Einblick

DISKUSSION UND FORSCHUNG ZUR HOMÖOPATHIE

Internationale Akademie für Integrative Wissenschaftlich Orientierte Homöopathie e. V.
International Academy of Science in Homeopathy and Integrative Medicine e. V.

Forschungs-Reader

www.akademie-wissenschaftliche-homoeopathie.org

v3.15

HOMÖOPATHIE
Wissenschaft und aktuelle Diskussion

Diese Zusammenstellung bietet einen Überblick zu wichtigen Forschungsarbeiten aus

- der Humanmedizin
- der Tiermedizin
- der Versorgungsforschung
- der Grundlagenforschung

Die Grundlagenforschung zeigt, dass spezifische physiko-chemische Effekte für potenzierte Substanzen wie Globuli messbar sind. Darüber hinaus werden Heilungserfolge in einer wachsenden Zahl von klinischen Studien beobachtet und quantifiziert. Daher entspricht eine Verbreitung pauschaler Negativurteile nicht dem Standard guter Forschungspraxis. Die hier wiedergegebenen Abstracts aus den einzelnen Forschungsfeldern ermöglichen dem Leser einen eigenständigen Einblick in die aktuelle Entwicklung einer modernen, evidenzbasierten Homöopathie.

Voreilige Urteile - Eine Hauptquelle der menschlichen Irrtumsfähigkeit

So informierte der für seine Erfindungen geadelte Physiker und Elektrizitätsforscher Lord Kelvin die Bürger und das englische Parlament, das er zu Forschungsfragen beriet.

Da wir als Menschen - wie als Wissenschaftler - ebenso irrtumsfähig wie erkenntnisbegabt sind, gründet sich die moderne evidenzbasierte Medizin bisher auf *drei Säulen:*

1. **Die Erfahrung und die Erkenntnis des Therapeuten**
2. **Die Werte und Wünsche sowie die Erfahrung des Erkrankten**
3. **Der aktuelle Stand der Wissenschaft und des medizinisch Wissbaren**

Die womöglich wichtigste Säule der evidenzbasierten Medizin wird in der aktuellen Debatte oft ausgelassen:

Es ist der Mensch, um den es geht.

Zur zentralen patientenorientierten, zweiten Säule der evidenzbasierten Medizin
Zu den Erfahrungen und Beobachtungen der betroffenen Bürger gibt es in der EU einen hohen Forschungsbedarf für komplementäre Methoden wie die Homöopathie.[1] Zugleich existiert interessante Evidenz durch Bürgerbefragungen: In Deutschland und Frankreich[2] leben fast 30 % der EU Bevölkerung. Laut repräsentativen, unabhängigen Befragungen haben in diesen beiden Ländern über 85 Millionen Menschen selbst Erfahrungen mit Homöopathie gemacht. 72 % von ihnen sind mit dem Ergebnis zufrieden oder sehr zufrieden.

- 73% der dazu befragten Bürger wünschen, dass die Homöopathie im Gesundheitssystem zur Verfügung steht und von den Krankenkassen finanziert wird.
- In Deutschland wünschen sich 85 % der Bevölkerung die Erforschung der Homöopathie an Universitäten.
- Rund 3 von 4 Bürgern erwarten, dass diese Erforschung durch fachkompetente Wissenschaftler auch vom Staat finanziert wird[3].

Das deutsche Grundgesetz schützt diese an der eigenen Gesundheitserfahrung orientierten und selbstbestimmten Wünsche seiner Bürger ausdrücklich:

Artikel 1
Die Würde des Menschen ist unantastbar.

Artikel 2, 1)
Jeder hat das Recht auf die freie Entfaltung seiner Persönlichkeit, soweit er nicht die Rechte anderer verletzt und nicht gegen die verfassungsmäßige Ordnung oder das Sittengesetz verstößt.

[1] What Attitudes and Needs Do Citizens in Europe Have in Relation to Complementary and Alternative Medicine? N. Nissen S. Schunder-Tatzber W.Weidenhammer H. Johannessen, Forschende Komplementärmedizin, 19/2012, 9-17
[2] Deutschland Bevölkerung 2019 | Bevölkerungsuhr, https://countrymeters.info/de/Germany: Unserer Schätzung zufolge umfasst die Bevölkerung Deutschland 81 402 348 Menschen Ende 2018. In Frankreich leben rund 65 649 091 Menschen https://www.laenderdaten.info/Europa/Frankreich/bevoelkerungswachstum.php; https://countrymeters.info/de/France
[3] Repräsentative Forsa Umfrage zur Homöopathie im Auftrag des BPI, Bund Pharmazeutischer Industrie, 2017

Artikel 2, 2)
Jeder hat das Recht auf Leben und körperliche Unversehrtheit. Die Freiheit der Person ist unverletzlich.

Nach den Erfahrungen von schwerem Missbrauch in deutschen Diktaturen stellt das Grundgesetz die Felder **Berufswahl**[4] **sowie Forschung und Lehre ausdrücklich frei**:

Artikel 5,3)
Kunst und Wissenschaft, Forschung und Lehre sind frei[5]**.**

Die entsprechenden Artikel in der EU-Charta der Grundrechte sind nahezu gleichlautend.

Zur ersten Säule der evidenzbasierten Medizin
Auf nationalen wie auf internationalen Fachtagungen berichten die homöopathischen Therapeuten übereinstimmend, dass überwiegend Patienten bei ihnen Hilfe suchen, bei deren Erkrankung andere, meist konventionelle Therapieverfahren nicht oder nicht ausreichend gewirkt haben oder wenn Antibiotika bei ihnen bakterielle Resistenzen erzeugt hatten. Wenn dann die Patienten, wie die zitierten Umfragen zeigen, häufig positive Erfahrungen mit der homöopathischen Therapie machen, kommen auch weitere Familienmitglieder mit ungelösten medizinischen Fragen zur homöopathischen Behandlung. Die Beobachtung umfassend ausgebildeter Therapeuten bestätigt die positiven Erfahrungen der meisten betroffenen Patienten.

Ärztliche Kollegen aus anderen Fachbereichen negieren diese Beobachtungen mitunter. Allerdings kennen sie selbst oft weder die therapeutischen Ergebnisse, noch die Eigenerfahrung der betroffenen Patienten, noch den Stand der Forschung. Dennoch entscheiden überwiegend fachfremd besetzte Ärztegremien in mehreren deutschen Bundesländern aktuell über den Fortbestand der ärztlichen Homöopathieausbildung. Hier zeichnet sich ein wichtiges, neues Forschungsfeld ab: Die Bedeutung und Auswirkung von Vorurteilen innerhalb jeder Säule der Evidenz.

Zur dritten wissenschaftlichen Säule der evidenzbasierten Medizin
Die bisherige Forschung weist anhand einer Reihe von gut durchgeführten Studien darauf hin, dass homöopathische Arzneimittel in klinischen Untersuchungen sowie in Grundlagenexperimenten

- wirksamer sind als Placebo und/oder
- bei bestimmten Indikationen ähnlich wirksam sind oder mitunter sogar wirksamer als eine alleinige konventionelle Standardtherapie.

[4] DGG, Artikel 12,1
[5] Diese Freiheit wird ausdrücklich im Kontext der anderen relevanten Artikel formuliert: Die Freiheit der Lehre entbindet nicht von der Treue zur Verfassung.

Auf den folgenden Seiten können Sie selbst Einblick in die Literatur zur Forschung über Homöopathie nehmen: Sie finden die zusammenfassenden Abstracts

- von klinischen Studien aus der Humanmedizin und Versorgungsforschung,
- von veterinärmedizinischen Studien,
- von Metastudien sowie aus der
- Grundlagenforschung.

Online genügt ein Klick im Inhaltsverzeichnis, um an die entsprechende Textstelle zu gelangen.

Wenn Sie einen Artikel ganz lesen möchten, finden Sie ihn unter dem Titel, der über dem Abstract steht, durch eine einfache Internetsuche. Wichtige Artikel, die frei zugänglich sind (open Access), sind in ihrer Ganzheit im Reader abgedruckt.

Vor die verschiedenen Forschungsgebiete haben wir jeweils eine Einleitung gesetzt. Seiten mit diesen einleitenden Gedanken haben zur besseren Erkennbarkeit einen blauen Randstreifen.

Am Ende des Readers finden Sie Informationen über die Akademie.

Wichtige klinische Studien

Die folgenden Studien zur Homöopathie zeigen entlang anerkannter Kriterien guter Forschungspraxis klare Hinweise für eine nebenwirkungsarme und gleichzeitig signifikante Wirksamkeit der homöopathischen Therapie. Sie erfüllen zentrale Kriterien für gut angelegte Studien und zeigen jede einzeln eine eindeutige Wirksamkeit der homöopathischen Therapie im Vergleich zu Placebo oder zu einer anderen konventionellen Standardtherapie.
Das erklärt womöglich, wie sich die Homöopathie über 200 Jahre, trotz starker theoretischer Hinterfragungen, zu einer der weltweit meist genutzten Einzeltherapien entwickeln konnte. Die Studien zeigen deutlich, wie wichtig es ist, die kompetente Forschung im Sinne der betroffenen Bürger zu fördern, um mehr über ihre Signifikanz, ihre sinnvolle Anwendung und über ihr Wirkprinzip zu erfahren.

Hintergrund: Die Homöopathie ist eine der nebenwirkungsärmsten und am häufigsten eingesetzten Einzeltherapien der Welt:

- Alleine in Indien gibt es über 100 Universitäten, die rein homöopathisch approbierte Ärzte ausbilden, die einen großen Teil der Bevölkerung ärztlich versorgen.
- Für Europa lässt sich abschätzen, dass mehr als 100 000 000 Menschen homöopathische Arzneien eingenommen haben. [6]
- Auf dem gesamten amerikanischen Kontinent und in Afrika wird die Homöopathie ebenfalls zunehmend angewandt.

Wie einleitend dargestellt, wünschen sich 85% der von Forsa befragten Bürger eine Erforschung der Homöopathie an Universitäten und fast ¾ der Bürger fordern eine staatliche Finanzierung. Gute Forschung muss heute sehr hohe Standards erfüllen. Das macht sie kostspielig und enorm zeitaufwendig: Für eine konventionelle medizinische Studie in der Medikamentenentwicklung rechnen Forschungsteams heute mit Kosten von 1-250 Millionen Euro.
Entgegen dem klar entwickelten Bürgerwillen sind die Bedingungen für homöopathische Forschung bislang ungewöhnlich ungünstig:

Es gibt - ganz anders als in der konventionellen Medizin und entgegen den Wahlversprechen fast aller Parteien – in Deutschland, wie in anderen EU Ländern - nahezu kei-

[6] Allein in Frankreich und Deutschland haben laut repräsentativen Befragungen über 80 000 000 Bürger homöopathische Arzneien ausprobiert. Von ihnen sind in beiden Ländern 72 % zufrieden oder sehr zufrieden (Forsa Umfrage zur Homöopathie im Auftrag des bpi 2017 und Umfrage des Ypsos Instituts, publiziert am 9.11.2018), https://www.ipsos.com/fr-fr/lhomeopathie-plebiscitee-par-les-francais

nerlei staatliche Förderung. Unter diesen in der Medizin ungewöhnlich harten, förderungsarmen Bedingungen entwickelt sich die Studienlage[7] zwar langsam, doch dafür erstaunlich positiv fort. In den Jahren seit der Jahrtausendwende ist das Niveau der homöopathischen Forschung kontinuierlich gestiegen und eine zunehmende Zahl von Studien erfüllt aktuell die für wichtig gehaltenen Kriterien einer evidenzbasierten Medizin. Das gilt für die klinische ebenso wie für die Grundlagenforschung.[8]

Qualitätskriterien für Studien

Zu den wichtigen aktuellen Qualitätsstandards für neue Studien gehören die Cochrane Kriterien: Zum essentiellen Goldstandard zählt hier eine Studie, die als **RCT**, also „randomised controlled" durchgeführt wurde, oder/und gegen den **SOC**, also den „Standard of Care" gemessen wurde. RCT heißt, dass es mindestens zwei Studienarme gibt, denen die Patienten zufällig zugewiesen werden. Je nach Zuweisung erhalten sie dann - wenn möglich doppelt verblindet - entweder die zu prüfende Therapie oder Placebo oder eine Standard-Therapie.

Für alle medizinischen Studien gilt:
Naturgemäß zeigt nicht jede Studie ein positives Ergebnis. Das kann an der Fragestellung ebenso liegen, wie an den Rahmenbedingungen oder an der konkreten Durchführung. Dies gilt in der Homöopathie genauso wie in der konventionellen Medizin. Ein aktueller Review zeigt, dass bei konventionellen medizinischen Studien zu neuen Wirkstoffen insgesamt nur 9,6% der Studien signifikant positive Ergebnisse zeigen. In der Psychiatrie sind es nur 6,2% und in der Onkologie sogar nur 5,1%[9]. Auch die über 90% falsifizierenden Studien ermöglichen oft wichtige Erkenntnisse, um sodann die nachfolgende Forschung im jeweiligen Fachgebiet besser auszurichten.

Wichtige Studien zu ADHS, Angststörungen, Depressionen und adjuvanter Krebstherapie finden Sie auf den folgenden Seiten.

[7] Frühe Studien erfüllten oft die heutigen Rahmenbedingungen für Studien noch nicht umfassend. Das gilt für ältere Studien in der konventionellen Medizin ähnlich.
[8] Siehe dazu den Survey zur Grundlagenforschung Seite 70, sowie Seite 71
[9] Siehe Clinical Development Success Rates 2006-2015, https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf

ADHS | Attention Deficit Hyperactivity Disorder

Eur J Pediatr (2005) 164: 758–767
DOI 10.1007/s00431-005-1735-7

ORIGINAL PAPER

Heiner Frei · Regula Everts · Klaus von Ammon
Franz Kaufmann · Daniel Walther
Shu-Fang Hsu-Schmitz · Marco Collenberg
Katharina Fuhrer · Ralph Hassink · Maja Steinlin
André Thurneysen

Homeopathic treatment of children with attention deficit hyperactivity disorder: a randomised, double blind, placebo controlled crossover trial

Received: 8 March 2005 / Revised: 23 May 2005 / Accepted: 1 June 2005 / Published online: 27 July 2005

Abstract An increasing number of parents turn to homeopathy for treatment of their hyperactive child. Two publications, a randomised, partially blinded trial and a clinical observation study, conclude that homeopathy has positive effects in patients with attention deficit hyperactivity disorder (ADHD). The aim of this study was to obtain scientific evidence of the effectiveness of homeopathy in ADHD. A total of 83 children aged 6–16 years, with ADHD diagnosed using the Diagnostic and Statistical Manual of Mental Disorders-IV criteria, were recruited. Prior to the randomised, double blind, placebo controlled crossover study, they were treated with individually prescribed homeopathic medications. 62 patients, who achieved an improvement of 50% in the Conners' Global Index (CGI), participated in the trial. Thirteen patients did not fulfill this eligibility criterion (CGI). The responders were split into two groups and received either verum for 6 weeks followed by placebo for 6 weeks (arm A), or vice-versa (arm B). At the beginning of the trial and after each crossover period, parents reported the CGI and patients underwent neuropsychological testing. The CGI rating was evaluated again at the end of each crossover period and twice in long-term follow-up. At entry to the crossover trial, cognitive performance such as visual global perception , impulsivity and divided attention, had improved significantly under open label treatment ($P < 0.0001$). During the crossover trial, CGI parent–ratings were significantly lower under verum (average 1.67 points) than under placebo ($P = 0.0479$). Long-term CGI improvement reached 12 points (63%, $P < 0.0001$). *Conclusion*: The trial suggests scientific evidence of the effectiveness of homeopathy in the treatment of attention deficit hyperactivity disorder, particularly in the areas of behavioural and cognitive functions.

Keywords Attention deficit hyperactivity disorder · Homeopathy · Individualised treatment · Randomised double blind trial · Treatment effectiveness

Abbreviations ADHD: attention deficit hyperactivity disorder · CGI: Conners' global index · CPRS: Conners' parent rating scale (long form) · CTRS: Conners teacher rating scale · DSM-IV: diagnostic and statistical manual of mental disorders · K-ABC: Kaufman assessment battery for children · QCB: questionnaire of change of behaviour · TAP: test battery for attention performance · VLMT: German version of the Rey auditory verbal learning test (RAVLT) · WISC-III: German version of Wechsler intelligence scale for children

H. Frei
Swiss Association of Homeopathic Physicians SAHP,
Lucerne, Switzerland

R. Everts · F. Kaufmann · D. Walther · K. Fuhrer
M. Steinlin (✉)
Division of Paediatric Neurology, University Children's Hospital,
Inselspital, 3010 Berne, Switzerland
E-mail: maja.steinlin@insel.ch
Tel.: +41-31-6329424
Fax: +41-31-6329500

K. von Ammon · A. Thurneysen
Kollegiale Instanz für Komplementärmedizin
(KIKOM)/Homeopathy, Imhoof Pavillon,
Inselspital, 3010 Berne, Switzerland
E-mail: andre.thurneysen@kikom.unibe.ch
Tel.: +41-31-6329758
Fax: +41-31-6324263

S.-F. Hsu-Schmitz · M. Collenberg
Department of Mathematical Statistics and Actuarial Science
(IMSV), University of Berne, Berne, Switzerland

R. Hassink
Zentrum für Entwicklungsförderung und pädiatrische
Neurorehabilitation, Bienne, Switzerland

Introduction

The attention deficit hyperactivity disorder (ADHD/ADD) is a combination of disturbed attention (visual,

Angststörungen und Depressionen | Anxiety and Depression

Grimaldi-Bensouda *et al. BMC Complementary and Alternative Medicine* (2016) 16:125
DOI 10.1186/s12906-016-1104-2

BMC Complementary and Alternative Medicine

RESEARCH ARTICLE Open Access

Homeopathic medical practice for anxiety and depression in primary care: the EPI3 cohort study

Lamiae Grimaldi-Bensouda[1,2*], Lucien Abenhaim[3,4], Jacques Massol[5], Didier Guillemot[6,7], Bernard Avouac[1], Gerard Duru[8], France Lert[9], Anne-Marie Magnier[10], Michel Rossignol[11], Frederic Rouillon[12], Bernard Begaud[13] and for the EPI3-LA-SER group

Abstract

Background: The purpose of the study was to compare utilization of conventional psychotropic drugs among patients seeking care for anxiety and depression disorders (ADDs) from general practitioners (GPs) who strictly prescribe conventional medicines (GP-CM), regularly prescribe homeopathy in a mixed practice (GP-Mx), or are certified homeopathic GPs (GP-Ho).

Methods: This was one of three epidemiological cohort studies (EPI3) on general practice in France, which included GPs and their patients consulting for ADDs (scoring 9 or more in the Hospital Anxiety and Depression Scale, HADS). Information on all medication utilization was obtained by a standardised telephone interview at inclusion, 1, 3 and 12 months.

Results: Of 1562 eligible patients consulting for ADDs, 710 (45.5 %) agreed to participate. Adjusted multivariate analyses showed that GP-Ho and GP-Mx patients were less likely to use psychotropic drugs over 12 months, with Odds ratio (OR) = 0.29; 95 % confidence interval (CI): 0.19 to 0.44, and OR = 0.62; 95 % CI: 0.41 to 0.94 respectively, compared to GP-CM patients. The rate of clinical improvement (HADS <9) was marginally superior for the GP-Ho group as compared to the GP-CM group (OR = 1.70; 95 % CI: 1.00 to 2.87), but not for the GP-Mx group (OR = 1.49; 95 % CI: 0.89 to 2.50).

Conclusions: Patients with ADD, who chose to consult GPs prescribing homeopathy reported less use of psychotropic drugs, and were marginally more likely to experience clinical improvement, than patients managed with conventional care. Results may reflect differences in physicians' management and patients' preferences as well as statistical regression to the mean.

Keywords: Anxiety, Depression, Homeopathy, Primary care

Background

Anxiety and depressive disorders (ADDs) are highly prevalent worldwide and represent a leading reason for consultation in primary care [1, 2]. Although systematic reviews and guidelines [3, 4] recognise the efficacy of antidepressant and psychotropic drugs for specific ADDs, heterogenity in the diagnostic approach of these patients in primary care is partly responsible for the non-optimal utilization of these drugs, particularly in mild and moderate cases [5]. The prevalence of ADDs in homeopathic care also ranks high, only surpassed by low-back pain [6]. Patients who seek homeopathic care differ from those preferring conventional medicine, but the diagnostic make-up of their consultations has been described as similar [7]. Evidence summarized in systematic reviews conducted to assess the benefit of homeopathy in ADDs is too limited to sufficiently draw firm conclusions regarding the efficacy or effectiveness of homeopathy in this indication [8–11]. However, its

* Correspondence: Lamiae.Grimaldi@la-ser.com
[1]LA-SER, 10 place de Catalogne, 75014 Paris, France
[2]Conservatoire national des arts et métiers (CNAM), 292 Rue Saint-Martin, 75003 Paris, France
Full list of author information is available at the end of the article

Complementary Therapies in Medicine
Volume 23, Issue 3, June 2015, Pages 309-317

Frass M[1], Friehs H[2], Thallinger C[3], Sohal NK[4], Marosi C[5], Muchitsch I[6], Gaertner K[7], Gleiss A[8], Schuster E[9], Oberbaum M[10].

Complement Ther Med. 2015 Jun;23(3):309-17. doi: 10.1016/j.ctim.2015.03.004. Epub 2015 Mar 23.

Influence of adjunctive classical homeopathy on global health status and subjective wellbeing in cancer patients - A pragmatic randomized controlled trial.

OBJECTIVES
The use of complementary and alternative medicine has increased over the past decade. The aim of this study was to evaluate whether homeopathy influenced global health status and subjective wellbeing when used as an adjunct to conventional cancer therapy.

DESIGN
In this pragmatic randomized controlled trial, 410 patients, who were treated by standard anti-neoplastic therapy, were randomized to receive or not receive classical homeopathic adjunctive therapy in addition to standard therapy. The study took place at the Medical University Vienna, Department of Medicine I, Clinical Division of Oncology.

MAIN OUTCOME MEASURES
The main outcome measures were global health status and subjective wellbeing as assessed by the patients. At each of three visits (one baseline, two follow-up visits), patients filled in two different questionnaires.

RESULTS
373 patients yielded at least one of three measurements. The improvement of global health status between visits 1 and 3 was significantly stronger in the homeopathy group by 7.7 (95% CI 2.3-13.0, p=0.005) when compared with the control group. A significant group difference was also observed with respect to subjective wellbeing by 14.7 (95% CI 8.5-21.0, p<0.001) in favor of the homeopathic as compared with the control group. Control patients showed a significant improvement only in subjective wellbeing between their first and third visits.

CONCLUSION
Results suggest that the global health status and subjective wellbeing of cancer patients improve significantly when adjunct classical homeopathic treatment is administered in addition to conventional therapy.

Add-on Therapien bei Carcinomen | Add-on Therapies in the Treatment of Cancer Patients

The Oncologist®

Clinical Trial Results

Homeopathic Treatment as an Add-On Therapy May Improve Quality of Life and Prolong Survival in Patients with Non-Small Cell Lung Cancer: A Prospective, Randomized, Placebo-Controlled, Double-Blind, Three-Arm, Multicenter Study

Michael Frass,[a] Peter Lechleitner,[b] Christa Gründling,[c] Claudia Pirker,[d] Erwin Grasmuk-Siegl,[d] Julian Domayer,[d] Maximilian Hochmair,[d] Katharina Gaertner,[e] Cornelia Duscheck,[f] Ilse Muchitsch,[g] Christine Marosi,[f] Michael Schumacher,[h] Sabine Zöchbauer-Müller,[f] Raj K. Manchanda,[i] Andrea Schrott,[j] Otto Burghuber[k]

[a]Medical University of Vienna, Department of Medicine I, Clinical Division of Oncology and Institute for Homeopathic Research, Vienna, Austria, and Scientific Society for Homeopathy (WissHom), Koethen, Germany; [b]Hospital of Lienz, Department of Medicine, Lienz, Austria; [c]General Practitioner, Enns, Austria; [d]Department of Respiratory and Critical Care Medicine, Respiratory Oncology Unit, Karl Landsteiner Institute of Lung Research and Pulmonary Oncology, Klinik Floridsdorf, Vienna, Austria; [e]Witten/Herdecke University, Faculty of Health Sciences, Witten, Germany; [f]Medical University of Vienna, Department of Medicine I, Clinical Division of Oncology, Vienna, Austria; [g]Austrian Chamber of Pharmacists, Department Vienna, HomResearch, Interdisciplinary Homeopathic Research Group, Vienna, Austria; [h]Elisabethinenspital, Department of Medicine, Linz, Austria; [i]Central Council for Research in Homeopathy, Ministry of AYUSH, Government of India and LMHI, West Delhi, Delhi, India; [j]StatistikAmbulanz, Consulting Company, Leobendorf, Austria; [k]Department of Respiratory and Critical Care Medicine and Ludwig Boltzmann Institute for Lung Health, Otto Wagner Hospital and Sigmund Freud University, Medical School, Vienna, Austria

Key Words. Additive homeopathy • Adult oncology • Complementary and alternative medicine • Global health status • Lung cancer • Survival

Trial Information

- **ClinicalTrials.gov Identifier:** NCT01509612
- **Sponsor:** Michael Frass
- **Principal Investigator:** Michael Frass
- **IRB Approved:** Yes

Lessons Learned

- Conventional medicine and homeopathy work well together.
- Quality of life improves with additive homeopathy in patients with non-small cell lung cancer (NSCLC).
- Survival improves with additive homeopathy in patients with NSCLC.

Abstract

Background. Patients with advanced non-small cell lung cancer (NSCLC) have limited treatment options. Alongside conventional anticancer treatment, additive homeopathy might help to alleviate side effects of conventional therapy. The aim of the present study was to investigate whether additive homeopathy might influence quality of life (QoL) and survival in patients with NSCLC.

Methods. In this prospective, randomized, placebo-controlled, double-blind, three-arm, multicenter, phase III study, we evaluated the possible effects of additive homeopathic treatment compared with placebo in patients with stage IV NSCLC, with respect to QoL in the two randomized groups and survival time in all three groups. Treated patients visited the outpatients' centers every 9 weeks: 150 patients with stage IV NSCLC were included in the study; 98 received either individualized homeopathic remedies (n = 51) or placebo (n = 47) in a double-blinded fashion; and 52 control patients without any homeopathic treatment were observed for survival only. The constituents of the different homeopathic remedies were mainly

Correspondence: Michael Frass, M.D., Medical University of Vienna, Department of Medicine I, Clinical Division of Oncology, Waehringer Guertel 18-20, A 1090 Vienna, and Institute for Homeopathic Research, Gaudenzdorfer Guertel 63, 1120 Vienna, Austria. Telephone: 0043-664-545-3040; e-mail: office@ordination-frass.at Received July 9, 2020; accepted for publication September 28, 2020; published Online First on November 7, 2020. http://dx.doi.org/10.1002/onco.13548

Rostock et al. BMC Cancer 2011, 11:19
http://www.biomedcentral.com/1471-2407/11/19

BMC Cancer

RESEARCH ARTICLE Open Access

Classical homeopathy in the treatment of cancer patients - a prospective observational study of two independent cohorts

Matthias Rostock[1,4*], Johannes Naumann[1,2], Corina Guethlin[2,5], Lars Guenther[2], Hans H Bartsch[1], Harald Walach[3]

Abstract

Background: Many cancer patients seek homeopathy as a complementary therapy. It has rarely been studied systematically, whether homeopathic care is of benefit for cancer patients.

Methods: We conducted a prospective observational study with cancer patients in two differently treated cohorts: one cohort with patients under complementary homeopathic treatment (HG; n = 259), and one cohort with conventionally treated cancer patients (CG; n = 380). For a direct comparison, matched pairs with patients of the same tumour entity and comparable prognosis were to be formed.
Main outcome parameter: change of quality of life (FACT-G, FACIT-Sp) after 3 months.
Secondary outcome parameters: change of quality of life (FACT-G, FACIT-Sp) after a year, as well as impairment by fatigue (MFI) and by anxiety and depression (HADS).

Results: HG: FACT-G, or FACIT-Sp, respectively improved statistically significantly in the first three months, from 75.6 (SD 14.6) to 81.1 (SD 16.9), or from 32.1 (SD 8.2) to 34.9 (SD 8.32), respectively. After 12 months, a further increase to 84.1 (SD 15.5) or 35.2 (SD 8.6) was found. Fatigue (MFI) decreased; anxiety and depression (HADS) did not change.
CG: FACT-G remained constant in the first three months: 75.3 (SD 17.3) at t0, and 76.6 (SD 16.6) at t1. After 12 months, there was a slight increase to 78.9 (SD 18.1). FACIT-Sp scores improved significantly from t0 (31.0 - SD 8.9) to t1 (32.1 - SD 8.9) and declined again after a year (31.6 - SD 9.4). For fatigue, anxiety, and depression, no relevant changes were found.
120 patients of HG and 206 patients of CG met our criteria for matched-pairs selection. Due to large differences between the two patient populations, however, only 11 matched pairs could be formed. This is not sufficient for a comparative study.

Conclusion: In our prospective study, we observed an improvement of quality of life as well as a tendency of fatigue symptoms to decrease in cancer patients under complementary homeopathic treatment. It would take considerably larger samples to find matched pairs suitable for comparison in order to establish a definite causal relation between these effects and homeopathic treatment.

Background

Many cancer patients use complementary and alternative medicine (CAM) treatments. Homeopathy is one of the most popular CAM modalities for cancer patients in seven out of 14 European countries [1]. Homeopathy has traditionally been very popular in India and South America too, and is increasingly sought after also in the US [2].

Developed in the 18th century by German physician Samuel Hahnemann, it is based on two principles, the Law of Similars ("similia similibus curentur: let likes be cured by likes") and Individualisation, and it makes use of a specific form of remedy preparation, the stepwise dilution and potentisation [3].

Homeopathy is discussed controversially as there is no plausible mode of action for the highly diluted remedies,

* Correspondence: matthias.rostock@usz.ch
[1]Tumour Biology Center at Albert Ludwig's University Freiburg, Germany
Full list of author information is available at the end of the article

Add-on Therapie bei beatmeten Intensivpatienten | Add-on Therapy on COPD

CHEST JOURNAL

CLINICAL INVESTIGATIONS IN CRITICAL CARE | VOLUME 127, ISSUE 3, P936-941, MARCH 01, 2005

Influence of Potassium Dichromate on Tracheal Secretions in Critically Ill Patients

Frass Michael, MD • Dielacher Christoph, RN • Linkesch Manfred, MD • ... Muchitsch Ilse, PhD • Schuster Ernst, PhD • Kaye Alan, MD • Show all authors

DOI: https://doi.org/10.1378/chest.127.3.936

Background

Stringy, tenacious tracheal secretions may prevent extubation in patients weaned from the respirator. This prospective, randomized, double-blind, placebo-controlled study with parallel assignment was performed to assess the influence of sublingually administered potassium dichromate C30 on the amount of tenacious, stringy tracheal secretions in critically ill patients with a history of tobacco use and COPD

Methods

In this study, 50 patients breathing spontaneously with continuous positive airway pressure were receiving either potassium dichromate C30 globules (group 1) [Deutsche Homoüopathie-Union, Pharmaceutical Company; Karlsruhe, Germany] or placebo (group 2). Five globules were administered twice daily at intervals of 12 h. The amount of tracheal secretions on day 2 after the start of the study as well as the time for successful extubation and length of stay in the ICU were recorded

Results

The amount of tracheal secretions was reduced significantly in group 1 ($p < 0.0001$). Extubation could be performed significantly earlier in group 1 ($p < 0.0001$). Similarly, length of stay was significantly shorter in group 1 (4.20 ± 1.61 days vs 7.68 ± 3.60 days, $p < 0.0001$ [mean ± SD])

Conclusion

These data suggest that potentized (diluted and vigorously shaken) potassium dichromate may help to decrease the amount of stringy tracheal secretions in COPD patients

Key words

COPD • double-blind, randomized, placebo-controlled study • extubation • homeopathy • tracheal secretions

Abbreviation:

APACHE (acute physiology and chronic health evaluation), BMI (body mass index), CPAP (continuous positive airway pressure), FIO2 (fraction of inspired oxygen)

Complementary Therapies in Clinical Practice 44 (2021) 101415

Contents lists available at ScienceDirect

Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctcp

Adjunctive homeopathic treatment of hospitalized COVID-19 patients (COVIHOM): A retrospective case series

Michael Takacs [a], Michael Frass [b,c,d,e,*], Gernot Walder [f], Philippa Fibert [g], Maria Rottensteiner [c], Walter Glück [c], Peter Lechleitner [a], Menachem Oberbaum [h], Ilse Leisser [i], Kavita Chandak [j], Peter Panhofer [c,d,k,l], Petra Weiermayer [b]

[a] Hospital of Lienz, Lienz, Austria
[b] WissHom: Scientific Society for Homeopathy, Koethen, Germany
[c] Umbrella Organization for Medical Holistic Medicine, Vienna, Austria
[d] Vienna International Academy for Holistic Medicine (GAMED), Otto Wagner Hospital Vienna, Austria
[e] Professor Emeritus, Medical University of Vienna, Department of Medicine I, Vienna, Austria
[f] Resident Specialist in Hygiene, Medical Microbiology and Infectious Diseases, Außervillgraten, Austria
[g] St Mary's University, London, UK
[h] Shaare Zedek Medical Center, The Center for Integrative Complementary Medicine, Jerusalem, Israel
[i] Apotheke Zum Weißen Engel – Homeocur, Retz, Austria
[j] Reeshabh Homeo Consultancy, Nagpur, India
[k] Chair of Complementary Medicine, Medical Faculty, Sigmund Freud University Vienna, Austria
[l] KLITM: Karl Landsteiner Institute for Traditional Medicine and Medical Anthropology, Vienna, Austria

ARTICLE INFO

Keywords:
Complementary therapies
COVID-19
Homeopathy
Intensive care unit
SARS-CoV-2

ABSTRACT

Background: and purpose. COVID-19 is a novel viral disease causing worldwide pandemia. The aim of this study was to describe the effect of adjunctive individualized homeopathic treatment delivered to hospitalized patients with confirmed symptomatic SARS-CoV-2 infection.

Patient presentation: Thirteen patients with COVID-19 were admitted. Mean age was 73.4 ± 15.0 (SD) years. Twelve (92.3%) were speedily discharged without relevant sequelae after 14.4 ± 8.9 days. A single patient admitted in an advanced stage of septic disease died in hospital. A time-dependent improvement of relevant clinical symptoms was observed in the 12 surviving patients. Six (46.2%) were critically ill and treated in the intensive care unit (ICU). Mean stay at the ICU of the 5 surviving patients was 18.8 ± 6.8 days. In six patients (46.2%) gastrointestinal disorders accompanied COVID-19.

Conclusion: The observations suggest that adjunctive homeopathic treatment may be helpful to treat patients with confirmed COVID-19 even in high – risk patients especially since there is no conventional treatment of COVID-19 available at present.

Sepsis

Homeopathy (2005) 94, 75–80
© 2005 The Faculty of Homeopathy
doi:10.1016/j.homp.2005.01.002, available online at http://www.sciencedirect.com

ORIGINAL PAPER

Adjunctive homeopathic treatment in patients with severe sepsis: a randomized, double-blind, placebo-controlled trial in an intensive care unit

M Frass[1,*], M Linkesch[2], S Banyai[2,3], G Resch[1], C Dielacher[2], T Löbl[2], C Endler[1], M Haidvogl[1], I Muchitsch[1] and E Schuster[4]

[1]*Ludwig Boltzmann Institute for Homeopathy, Graz, Austria*
[2]*II Department of Internal Medicine, University of Vienna, Vienna, Austria*
[3]*Cantonal Hospital of Lucerne, Switzerland*
[4]*Department of Medical Computer Sciences, University of Vienna, Vienna, Austria*

***Background*: Mortality in patients with severe sepsis remains high despite the development of several therapeutic strategies. The aim of this randomized, double-blind, placebo-controlled trial was to evaluate whether homeopathy is able to influence long-term outcome in critically ill patients suffering from severe sepsis.**
***Methods*: Seventy patients with severe sepsis received homeopathic treatment ($n = 35$) or placebo ($n = 35$). Five globules in a potency of 200c were given at 12 h interval during the stay at the intensive care unit. Survival after a 30 and 180 days was recorded.**
***Results*: Three patients (2 homeopathy, 1 placebo) were excluded from the analyses because of incomplete data. All these patients survived. Baseline characteristics including age, sex, BMI, prior conditions, APACHE II score, signs of sepsis, number of organ failures, need for mechanical ventilation, need for vasopressors or veno-venous hemofiltration, and laboratory parameters were not significantly different between groups. On day 30, there was non-statistically significantly trend of survival in favour of homeopathy (verum 81.8%, placebo 67.7%, $P = 0.19$). On day 180, survival was statistically significantly higher with verum homeopathy (75.8% *vs* 50.0%, $P = 0.043$). No adverse effects were observed.**
***Conclusions*: Our data suggest that homeopathic treatment may be an useful additional therapeutic measure with a long-term benefit for severely septic patients admitted to the intensive care unit. A constraint to wider application of this method is the limited number of trained homeopaths.** *Homeopathy* (2005) **94,** 75–80.

Keywords: APACHE II; homeopathy; critically ill patients; intensive care unit; sepsis; survival; double-blind; randomized prospective; placebo-controlled study

Introduction

The incidence of severe sepsis is 70,000 to 300,000 patients in the United States each year.[1] Septic shock is associated with mortality rates ranging from 40% to 90%.[2] Several new therapeutic approaches have failed during the last decades. Recent guidelines[1] recommend use of goal directed therapy, low-tidal ventilation, administration of recombinant Protein C (aPC), close monitoring of blood glucose with a target value of 80–100 mg/dl, and administration of hydrocortisone. Despite these therapeutic strategies, mortality has remained almost unchanged during the last few years.

Homeopathic medicine has been used for about two centuries. Several studies describe its superiority above placebo.[3–5] Experimental studies demonstrate the

*Correspondence: M Frass, Ludwig Boltzmann Institute for Homeopathy, Duerergasse 4, A 8010 Graz, Austria.
E-mail: michael.frass@kabsi.at
Received 3 August 2004; revised 11 January 2005; accepted 26 January 2005

Rheumatology 2004;43:577–582 doi:10.1093/rheumatology/keh111
Advance Access publication 20 January 2004

Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo

I. R. Bell[1,2,3,4,6,8], D. A. Lewis II[9], A. J. Brooks[3], G. E. Schwartz[3,5,6], S. E. Lewis[9], B. T. Walsh[4] and C. M. Baldwin[3,4,7,8]

Objective. To assess the efficacy of individualized classical homeopathy in the treatment of fibromyalgia.
Methods. This study was a double-blind, randomized, parallel-group, placebo-controlled trial of homeopathy. Community-recruited persons ($N = 62$) with physician-confirmed fibromyalgia (mean age 49 yr, S.D. 10 yr, 94% women) were treated in a homeopathic private practice setting. Participants were randomized to receive oral daily liquid LM (1/50 000) potencies with an individually chosen homeopathic remedy or an indistinguishable placebo. Homeopathic visits involved joint interviews and concurrence on remedy selection by two experienced homeopaths, at baseline, 2 months and 4 months (prior to a subsequent optional crossover phase of the study which is reported elsewhere). Tender point count and tender point pain on examination by a medical assessor uninvolved in providing care, self-rating scales on fibromyalgia-related quality of life, pain, mood and global health at baseline and 3 months, were the primary clinical outcome measures for this report.
Results. Fifty-three people completed the treatment protocol. Participants on active treatment showed significantly greater improvements in tender point count and tender point pain, quality of life, global health and a trend toward less depression compared with those on placebo.
Conclusions. This study replicates and extends a previous 1-month placebo-controlled crossover study in fibromyalgia that pre-screened for only one homeopathic remedy. Using a broad selection of remedies and the flexible LM dose (1/50 000 dilution factor) series, the present study demonstrated that individualized homeopathy is significantly better than placebo in lessening tender point pain and improving the quality of life and global health of persons with fibromyalgia.

KEY WORDS: Fibromyalgia, Homeopathy, Chronic pain, Global health.

The use of homeopathy as a complementary medical treatment for a wide range of acute and chronic conditions is increasing [1, 2], with high levels of patient satisfaction with homeopathic care [3]. Clinicians often report benefit of individualized constitutional homeopathic remedies in patients having overlapping, polysymptomatic disorders, for example fibromyalgia (FM), chronic fatigue syndrome and multiple chemical sensitivity with low-level chemical intolerance, for which conventional medicine has limited options. Fibromyalgia is a chronic diffuse musculoskeletal pain disorder involving concomitant fatigue, sleep disturbance and, often, co-morbid depression [4]. The prevalence in the United States is 2% [5]. Fibromyalgia disproportionately affects women. One randomized, double-blind crossover study of patients meeting criteria for a single homeopathic remedy, Rhus toxicodendron, documented greater improvements over 1 month in number of painful tender points and better sleep on active versus placebo treatment [6].

Although systematic reviews of homeopathy have found that active treatment has an advantage over placebo across various conditions, investigators have called for greater efforts to replicate and extend homeopathic studies on specific conventional diagnostic entities [7]. The debate over poor reproducibility of findings, methodological shortcomings, and interpretation of data from previous studies has been vigorous [8]. The purpose of this study was to perform a randomized, double-blind, placebo-controlled feasibility trial of individualized homeopathy in fibromyalgia using daily LM (1/50 000 dilution factor) potencies.

Methods

Design

A double-blind, parallel group design of randomly assigned active versus placebo individualized, pragmatic homeopathic treatment was implemented. Patients had homeopathic visits at a private clinic in Phoenix, Arizona, at baseline, 2 months, 4 months and 6 months of treatment. They were evaluated with the same battery of outcome measures during laboratory assessment visits at the University of Arizona (Tucson) at baseline, 3 months and 6 months. An optional crossover treatment phase of the study was implemented immediately after the 4-month homeopathic visit and occurred over months 5 and 6 (post-crossover laboratory and clinical results are reported elsewhere [9]).

The 3-month laboratory evaluation and 4-month homeopathic visits were separated in time because of (1) practical considerations

[1]Program in Integrative Medicine, [2]Departments of Psychiatry, [3]Psychology, [4]Medicine, [5]Neurology, [6]Surgery, the [7]Arizona Respiratory Center and the [8]Mel and Enid Zuckerman Arizona College of Public Health at the University of Arizona, Tucson, Arizona, and [9]Saybrook Graduate School and Research Institute, San Francisco, California, USA.

Submitted 9 July 2003; revised version accepted 12 November 2003.

Correspondence to: I. R. Bell, Program in Integrative Medicine, The University of Arizona Health Sciences Center, 1249 N. Mountain Avenue, Tucson, AZ 85719, USA. E-mail: IBELL@U.ARIZONA.EDU

Menopausales Syndrom | Menopausal Syndrom

ORIGINAL RESEARCH ARTICLE

Drugs R D 2012; 12 (3): 107-119
1179-6901/12/0003-0107

Efficacy of a Non-Hormonal Treatment, BRN-01, on Menopausal Hot Flashes

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

Jean-Claude Colau,[1] *Stéphane Vincent,*[2] *Philippe Marijnen*[2] and *François-André Allaert*[3]

1 Department of Gynaecology, Hospital Foch, Suresnes, France
2 Laboratoires Boiron, Sainte Foy-lès-Lyon, France
3 Chaire d'Evaluation Médicale Ceren ESC et Dim, CHU Dijon, Dijon, France

Abstract

Background: Homeopathic medicines have a place among the non-hormonal therapies for the treatment of hot flashes during the menopause.

Objective: The objective of this study was to evaluate the efficacy of the non-hormonal treatment BRN-01 in reducing hot flashes in menopausal women.

Study Design: This was a multicenter, randomized, double-blind, placebo-controlled study carried out between June 2010 and July 2011.

Setting: The study was conducted in 35 active centers in France (gynecologists in private practice).

Patients: One hundred and eight menopausal women, ≥50 years of age, were enrolled in the study. The eligibility criteria included menopause for <24 months and ≥5 hot flashes per day with a significant negative effect on the women's professional and/or personal life.

Intervention: Treatment was either BRN-01 tablets, a registered homeopathic medicine containing *Actaea racemosa* (4 centesimal dilutions [4CH]), *Arnica montana* (4CH), *Glonoinum* (4CH), *Lachesis mutus* (5CH), and *Sanguinaria canadensis* (4CH), or identical placebo tablets, prepared by Laboratoires Boiron according to European Pharmacopoeia standards. Oral treatment (2 to 4 tablets per day) was started on day 3 after study enrollment and was continued for 12 weeks.

Main Outcome Measure: The main outcome measure was the hot flash score (HFS) compared before, during, and after treatment. Secondary outcome criteria were the quality of life (QoL) [measured using the Hot Flash Related Daily Interference Scale (HFRDIS)], severity of symptoms (measured using the Menopause Rating Scale), evolution of the mean dosage, and compliance. All adverse events (AEs) were recorded.

Results: One hundred and one women were included in the final analysis (intent-to-treat population: BRN-01, n = 50; placebo, n = 51). The global HFS over the 12 weeks, assessed as the area under the curve (AUC) adjusted for

baseline values, was significantly lower in the BRN-01 group than in the placebo group (mean ± SD 88.2 ± 6.5 versus 107.2 ± 6.4; p = 0.0411). BRN-01 was well tolerated; the frequency of AEs was similar in the two treatment groups, and no serious AEs were attributable to BRN-01.

Conclusion: BRN-01 seemed to have a significant effect on the HFS, compared with placebo. According to the results of this clinical trial, BRN-01 may be considered a new therapeutic option with a safe profile for hot flashes in menopausal women who do not want or are not able to take hormone replacement therapy or other recognized treatments for this indication.

Trial registration number (EudraCT): 2009-016959-21.

Multimorbide Patienten | Multimorbid Patients

Homeopathy (2015) 104, 57–65

http://dx.doi.org/10.1016/j.homp.2014.09.001, available online at http://www.sciencedirect.com

ORIGINAL PAPER

Homeopathic treatment of multimorbid patients: a prospective outcome study with polarity analysis

Heiner Frei*

University of Berne, Kreuzplatz 6, CH-3177 Laupen, Switzerland

Background: **The treatment of multimorbid patients who have a combination of three or more concurrent complaints is one of the core competencies of homeopathy. In this article we introduce the application of polarity analysis (PA) in multimorbidity. PA came to prominence through the Swiss homeopathic ADHD double-blind study, which successfully demonstrated a significant difference between highly dilute homeopathic remedies and placebo. PA enables homeopaths to calculate a relative healing probability, based on Boenninghausen's grading of polar symptoms. After its evaluation in the treatment of a variety of acute and chronic disease, which showed improved results compared to a conventional homeopathic approach, it was a challenge to test PA with multimorbid patients. Since such patients almost invariably have a multiple symptoms, the question was whether we can nevertheless successfully use Polarity Analysis or whether the method is rendered ineffective by the multitude of symptoms.**
Methods: **We treated 50 multimorbid patients with PA and prospectively followed them over one year.**
Results: **43 patients (86%) completed the observation period, achieving an average improvement of 91% in their initial symptoms. Six patients dropped out, and one did not achieve an improvement of 80%, and was therefore also counted as a treatment failure. The cost of homeopathic treatment was 41% of projected equivalent conventional treatment.**
Conclusions: **Polarity Analysis is an effective method for treating multimorbidity. The multitude of symptoms does not prevent the method from achieving good results. Homeopathy may be capable of taking over a considerable proportion of the treatment of multimorbid patients, at lower costs than conventional medicine.** *Homeopathy* (2015) **104**, 57–65.

Keywords: Homeopathy; Multimorbid patients; Polarity analysis; Prospective outcome study; Treatment costs

Introduction

Polarity analysis (PA) is a defined method of homeopathic treatment, enabling illness to be healed with greater reliability.[1] In the Swiss double-blind study on attention deficit hyperactivity disorder (ADHD), PA enabled the hit rate to be raised to the level of proof required to successfully demonstrate a statistically significant difference between placebo and high-potency homeopathic remedies.[2] When evaluated in prospective outcome analyses with acute and chronic illness, PA has also been found to improve the results in comparison with conventional homeopathic treatment.[1,3]

The present work aimed at a prospective evaluation of Polarity Analysis in the normal treatment of patients with

*Correspondence: Heiner Frei, University of Berne, Kreuzplatz 6, CH-3177 Laupen, Switzerland.
E-mail: heiner.frei@hin.ch
Received 13 March 2014; revised 27 August 2014; accepted 2 September 2014

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Treatment of Acute Childhood Diarrhea With Homeopathic Medicine: A Randomized Clinical Trial in Nicaragua

Jennifer Jacobs, MD, MPH; L. Margarita Jiménez, MD, MPH; Stephen S. Gloyd, MD, MPH; James L. Gale, MD; and Dean Crothers, MD

ABSTRACT. ***Objective.*** **Acute diarrhea is the leading cause of pediatric morbidity and mortality worldwide. Oral rehydration treatment can prevent death from dehydration, but does not reduce the duration of individual episodes. Homeopathic treatment for acute diarrhea is used in many parts of the world. This study was performed to determine whether homeopathy is useful in the treatment of acute childhood diarrhea.**

Methodology. **A randomized double-blind clinical trial comparing homeopathic medicine with placebo in the treatment of acute childhood diarrhea was conducted in León, Nicaragua, in July 1991. Eighty-one children aged 6 months to 5 years of age were included in the study. An individualized homeopathic medicine was prescribed for each child and daily follow-up was performed for 5 days. Standard treatment with oral rehydration treatment was also given.**

Results. **The treatment group had a statistically significant ($P < .05$) decrease in duration of diarrhea, defined as the number of days until there were less than three unformed stools daily for 2 consecutive days. There was also a significant difference ($P < .05$) in the number of stools per day between the two groups after 72 hours of treatment.**

Conclusions. **The statistically significant decrease in the duration of diarrhea in the treatment group suggests that homeopathic treatment might be useful in acute childhood diarrhea. Further study of this treatment deserves consideration.** ***Pediatrics* 1994;93:719–725; *diarrhea, diarrhea, infantile; homeopathy, Nicaragua.***

ABBREVIATION. ORT, oral rehydration treatment.

Alternative medicine is controversial within the scientific community. It is used widely by the general population, yet few scientifically rigorous studies have been published demonstrating its efficacy. A recent survey published in the *New England Journal of Medicine* found that >30% of the US population had used alternative medical practices in 1990 to treat serious medical conditions and that 10% had visited practitioners of alternative medicine.[1] The lack of research in this area prompted Congress, in 1992, to establish the Office of Alternative Medicine within the National Institutes of Health to investigate various alternative medical practices (*New York Times*. January 10, 1993:1).

Homeopathy is a type of alternative medicine that is practiced extensively worldwide, especially in Europe, Latin America, and Asia.[2–4] In the United States, it has been estimated that 1% of the population used homeopathy in 1990.[1] Homeopathic theory is based on the premise whereby a substance that can cause certain symptoms when given in large doses to a healthy person is said to cure those same symptoms when given in very small doses to someone who is sick.

Homeopathic treatment is individualized, whereby two or more people with the same diagnosis may be given different medicines, depending on the specific symptoms of illness in each person. For example, a patient with acute diarrhea may be prescribed one of six or seven common remedies for this illness, based on the appearance and odor of the stool, whether or not there is abdominal pain or vomiting, what time of day the diarrhea is worse, the emotional state of the patient, and such general symptoms as body temperature, degree of thirst, and appetite.

There has been much debate about the efficacy of homeopathy since its inception in Germany in the late 18th century. Homeopathic medicines, made from plant, animal, and mineral substances, are diluted in a water/alcohol solution to extremely small concentrations. This dilution of homeopathic medicines to infinitessimal doses has led many scientists to reject homeopathic theory (*Consumer Reports*. March 1994: 201–206).[5] Currently, there is no scientific explanation for the mechanism of action of homeopathic medicines, although several hypotheses exist.[6,7]

Recent clinical trials in Europe have suggested a positive treatment association when homeopathic medicines are compared with placebo in the treatment of allergic rhinitis,[8] fibrositis,[9] and influenza,[10] whereas an earlier study showed no apparent treatment effect in rheumatoid arthritis.[11] In 1991, the *British Medical Journal* published a meta-analysis of homeopathic clinical trials which found that 15 of 22 well-designed studies showed positive results. The authors concluded that more methodologically rigorous trials should be performed to address the question of efficacy of homeopathic treatment.[12]

Acute diarrhea is the leading cause of pediatric morbidity and mortality worldwide. In the developing world, there are an estimated 1.3 billion episodes

From the Department of Epidemiology and the International Health Program, School of Public Health and Community Medicine, University of Washington, Seattle, Washington.
Dr Jiménez is a member of the Faculty of Medicine, University of Guadalajara, Jalisco, Mexico.
Dr Crothers' current affiliation is the Evergreen Center for Homeopathic Medicine, Edmonds, Washington.
Received for publication Dec 22, 1992; accepted Oct 25, 1993.
Reprint requests to (J.J.) 23200 Edmonds Way, Edmonds, WA 98026.

Neurodermitis | Atopic Dermatitis

Homeopathy (2016) 105, 217–224

http://dx.doi.org/10.1016/j.homp.2016.03.001, available online at http://www.sciencedirect.com

ORIGINAL PAPER

Homeopathic therapy in pediatric atopic diseases: short- and long-term results

Elio Rossi*, Marco Picchi, Paola Bartoli, Marialessandra Panozzo, Chiara Cervino and Linda Nurra

Homeopathic Clinic, Campo di Marte Hospital, Local Health Unit No. 2, Lucca, Italy

Aim: **To study the outcomes of atopic diseases in children treated with homeopathy at the Homeopathic Clinic of Lucca (Italy) and related long-term results after approximately an 8-year period.**
Materials and methods: **Our data derive from an observational longitudinal study carried out on 857 pediatric patients who consecutive visited from 1998 to 2014. Children with atopic diseases were 325 (37.9%), 126 (39%) suffered from atopic dermatitis, 72 (22%) from allergic rhinitis, and 127 (39%) from asthma. Moreover, a long-term study was conducted on a subset of 107/165 patients, consecutively visited from 1998 to 2006, and with ≥5 years follow-up. The study also investigated the evolution of overall symptoms in those patients with a complex atopic symptomatology.**
Results: **75.8% of atopic children had moderate or major improvement (67.1% with asthma as the primary disease; 84.2% rhinitis; 84.2% dermatitis). At re-evaluation after 5–10 years, complete remission of atopic symptoms was obtained in 70.1% of the children: 84.2% in dermatitis; 48.1% in allergic rhinitis; 71.4% in asthma. Children with two or three atopic diseases at the first visit were completely cured in 40% of cases.**
Conclusion: **The results seem to confirm that homeopathic medicine produces positive therapeutic response in atopic children.** *Homeopathy* (2016) **105**, 217–224.

Keywords: Atopic diseases; Homeopathy; Dermatitis; Allergic rhinitis; Asthma; Short and long term results

Introduction

Childhood atopic diseases consist of the triad of atopic dermatitis, allergic rhinitis, and asthma. All share a common pathogenesis, being mediated by IgE, and are frequently present together in the same individual and family. Atopic diseases are the most common chronic childhood conditions and, in recent decades, asthma and allergy have reached epidemic proportions in most Western societies.

It has been calculated that over 500 million people suffer from allergic rhinitis[1]; according to World Health Organization (WHO) statistics, hundreds of millions of subjects in the world suffer from rhinitis,[2] but the prevalence of allergic rhinitis varies from one country to another (5–40%). One out of 5 children and adults has been shown to suffer from this condition.[3,4]

Asthma is a chronic inflammatory disease of the airways. More than 300 million children worldwide have asthma and the numbers are increasing in many countries.[5] Episodic wheeze occurs in about 30% of all children, while persistent asthma occurs in about 10% of all children and 5% of adults, even though this varies greatly across geographic regions.[4] In the United States, asthma affects more than 22 million people. It is one of the most common chronic childhood diseases, affecting more than 10 million U.S. children ages 17 and younger (14%).[6] Atopy is present in about 75% of all children with asthma but only in 50%, or even less, of adults.[7]

Atopic dermatitis is a serious and widespread health problem, with a prevalence in children that varies, according to different authors, between 10 and 20%[8] or 18 and 25%[9] and it has been calculated that about 20% of all children develop symptoms of atopic dermatitis at some point in their lives.[10] The 2010 and 2012 National Health

*Correspondence: Elio Rossi, Ambulatorio di omeopatia, Padiglione B, Cittadella della Salute – Ospedale Campo di Marte, 55100 Lucca, Italy.
E-mail: omeopatia@usl2.toscana.it
Received 18 July 2015; revised 4 March 2016; accepted 9 March 2016

OPEN ACCESS Freely available online

PLOS | ONE

Management of Upper Respiratory Tract Infections by Different Medical Practices, Including Homeopathy, and Consumption of Antibiotics in Primary Care: The EPI3 Cohort Study in France 2007–2008

Lamiae Grimaldi-Bensouda[1,2]*, Bernard Bégaud[3], Michel Rossignol[4,5], Bernard Avouac[1], France Lert[6], Frederic Rouillon[7], Jacques Bénichou[8,9], Jacques Massol[10], Gerard Duru[11], Anne-Marie Magnier[12], Lucien Abenhaim[13,14], Didier Guillemot[15,16]

1 LA-SER, Paris, France, **2** Pharmacoepidemiology and Infectious Diseases Research Group, Pasteur Institute, Paris, France, **3** INSERM U657, University of Bordeaux Segalen, U657, Bordeaux, France, **4** Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Canada, **5** LA-SER Center for Risk Research, Montreal, Canada, **6** INSERM U1018, Center for Epidemiology and Population Health, Villejuif, France, **7** Sainte-Anne Hospital, University of Paris V René Descartes, Paris, France, **8** INSERM U657, Pharmacoepidemiology and evaluation of the impact of health products on human health, Department of Pharmacology, University Victor Segalen Bordeaux 2, Tondu Hospital – Case 41, Bordeaux, France, **9** Department of Biostatistics, University Hospital of Rouen, Rouen, France, **10** Faculty of Medicine, University of Franche Comté, Besançon, France, **11** Cyklad Group, Rillieux la Pape, France, **12** Faculty of Medicine, University Pierre and Marie Curie, Paris, France, **13** Department of Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom, **14** LA-SER Europe Limited, London, United Kingdom, **15** Pasteur Institute, Paris, France, **16** Faculty of Medicine, University of Paris-Ile de France Ouest, Guyancourt, Paris, France

Abstract

Background: Prescribing of antibiotics for upper respiratory tract infections (URTI) varies substantially in primary care.

Objectives: To describe and compare antibiotic and antipyretic/anti-inflammatory drugs use, URTI symptoms' resolution and occurrence of potentially-associated infections in patients seeking care from general practitioners (GPs) who exclusively prescribe conventional medications (GP-CM), regularly prescribe homeopathy within a mixed practice (GP-Mx), or are certified homeopathic GPs (GP-Ho).

Method: The EPI3 survey was a nationwide population-based study of a representative sample of 825 GPs and their patients in France (2007–2008). GP recruitment was stratified by self-declared homeopathic prescribing preferences. Adults and children with confirmed URTI were asked to participate in a standardized telephone interview at inclusion, one-, three- and twelve-month follow up. Study outcomes included medication consumption, URTI symptoms' resolution and potentially-associated infections (sinusitis or otitis media/externa) as reported by patients. Analyses included calibration to account for non-respondents and groups were compared using multivate analyses adjusting for baseline differences with a propensity score.

Results: 518 adults and children with URTI (79.3% rhinopharyngitis) were included (36.9% response rate comparable between groups). As opposed to GP-CM patients, patients in the GP-Ho group showed significantly lower consumption of antibiotics (Odds ratio (OR) = 0.43, 95% confidence interval (CI): 0.27–0.68) and antipyretic/anti-inflammatory drugs (OR = 0.54, 95% CI: 0.38–0.76) with similar evolution in related symptoms (OR = 1.16, 95% CI: 0.64–2.10). An excess of potentially-associated infections (OR = 1.70, 95% CI: 0.90–3.20) was observed in the GP-Ho group (not statistically significant). No difference was found between GP-CM and GP-Mx patients.

Conclusion: Patients who chose to consult GPs certified in homeopathy used less antibiotics and antipyretic/anti-inflammatory drugs for URTI than those seen by GPs prescribing conventional medications. No difference was observed in patients consulting GPs within mixed-practice. A non-statistically significant excess was estimated through modelling for associated infections in the GP-Ho group and needs to be further studied.

Citation: Grimaldi-Bensouda L, Bégaud B, Rossignol M, Avouac B, Lert F, et al. (2014) Management of Upper Respiratory Tract Infections by Different Medical Practices, Including Homeopathy, and Consumption of Antibiotics in Primary Care: The EPI3 Cohort Study in France 2007–2008. PLoS ONE 9(3): e89990. doi:10.1371/journal.pone.0089990

Editor: C. Mary Schooling, CUNY, United States of America

Received January 16, 2013; **Accepted** January 28, 2014; **Published** March 19, 2014

Funding: This study was funded by Laboratoires Boiron, France. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have the following interests: LGB, BA and MR are employees of LA-SER, the company conducting the study. LG-B was the recipient of a research fellowship from INSERM (French National Institute of Health and Medical Research) at the time of the study. LA is a stockholder in LA-SER. GD is employed by Cyklad Group. FR and DG received a consulting fee or honorarium from LA-SER for the submitted work. This study was funded by Laboratoires Boiron, France. There are no patents, products in development or marketed products to declare. This does not alter the authors' adherence to all the PLoS ONE policies on sharing data and materials.

* E-mail: Lamiae.grimaldi@la-ser.com

Otitis Media

The Pediatric Infectious Disease Journal
An official publication of the European Society for Paediatric Infectious Diseases

ORIGINAL STUDIES

Homeopathic treatment of acute otitis media in children: a preliminary randomized placebo-controlled trial

JACOBS, JENNIFER MD, MPH; SPRINGER, DAVID A. MD, MPH; CROTHERS, DEAN MD

The Pediatric Infectious Disease Journal: February 2001 - Volume 20 - Issue 2 - p 177-183
From the Department of Epidemiology, School of Public Health and Community Medicine, University of Washington (JJ), and Wallingford Pediatrics (DAS), Seattle, WA; and Evergreen Center for Homeopathic Medicine, Edmonds, WA (DC).
Accepted for publication Sept. 22, 2000.

BACKGROUND
The use of antibiotics in the initial treatment of acute otitis media is currently being questioned. Homeopathy has been used historically to treat this illness, but there have been no methodologically rigorous trials to determine whether there is a positive treatment effect.

METHODS
A randomized double blind placebo control pilot study was conducted in a private pediatric practice in Seattle, WA. Seventy-five children ages 18 months to 6 years with middle ear effusion and ear pain and/or fever for no more than 36 h were entered into the study. Children received either an individualized homeopathic medicine or a placebo administered orally three times daily for 5 days, or until symptoms subsided, whichever occurred first. Outcome measures included the number of treatment failures after 5 days, 2 weeks and 6 weeks. Diary symptom scores during the first 3 days and middle ear effusion at 2 and 6 weeks after treatment were also evaluated.

RESULTS
There were fewer treatment failures in the group receiving homeopathy after 5 days, 2 weeks and 6 weeks, with differences of 11.4, 18.4 and 19.9%, respectively, but these differences were not statistically significant. Diary scores showed a significant decrease in symptoms at 24 and 64 h after treatment in favor of homeopathy ($P < 0.05$). Sample size calculations indicate that 243 children in each of 2 groups would be needed for significant results, based on 5-day failure rates.

CONCLUSION
These results suggest that a positive treatment effect of homeopathy when compared with placebo in acute otitis media cannot be excluded and that a larger study is justified.

Übersichtsstudie zu Muskuloskeletalen Erkrankungen

Musculoskeletal Disorders

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2012; **21**: 1093–1101
Published online 11 July 2012 in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3316

ORIGINAL REPORT

Impact of physician preferences for homeopathic or conventional medicines on patients with musculoskeletal disorders: results from the EPI3-MSD cohort

Michel Rossignol[1,2*], Bernard Begaud[3], Pierre Engel[4], Bernard Avouac[4], France Lert[5], Frederic Rouillon[6], Jacques Bénichou[7,8], Jacques Massol[9], Gerard Duru[10], Anne-Marie Magnier[11], Didier Guillemot[12,13], Lamiae Grimaldi-Bensouda[4,14], Lucien Abenhaim[15,16] and for the EPI3-LA-SER group

[1]*Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Canada*
[2]*LA-SER Centre for Risk Research, Montreal, Canada*
[3]*INSERM U657, University of Bordeaux Segalen, Bordeaux, France*
[4]*LA-SER, Paris, France*
[5]*INSERM U1018, Centre for Epidemiology and Population Health, Villejuif, France*
[6]*Sainte-Anne Hospital, University of Paris V René Descartes, Paris, France*
[7]*INSERM U657, Pharmacoepidemiology and evaluation of the impact of health products on human health, Rouen, France*
[8]*Department of Biostatistics, University Hospital of Rouen, Rouen, France*
[9]*Faculty of Medicine, University of Franche Comté, Besançon, France*
[10]*CYKLAD GROUP, Rillieux la Pape, France*
[11]*Faculty of Medicine, University Pierre and Marie Curie, Paris, France*
[12]*Pasteur Institute, Paris, France*
[13]*Faculty of Medicine, University of Paris-Ile de France Ouest, Paris, France*
[14]*Pharmacoepidemiology and Infectious Diseases Research Group, Pasteur Institute, Paris, France*
[15]*Department of Epidemiology, London School of Hygiene and Tropical Medicine, London, UK*
[16]*LA-SER Europe Limited, London, UK*

ABSTRACT

Objective The **objective** of this study was to assess the effect of physician practicing preferences (PPP) in primary care for homeopathy (Ho), CAM (Complementary and alternative medicines) with conventional medicine (Mx) or exclusively conventional medicine (CM) on patients with musculoskeletal disorders (MSDs), with reference to clinical progression, drug consumption, side effects and loss of therapeutic opportunity.
Methods The EPI3-MSD study was a nationwide observational cohort of a representative sample of general practitioners (GP) and their patients in France. Recruitment of GP was stratified by PPP, which was self-declared. Diagnoses and comorbidities were recorded by GP at inclusion. Patients completed a standardized telephone interview at inclusion, one, three and twelve months, including MSD-functional scales and medication consumption.
Results 1153 MSD patients were included in the three PPP groups. Patients did not differ between groups except for chronicity of MSDs (>12 weeks), which was higher in the Ho group (62.1%) than in the CM (48.6%) and Mx groups (50.3%). The twelve-month development of specific functional scores was identical across the three groups after controlling for baseline score ($p > 0.05$). After adjusting for propensity scores, NSAID use over 12 months was almost half in the Ho group (OR, 0.54; 95%CI, 0.38–0.78) as compared to the CM group; no difference was found in the Mx group (OR, 0.81; 95% CI: 0.59–1.15).
Conclusion MSD patients seen by homeopathic physicians showed a similar clinical progression when less exposed to NSAID in comparison to patients seen in CM practice, with fewer NSAID-related adverse events and no loss of therapeutic opportunity. Copyright © 2012 John Wiley & Sons, Ltd.

KEY WORDS—musculoskeletal disease; cohort; homeopathy; exposure to NSAID; pharmacoepidemiology

Received 27 January 2012; Revised 10 May 2012; Accepted 01 June 2012

*Correspondence to: M. Rossignol, 1301 Sherbrooke street EastMontreal, QC CANADA H2L 1M3. E-mail: Michel.Rossignol@CRR-Intl.com

Übersichtsstudie bei chronischen Rückenschmerzen:

Chronischer Rückenschmerz | Chronic Low Back Pain

ORIGINAL ARTICLE

Homeopathic Treatment of Patients With Chronic Low Back Pain

A Prospective Observational Study With 2 Years' Follow-up

Claudia M. Witt, MD, MBA, Rainer Lüdtke, MSc,† Roland Baur, MD,* and Stefan N. Willich, MD, MPH, MBA**

Objectives: To evaluate the details and effects of an individualized homeopathic treatment in patients with chronic low back pain in usual care.

Methods: Prospective multicenter observational study. Consecutive patients beginning homeopathic treatment in primary care practices were evaluated over 2 years by using standardized questionnaires. Diagnoses (ICD-9) and symptoms with severity, health-related quality of life (QoL), medical history, consultations, homeopathic and conventional treatments, and other health service use were recorded.

Results: One hundred twenty-nine adults (64.3% women, mean age 43.6 ± 12.7 y) were treated by 48 physicians. The patients mainly had chronic low back pain (average duration 9.6 ± 9.0 y) and other chronic diseases. Nearly all the patients (91.3%) had been pretreated. The initial case-taking took 113 ± 36, and the case analysis took 31 ± 38 minutes. The 7.4 ± 8.1 subsequent consultations (duration: 23.7 ± 15.2 min) cumulated to 204.5 ± 184.6 minutes. The patients received an average of 6.8 ± 6.3 homeopathic prescriptions. The severity of the diagnoses and complaints showed marked and sustained improvements with large effect sizes (Cohen's d from 1.67 to 2.55) and QoL improved accordingly (SF-36 physical component scale $d = 0.33$; mental component scale $d = 0.54$). The use of conventional treatment and health services decreased markedly: the number of patients using low back pain-related drugs was half of the baseline.

Discussion: Classic homeopathic treatment represents an effective treatment for low back pain and other diagnoses. It improves health-related QoL and reduces the use of other healthcare services.

Key Words: low back pain, homeopathy, prospective observational study, utilization, usual care

(*Clin J Pain* 2009;25:334–339)

Low back pain is a common musculoskeletal disorder with a 70% lifetime prevalence that causes major economic losses through medical and lost workdays costs.[1–3] Pains in the lumbal or sacroiliacal region can be acute or chronic and may radiate down the legs. They may come from physical causes (eg, trauma, osteoarthritis, intervertebral disc degeneration, or herniation) or psychologic issues.[4] Current treatment strategies are mostly symptomatic (analgesics, non steroidal anti inflammatory drugs, local anesthetics) and are designed to maintain mobility and avoid chronification. In chronic cases, treatment can be complemented with education, physiotherapy, back training,[4] and acupuncture.[5,6]

Homeopathy is practiced in many regions of the world,[7] especially in high-income countries where it ranks the most popular among traditional, complementary, or alternative medicines.[7–9] Following its "law of similarity," patients are treated with a remedy that in healthy proband has produced symptoms that are similar to those of the patients disease. A diagnosis can be treated with different remedies in different patients ("individualization"), depending on varying side symptoms. The "classic" homeopathic case evaluation usually includes all symptoms of the patient, not only those of the main complaints, and in some schools even those of no pathologic value.

Homeopathic drugs ("remedies") are produced by alternating steps of diluting and agitating a starting substance; the resulting "potencies" quickly reach dilutions beyond Avogadro's number, where the probability of even 1 molecule of the starting substance being present in an applied dose approaches zero. Such "high potencies" are often prescribed and their effects constitute a subject of scientific controversy.[10] Meta-analyses of placebo-controlled studies have shown inconsistent results.[11,12] In contrast to placebo-controlled trials that focus on the specific effect of a homeopathic medicine, the aim of this study was to research homeopathy as a whole treatment system.

This study evaluated the use, consultation, and prescription patterns as well as the effects of the whole treatment system of homeopathy under conditions of usual care. To this effect, we investigated 3981 patients in a prospective observational study,[13–15] of whom this paper presents a subgroup of 129 adults consulting a homeopathic physician because of low back pain caused by any etiology.

METHODS

In this prospective multicenter observational study, the patients were included consecutively upon their first consultation with a participating physician and were followed up for 24 months by using standardized questionnaires. To ensure consecutive recruitment, the physicians

Received for publication July 7, 2008; revised September 23, 2008; accepted October 6, 2008.
From the *Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, Berlin; and †Karl and Veronica Carstens-Foundation, Am Deimelsberg 36, Essen, Germany.
Supported by a grant by the Karl und Veronica Carstens Foundation, D-Essen.
Reprints: Claudia M. Witt, MD, MBA, Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, D-10098 Berlin, Germany (e-mail: claudia.witt@charite.de).

BMC Public Health

BioMed Central

Research article

Open Access

Homeopathic medical practice: Long-term results of a cohort study with 3981 patients

Claudia M Witt*[1], Rainer Lüdtke[2], Roland Baur[1] and Stefan N Willich[1]

Address: [1]Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, D-10098 Berlin, Germany and [2]Karl und Veronica Carstens Foundation, Am Deimelsberg 36, D-45276 Essen, Germany

Email: Claudia M Witt* - claudia.witt@charite.de; Rainer Lüdtke - r.luedtke@carstens-stiftung.de; Roland Baur - claudia.witt@charite.de; Stefan N Willich - stefan.willich@charite.de

* Corresponding author

Published: 03 November 2005

BMC Public Health 2005, 5:115 doi:10.1186/1471-2458-5-115

Received: 09 May 2005
Accepted: 03 November 2005

This article is available from: http://www.biomedcentral.com/1471-2458/5/115

Abstract

Background: On the range of diagnoses, course of treatment, and long-term outcome in patients who chose to receive homeopathic medical treatment very little is known. We investigated homeopathic practice in an industrialized country under everyday conditions.

Methods: In a prospective, multicentre cohort study with 103 primary care practices with additional specialisation in homeopathy in Germany and Switzerland, data from all patients (age >1 year) consulting the physician for the first time were observed. The main outcome measures were: Patient and physician assessments (numeric rating scales from 0 to 10) and quality of life at baseline, and after 3, 12, and 24 months.

Results: A total of 3,981 patients were studied including 2,851 adults (29% men, mean age 42.5 ± 13.1 years; 71% women, 39.9 ± 12.4 years) and 1,130 children (52% boys, 6.5 ± 3.9 years; 48% girls, 7.0 ± 4.3 years). Ninety-seven percent of all diagnoses were chronic with an average duration of 8.8 ± 8 years. The most frequent diagnoses were allergic rhinitis in men, headache in women, and atopic dermatitis in children. Disease severity decreased significantly ($p < 0.001$) between baseline and 24 months (adults from 6.2 ± 1.7 to 3.0 ± 2.2; children from 6.1 ± 1.8 to 2.2 ± 1.9). Physicians' assessments yielded similar results. For adults and young children, major improvements were observed for quality of life, whereas no changes were seen in adolescents. Younger age and more severe disease at baseline were factors predictive of better therapeutic success.

Conclusion: Disease severity and quality of life demonstrated marked and sustained improvements following homeopathic treatment period. Our findings indicate that homeopathic medical therapy may play a beneficial role in the long-term care of patients with chronic diseases.

Background

Homeopathy is one of the most frequently used and controversial systems of complementary and alternative medicine. It is based on the 'principle of similars', whereby highly diluted preparations of substances that cause symptoms in healthy individuals are used to stimulate healing in patients who have similar symptoms when ill [1]. When a single homeopathic remedy is selected based on a patient's total symptom picture, it is called 'classical' homeopathy [2]. According to a survey in the US [3], the proportion of patients obtaining homeopathic care has quadrupled in the last seven years. A survey in Britain [4]

estimated that annual expenditures reached £34.04 million (out-of-pocket £30.74 million, NHS £3.3 million). For Germany, the country in which classical homeopathy originated, a recent survey demonstrated that approximately 10% of men and 20% of women in the general population used homeopathic medicines during the previous year [5]. General trends show a rise in the number of individuals utilising naturopathic and homeopathic therapeutic methods [6].

The General Medical Council in Germany grants an official certification in homeopathy to physicians upon successful completion of a three-year-long training programme. Approximately 4,500 physicians in Germany hold this additional certification [6]. However, with the exception of some randomised, controlled trials including patients with selected diagnoses [2,7] there is no data on the health care offered by classical homeopathic medical practices. Therefore, it is impossible to assess the state of homeopathic health care and its effectiveness. We designed this project with the goal of systematically collecting data in the area of homeopathic health care for the first time in Germany. The aim of the present study was to determine the spectrum of diagnoses and treatments, as well as the course of disease over time among patients who chose to receive homeopathic treatment.

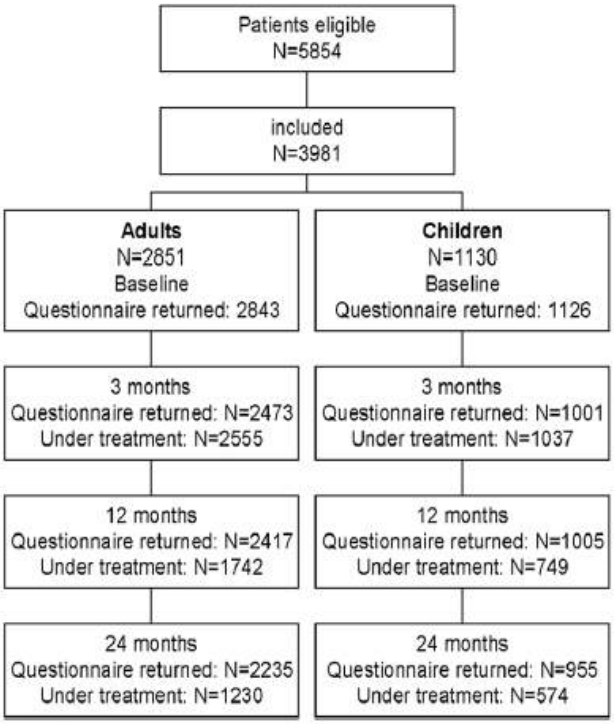


Figure 1
Patient selection.

Methods

Patients were included consecutively in this prospective, multi-centre observational study upon their first consultation with a participating physician and were followed up for a total of 24 months. Evaluations were made using standardised questionnaires. In order to provide as representative a picture of homeopathic health care as possible, patients were included in the study regardless of their diagnosis. Patients were eligible for the study if they were consulting the participating physician for the first time and were at least 1 year of age. In order to participate in the study, physicians were required to have passed certified training in classical homeopathy and at least three years of experience in its practice. A total of 187 physicians belonging to four different working groups were contacted either by post or telephone and informed about the study. Of these, 103 physicians chose to participate. Each participating physician was trained in study procedures and was subject to at least one monitoring visit during the study period. All study participants provided written, informed consent, and the study protocol was approved by the appropriate ethics review boards.

Outcome measures

For patients, we developed different questionnaires for three different age groups: 1–6 years of age, 7–16 years of age, adults (>16 years of age). All questionnaires were designed to document sociodemographic data, as well as information on prior medical history, patient symptoms and complaints, quality of life, and the use of any treatment other than homeopathy. At baseline, patients recorded the complaints that led them to consider homeopathic treatment. Independently of their physicians, patients rated the severity of their complaints on a numeric rating scale (0 = no complaints, 10 = maximum severity) [8]. All complaints listed by patients in their baseline questionnaire were transferred to their follow-up questionnaires by the study office personnel. This ensured that each baseline complaint was assessed at each subsequent follow-up. For children between 1 and 6 years of age, the KITA questionnaire [9] was used to assess general health-related quality of life. It was completed by the children's parents. Patients between 7 and 16 years of age completed the KINDL questionnaire [10,11]. In additional, parents were asked to provide the required medical information. For the adults, general health-related quality of life was assessed using the MOS SF-36 questionnaire [12]. The results of the SF-36 are presented in normalised scores, the results being scaled in such a way that the normal German population has a mean score of 0 and a standard deviation of 1.

The first questionnaire was distributed to the patients by the study physician and completed prior to the start of therapy (baseline). Patients sent their completed ques-

tionnaires to the study office in sealed envelopes. Follow-up questionnaires were sent to all patients by the study office at 3, 12, and 24 months.

For physicians, we developed a standardised questionnaire that allowed for continuous documentation during the treatment/follow-up period (24 months), as well as standardised points of assessment at 0, 3, 12 and 24 months. At each of these time points, the severity of a maximum of 4 diagnoses and maximum of 8 symptoms was rated by participating physicians using a numerical rating scale [8]. This information was then forwarded to the study office. The type of homeopathic treatment, the use of any conventional therapy, as well as any referrals to other physicians were recorded on a continuous basis.

Statistics

Data was double entered manually into an ACCESS® database and subsequently compared using the SAS® system followed by plausibility data checks if necessary. The diagnoses, documented by study physicians, were encoded in ICD-9 format and recorded by two specially trained study staff members using DIACOS.® Statistical analysis was performed using SAS/STAT® software (Version 8.2).

Data for adults (>16 years) and for children/adolescents were analysed separately. In order to calculate the average severity of the physicians' diagnoses, we took the four diagnoses named first for each patient during the baseline examination. For each of the follow-up assessment points (i.e. at 3, 12, and 24 months) we ascertained the respective severity ratings made by study physicians.

All results reported here are based on the intention-to-treat approach, i.e. each included patient entered the final analyses. If patients dropped out or withdrew from the study we replaced the respective missing values: baseline complaints that had been cured were given a severity rating of 0 in all following examinations. For patients who died during the study, we inserted the maximum severity rating of 10. Other missing values were multiply imputed following the suggestions of Rubin [13]. Instead of filling in a *single* value as a substitute for a missing value, multiple imputation is a strategy by which each missing value is replaced simultaneously by a *set* of plausible values that represents the uncertainty about the right value to impute. Thus, the missing values are filled in several times generating several distinct data tables, each with a complete set of data without any missing value. These complete data tables are analyzed separately using appropriate statistical models. Afterwards, the results from all statistical analyses are pooled to generate treatment effects and p-values. In our study we used the MCMC (Marcov chain Monte Carlo) replacement method and created 5 multiple imputed data tables.

Table 1: Baseline characteristics of study population

	Adults	Children
Gender (% female)	70.8	48.3
Age (years, mean ± std)	40.7 ± 12.7	6.7 ± 4.1
Marital status (% living in partnership)	84.0	/
Education (% attending school >10 years)	85.0	/
Belief in homeopathy (%)	65.7	68.6†
Duration of disease (years, mean ± std)	10.3 ± 9.8	4.3 ± 3.7
Intake of conventional drugs (%)	50.2	31.7

† Parents' perspective

For each imputed data set, treatment effects were estimated on the basis of generalized linear regression models. Generalized linear regression models are flexible and powerful tools to describe data from cohort studies [14]. They are generalizations of the well known and often applied multiple regression models which often appear to be too simple to describe longitudinal data adequately. A generalized linear model is best described by two components. First, the mean course of the outcome, and second, the correlation structure for measurements taken at the same individual at different times. In our study we divided the 2-year follow-up period into two parts. During the first part (months 0–3) we assumed that mean outcome increases (or decreases) linearly. For the second part (months 3–21) we assumed that the mean outcome increases (or decreases) according to a quadratic term. Moreover, we assumed that the correlation between two measurements can be described by a simple exponential function. This essentially means, that the correlation only depends from the time span between the two measurements, and it decreases the bigger this time span is. This approach is completely analogous to the recommendations given by Diggle, Liang, and Zeeger in their standard text book on the analysis of longitudinal data [14].

Subgroup analyses are based on essentially the same statistical approach adding the respective factors as a fixed covariate into the models. For subgroup analyses adults' and children's data were pooled.

Usually, patients for clinical studies are not selected randomly from a target population but according to some selection criteria that sample patients according to extreme measurements (high blood pressure, severe pain, low quality of life, ...). This inevitably leads to regression-to-the-mean, a statistical phenomenon that makes natural variation look like real changes [15]. Separating regression-to-the-mean effects from true treatment effects can be difficult but is at least feasible when the mean and the standard deviation of the target population are known. In this situation it is possible to calculate the expected outcome for each patient when regression-to-the-mean

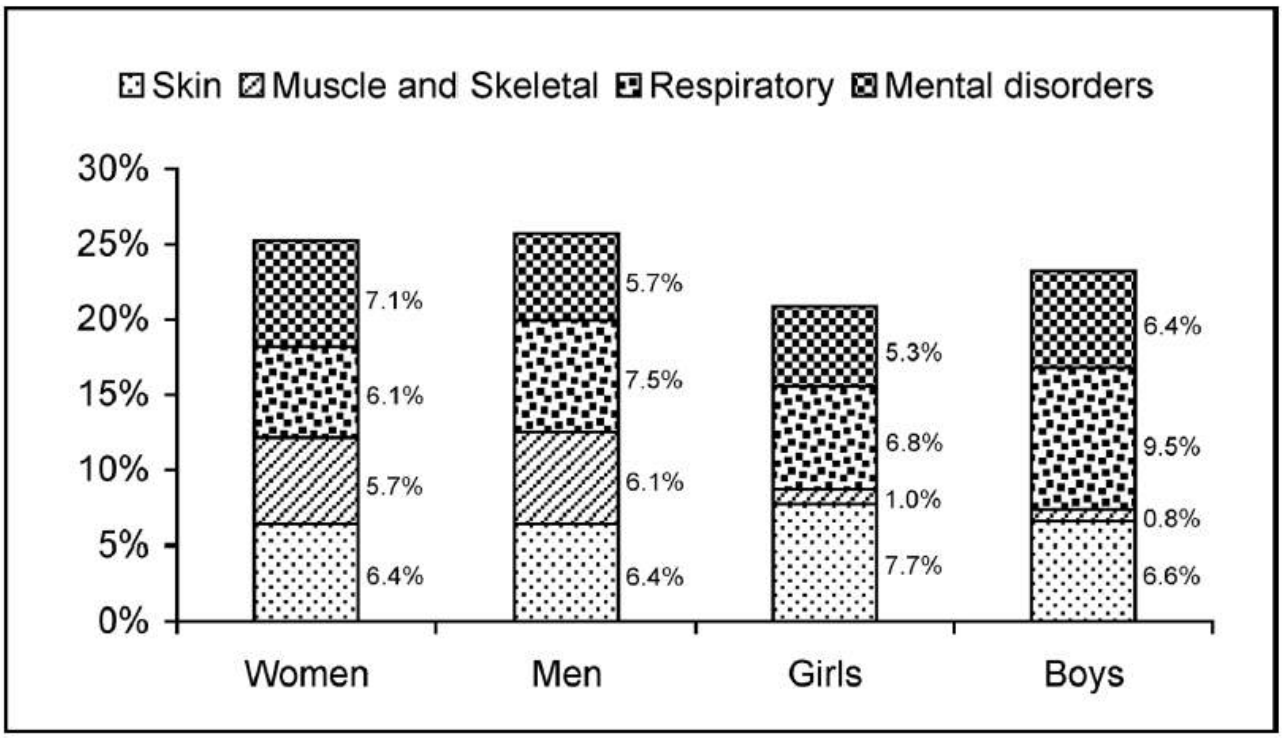


Figure 2
Most common medical complaints as reported by the homeopathy physicians (in % of documented complaints).

occurs [16]. In our study we made a rather conservative assumption on the target population (chronically ill patients seeking homeopathic care): to have the same quality of life as the general German population (i.e. a mean SF-36 score of 0 and a standard deviation of 1). From this we calculated the expected regression-to-the mean effect and compared it to the actually observed change of the SF-36 scores.

Results

A total of 103 physicians participated in the study (51 male, 45 ± 7 years of age; 52 female, 45 ± 7 years of age). Twenty-six percent of the participating physicians were specialists (10% internists, 9% paediatricians, 7% other) and 74% were general practitioners. The average duration of overall medical practice was 17.4 ± 8.4 years with 9.0 ± 4.4 years of practice in homeopathy (range 3–20 years). Forty percent of the physicians were certified to work in the public health care system, and 60% were in private practice.

Patients were recruited for the study between September 1997 and December 1999. Of the patients who met the inclusion criteria, 3981 (68%) chose to participate and were included in the study (for patient selection see Figure 1). Of these, 2851 were adults (71% women) and 1130 were children (48% girls). The baseline characteristics are listed in Table 1.

On average, the homeopathic physicians made 2.6 ± 1.2 diagnoses per patient (2.8 ± 1.1 in adults, 2.3 ± 1.1 in children). Ninety-seven percent of all diagnoses were classified by these physicians as chronic with a median duration of 4.3 ± 2.7 years in children and 10.3 ± 9.8 years in adults. Almost all patients had received conventional treatment (95%) or had already contacted another physician (95%) prior to the start of this study. The most common diagnosis in women was migraine (9.7%), in men allergic rhinitis (10.3%), and in children of both genders atopic dermatitis (20%), for details see [17]. For the most common disease groups see Figure 2.

All patients underwent an initial homeopathic anamnesis, lasting an average of 2.0 ± 0.7 hours. Following enrolment in the study, patients had to wait an average of 57 ± 84 days before undergoing the initial anamnesis. During the 24-month observation period, patients consulted their physicians an average of 7.8 ± 8.4 times. During the study period, half of the patients (50.3%, adults: 50.8%, children 48.9%) noted additional visits to non-study physicians (gynaecologists and dentists excluded). The intake of conventional medication decreased from 45.0% at

Table 2: Course of outcome parameters and estimated mean changes of outcome parameters

					Estimated changes compared to baseline†		
	Baseline mean ± SD	**3 months** mean ± SD	**12 months** mean ± SD	**24 month** mean ± SD	**Δ 3 months** mean (95%CI)	**Δ 12 months** mean (95%CI)	**Δ 24 months** mean (95%CI)
Adults							
Patients assessments (NRS) ‡	6.2 ± 1.7	3.8 ± 2.2*	3.3 ± 2.1*	2.9 ± 2.2*	-2.4 (-2.5 to -2.3)	-2.8 (-2.9 to -2.7)	-3.1 (-3.2 to -3.0)
Physicians assessments (NRS) ‡	6.0 ± 1.6	3.9 ± 2.1*	2.8 ± 2.1*	2.1 ± 2.0*	-2.1 (-2.2 to -2.0)	-3.1 (-3.2 to -3.0)	-3.7 (-3.8 to -3.6)
SF-36 QoL physical scale	46.5 ± 10.1	49.1 ± 9.5*	50.1 ± 9.6*	50.7 ± 9.5*	2.6 (2.3 to 2.9)	3.5 (3.0 to 3.9)	4.1 (3.5 to 4.6)
SF-36 QoL mental scale	39.3 ± 11.8	44.6 ± 10.8*	45.5 ± 10.8*	46.4 ± 10.6*	5.6 (5.2 to 6.0)	6.2 (5.7 to 6.7)	6.9 (6.3 to 7.6)
Children							
Patients assessments (NRS) ‡	6.1 ± 1.8	3.2 ± 2.3*	2.5 ± 2.1*	2.2 ± 2.0*	-3.1 (-3.3 to -2.9)	-3.5 (-3.7 to -3.4)	-3.9 (-4.0 to -3.7)
Physicians assessments (NRS) ‡	5.9 ± 1.7	3.2 ± 2.2*	2.0 ± 1.5*	1.5 ± 1.8*	-2.7 (-2.8 to -2.6)	-3.8 (-4.0 to -3.7)	-4.4 (-4.6 to -4.3)
KINDL QoL	69.3 ± 13.3	72.1 ± 12.6	68.0 ± 9.2	67.3 ± 9.9*	2.7 (1.7 to 3.7)	-0.4 (-1.5 to 0.8)	-2.2 (-3.6 to -0.8)
KITA QoL mental/ physical dimension	67.6 ± 16.9	75.4 ± 14.6*	77.0 ± 14.1*	77.5 ± 14.3*	8.3 (6.6 to 10.0)	9.3 (7.7 to 10.8)	10.0 (8.3 to 11.6)
KITA QoL aspects of daily living	58.6 ± 18.3	66.9 ± 15.9*	69.1 ± 16.7*	70.6 ± 16.0*	8.5 (7.2 to 9.8)	10.4 (8.8 to 12.0)	11.6 (9.7 to 13.5)

† estimations are based on generalised linear models, see text; ‡ = lower values indicate better status and negative Δ indicates improvement
QoL = quality of life; NRS = numeric rating scale, * $p < 0.001$ versus baseline

baseline (adults: 50.2%, children 31.7%) to 26.8% after 24 months (adults: 31.8%, children 14.2%).

According to patient assessments, disease severity decreased significantly between baseline and 12 months, as well as between 12 months and 24 months (see Table 2). According to physician assessments, 25.7% (adults: 21.9%, children: 37.6%) of the diagnoses were no longer present at 24 months, whereas patients judged 23.0% (adults 19.7%, children 32.8%) of the medical complaints to have resolved by this point. Thirteen percent of the patients documented that they had no complaints whatsoever at 24 months.

In adults, large improvements in quality of life were observed on both component scales (mental and physical) during the first three months of treatment, and continued to improve during the course of the study (see Table 2). Even with the pessimistic assumption that the test-retest correlation of the SF-36 is only 0.7 and that the study population is no more ill than a random sample of the general population, one could expect an improvement of only 3.8 (1.2) score points on the mental (physical) component scale, attributable to regression-to-the-mean [16], markedly lower than the 5.6 (2.6) score points observed in our study (Table 2). Statistically, the baseline quality of life of non-completers was not significantly lower than in other patients (p-values: MCS: $p = 0.37$; PCS: $p = 0.48$, Wilcoxon-tests).

Quality of life in young children (age 1–6 years) also improved markedly during the observation period (Table 2), having already risen during the first three months of study therapy as measured on both scales of the KITA questionnaire (mental-physical dimension and aspects of daily living, each $p < 0.001$, see Table 2). These improvements continued over the course of treatment ($p < 0.001$, see Table 2). In school children and adolescents, however, an improvement in quality of life was only visible during the first three months of study therapy ($p < 0.001$, see Table 2).

The diagnosis had no relevant influence on the changes in patient complaints or quality of life as measured in this investigation.

In patient and physician assessments, younger patients showed greater improvements than did older patients and more severe disease at baseline was followed by greater improvements compared to less severe disease (see Table 3). Gender, duration of disease and belief in homeopathy had only a minor influence on improvements.

Discussion

Patient and physician assessments of disease severity and quality of life consistently demonstrated substantial improvements following homeopathic treatment, which were maintained through 24 months' follow up. Improvements were more pronounced in younger patients and in

Table 3: Subgroup analyses for patients and physicians assessments (mean changes of outcome parameters after 24 months compared to baseline, negative Δ indicates improvement)

	Patients assessments (NRS)			Physicians assessments (NRS)		
	Mean†	95%-CI	p value*	Mean†	95%-CI	p value*
Total (n = 3981)	-3.3	-3.4 to -3.2		-3.9	-4.0 to -3.8	0,060
Gender						
Female (n = 2560)	-3.4	-3.5 to -3.2		-3.9	-4.0 to -3.8	
Male (n = 1412)	-3.3	-3.4 to -3.1	0.387	-3.9	-4.0 to -3.8	0,060
Age groups (years)						
<10 (n = 839)	-4.0	-4.2 to -3.8		-4.4	-4.6 to -4.2	
10–19 (n = 355)	-3.5	-3.7 to -3.2	<0.001	-4.3	-4.5 to -4.0	0.149
20–39 (n = 1456)	-3.4	-3.6 to -3.3	<0.001	-3.7	-3.8 to -3.6	<0.001
40–59 (n = 1041)	-2.8	-3.8 to -2.0	<0.001	-3.6	-3.8 to -3.5	<0.001
≥ 60 (n = 281)	-2.6	-2.9 to -2.2	<0.001	-3.5	-3.8 to -3.2	<0.001
Baseline severity of disease						
NRS < 6.0 (n = 1660)	-2.1	-2.3 to -2.0		-3.1	-3.2 to -3.0	
NRS ≥ 6.0 (n = 2310)	-4.1	-4.2 to -4.0	<0.001	-4.6	-4.7 to -4.5	<0.001
Duration of disease in adults (years)						
< 10 (n = 1878)	-3.2	-3.4 to -3.1		-3.7	-3.8 to -3.6	
≥ 10 (n = 927)	-2.9	-3.1 to -2.7	<0.001	-3.6	-3.7 to -3.4	0.043
Intake of conventional drugs at baseline						
Yes (n = 1788)	-3.3	-3.5 to -3.2		-3.8	-3.9 to -3.7	
No (n = 2188)	-3.3	-3.5 to -3.2	0.157	-3.9	-4.0 to -3.9	0.029
Belief in homeopathy						
Strong (n = 2656)	-3.4	-3.5 to -3.1		-3.9	-4.0 to -3.8	
Weak (n = 1316)	-3.1	-3.3 to -3.0	<0.001	-3.8	-3.9 to -3.7	0.563

† estimations are based on generalised linear models, NRS = numeric rating scale; * per item each subgroup compared to the first listed subgroup

those with greater disease severity compared to older patients and those with less severe disease at baseline.

To our knowledge, the present study is the first to evaluate systematically the range of diagnoses and therapies in classical homeopathic medical practices in Germany and Switzerland. In addition, the study provided information on the course of illness in patients receiving homeopathic treatment, as assessed by patients and physicians.

The methodological strengths of our study include consecutive enrolment of a large sample size, the participation of approximately 2% of all physicians certified to practice homeopathy in Germany and 28% of all members of the Hahnemann Association (an organisation for physicians practicing only 'classical' homeopathy) and the use of standardised outcome instruments also used in studies on conventional therapy.

One limitation of our study is that the observed effects cannot be categorized with respect to specificity, i.e. we cannot draw conclusions as to the beneficial mechanisms. Furthermore patients were allowed to use conventional therapies during the study period in addition to homeopathic treatment. Thus, the observed improvement cannot be attributed to homeopathic treatment alone. The aim of the investigation, however, was not to test the effectiveness of homeopathic treatment alone, but rather provide systematic and detailed information about the current status of homeopathic medical care in routine practice and its effectiveness. These data may also be helpful in the planning of further research projects on homeopathy.

The effects observed by patient and the physician assessment, as well as those seen with regard to quality of life, deserve additional comments. The average severity of the

chronic diseases was reduced by approximately 50% after only 3 months of homeopathic treatment, and remained around this level during the follow-up period. Physician assessments tended to be more positive than patient assessments.

The improvements we observed in our patients cannot be attributed solely to regression-to-the-mean, because the improvements were greater than could be expected even under conservative model assumptions. This is supported by the fact that patients did not visit the study physicians when they were feeling the worst, but rather after a long waiting period.

A strength of this study is that patients with all diagnoses were included. Therefore, no disease-specific measurement instruments could be used. To assess the severity of different medical complaints, there is no other generally accepted measuring instrument available. Instead numerical rating scales [8] were applied, which would allow for the determination of illness severity in a diagnosis-independent manner.

Compared to the other quality two of life questionnaires used in our study, the KINDL questionnaire for the age group 7 to 16 years was not sensitive to change, as has been shown in other studies [18,19]. Other explanations might be that children adapt easier to perceived quality of life and that the dimensions of Quality of life used for adults are not transferable to children. However, there is no other generally accepted measuring instrument available in German-speaking countries.

In the range of baseline diagnoses, chronic illnesses clearly predominated (>95% of diagnoses). Among these, headache and atopic disease (allergic rhinitis, asthma and atopic dermatitis) were the most common diagnoses. As the clinical histories of our patients showed, most of our patients decided to consult a homeopathic physician only after having received conventional treatment. This, together with the extensive initial case taking and the reputation of homeopathy as a "medicine designed to treat the individual as a whole"' causes a selection for chronic illnesses.

We were unable to confirm the common notion that homeopathy is frequently used for trivial complaints or diseases. The duration of disease in study patients was very long and their symptoms were, on average, of moderate severity.

In this study we were not able to evaluate different types of homeopathic strategies. For quality assurance purposes, we avoided selecting a random sample of homeopathic physicians for the study, choosing instead to recruit physicians schooled and certified in 'classical' homeopathy. The results of our study are, therefore, representative only for the classical type of homeopathy that was practised by participating physicians. Compared to conventional medical practices, headache and atopic disease (allergic rhinitis, asthma and atopic dermatitis) were the most common diagnoses in homeopathic practices (as opposed to hypertension, hyperlipidemia and low back pain in 70,000 patients treated conventionally) [9]. An American study [20] found asthma, depression, otitis media, and allergic rhinitis to be the most common diagnoses treated in homeopathic practices, compared to hypertension, upper respiratory tract infection, otitis media and diabetes mellitus, which were treated most commonly in conventional practices.

A health insurance company project that included about 900 patients treated with homeopathy in routine care [21] showed an improvement in quality of life and in physician assessment. In Güthlin's study [21], however, only physicians certified to work in the public health care system were able participate. Homeopaths working in private practices (i.e. the great majority in Germany) were excluded. The advantage of the present study is that doctors in private practice were also included, thus providing a more detailed and broader basis for describing the current status of homeopathic health care. Another controlled study in cooperation with a German health insurance company [22], indicated similar overall effectiveness of homeopathically versus conventionally treated patients for selected diagnoses and in some groups, superiority of homeopathic treatment.

Conclusion

We evaluated for the first time the range of diagnoses and therapies at medical practices offering classical homeopathic treatment in Germany and Switzerland. The findings of our study demonstrate that patients who seek homeopathic treatment are primarily those suffering from long-standing, chronic disease. Both according to physician and patient assessments, the severity of complaints decreased markedly over the 24-month observation period. Younger patients and those with more severe disease appear to benefit most from homeopathic treatment. Among adults and children, we observed an increase in quality of life. Our findings indicate that homeopathic medical therapy may play a beneficial role in the long-term care of patients with chronic diseases.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

CW participated in the design of the study, coordination and statistical analysis. RL participated in its design and performed the statistical analysis. RB participated in the design of the study and data acquisition. SNW conceived of the study, and participated in its design and statistical analysis and had the overall scientific responsibility. All authors helped to draft the manuscript, read and approved the final manuscript.

Acknowledgements

This study was supported by a grant from the Karl and Veronica Carstens Foundation. We thank all participating physicians and patients.

References

1. Jonas W, Jacobs J: *Healing With Homeopathy* New York, Warner Books; 1996.
2. Linde K, Clausius N, Ramirez G, Melchart D, Eitel F, Hedges LV, Jonas WB: **Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials.** *Lancet* 1997, **350**:834-843.
3. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, Kessler RC: **Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey.** *JAMA* 1998, **280**:1569-1575.
4. Thomas KJ, Nicholl JP, Coleman P: **Use and expenditure on complementary medicine in England: a population based survey.** *Complement Ther Med* 2001, **9**:2-11.
5. Härtel U, Volger E: **Inanspruchnahme und Akzeptanz von klassischen Naturheilverfahren und alternativen Heilmethoden in Deutschland. Ergebnisse einer repräsentativen Bevölkerungsstudie.** *Das Gesundheitswesen* 2003, **65**:A35.
6. G M, S M: *Gesundheitsberichtserstattung des Bundes - Inanspruchnahme alternativer Methoden in der Medizin* Edited by: T Z. Berlin, Robert Koch Institut; 2002.
7. Kleijnen J, Knipschild P, ter Riet G: **Clinical trials of homoeopathy.** *BMJ* 1991, **302**:316-323.
8. Huskisson EC, Scott J: **VAS Visuelle Analog-Skalen; auch VAPS Visual Analogue Pain Scales, NRS Numerische Rating-Skalen; Mod. Kategorialskalen.** In *Handbuch psychosozialer Meßinstrumente - ein Kompendium für epidemiologische und klinische Forschung zu chronischer Krankheit* Edited by: Westhoff G. Göttingen, Hogrefe; 1993:881-885.
9. Wittorff M: **KITA Fragebogen zur Erfassung der gesundheitsbezogenen Lebensqualität von Kleinkindern zwischen 1-6 Jahren.** 2002.
10. Bullinger M, Mackensen S, Kirchberger I: **KINDL - ein Fragebogen zur Erfassung der gesundheitsbezogenen Lebensqualität von Kindern.** *Zeitschrift für Gesundheitspsychologie* 1994, **II**:64-77.
11. U. RS, Bullinger M: **Assessing health-related quality of life in chronically ill children with the German KINDL: first psychometric and content analytical results.** *Qual Life Res* 1998, **7**:399-407.
12. Bullinger M, Kirchberger I: *SF-36 Fragebogen zum Gesundheitszustand* Göttingen, Hogrefe; 1998.
13. Rubin DB: *Multiple Imputation for Nonresponsense in Surveys* New York, John Wiley & Sons; 1987.
14. Diggle PJ, Liang KY, Zeger SL: *Analysis of Longitudinal Data* Oxford, Clarendon,Press; 1994.
15. Barnett AG, van der Pols JC, Dobson AJ: **Regression to the mean: what it is and how to deal with it.** *Int J Epidemiol* 2005, **34**:215-220.
16. Hannan PJ, Jacobs DRJ, McGovern P, Klepp KI, Elmer P: **Estimating the effect of regression toward the mean under stochastic censoring.** *Am J Epidemiol* 1994, **139**:422-431.
17. Becker-Witt C, Lüdtke R, Weisshuhn TE, Willich SN: **Diagnoses and treatment in homeopathic medical practice.** *Forsch Komplementarmed Klass Naturheilkd* 2004, **11**:98-103.
18. Becker M: **Duft-Qigongunterricht für Schulkinder - Eine kontrollierte Pilotstudie zur Evaluation von Durchführbarkeit und Nutzen.** Humboldt-Universität zu Berlin; 2002.
19. Keil T, Becker-Witt C, Vance W, Roll S, Wegscheider K, Willich SN: **Vergleich von homöopathischer und konventioneller Therapie bei Kindern mit Neurodermitis.** *Informatik, Biometrie und Epidemiologie in Medizin und Biologie* 2002, **33**:283.
20. Jacobs J, Chapman EH, Crothers D: **Patient characteristics and practice patterns of physicians using homeopathy.** *Arch Fam Med* 1998, **7**:537-540.
21. Güthlin C, Lange O, Walach H: **Measuring the effects of acupuncture and homoeopathy in general practice: An uncontrolled prospective documentation approach.** *BMC Public Health* 2004, **4**:6.
22. Becker-Witt C, Keil T, Roll S, Menke D, Vance W, Wegscheider K, Willich SN: **Effectiveness and costs of homeopathy compared to conventional medicine-a prospective multicenter cohort study.** *Volume 4*. Edited by: Hospital TRLH. London, The Royal London Homeopathic Hospital; 2003:57-60.

Pre-publication history

The pre-publication history for this paper can be accessed here:

http://www.biomedcentral.com/1471-2458/5/115/prepub

THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 11, Number 5, 2005, pp. 793–798

Homeopathic Treatment for Chronic Disease: A 6-Year, University-Hospital Outpatient Observational Study

DAVID S. SPENCE, M.B., B.S., F.F.Hom., M.R.C.S., L.R.C.P., D.R.C.OG.,[1]
ELIZABETH A. THOMPSON, B.A., M.B., B.S., M.R.C.P., F.F.Hom.,[2] and S.J. BARRON, B.Sc.[1]

ABSTRACT

Objective: The aim of this study was to assess health changes seen in routine homeopathic care for patients with a wide range of chronic conditions who were referred to a hospital outpatient department.

Design: This was an observational study of 6544 consecutive follow-up patients during a 6-year period.

Setting: Hospital outpatient unit within an acute National Health Service (NHS) Teaching Trust in the United Kingdom.

Participants: Every patient attending the hospital outpatient unit for a follow-up appointment over the study period was included, commencing with their first follow-up attendance.

Main outcome measure: Outcomes were based on scores on a 7-point Likert-type scale at the end of the consultation and were assessed as overall outcomes compared to the initial baseline assessments.

Results: A total of 6544 consecutive follow-up patients were given outcome scores. Of the patients 70.7% ($n = 4627$) reported positive health changes, with 50.7% ($n = 3318$) recording their improvement as better (+2) or much better (+3).

Conclusions: Homeopathic intervention offered positive health changes to a substantial proportion of a large cohort of patients with a wide range of chronic diseases. Additional observational research, including studies using different designs, is necessary for further research development in homeopathy.

INTRODUCTION

Homeopathic medicine is a system of therapeutics that appears to work by stimulating the body's autoregulatory mechanisms using microdoses of toxins.[1] The principle was first expounded by Hippocrates, the so-called father of medicine, in 450 BC and was rationalized into a clinical system by a German physician, Samuel Hahnemann, in the late 18th century. Its clinical use spread widely through western Europe in the 19th century and then to the rest of the world. Homeopathy is extremely popular with patients and its use has steadily increased in recent years.

Much skepticism within the medical profession has always existed because the exact mechanism of action of homeopathic medicines is not fully understood, and any beneficial action has often been attributed to the placebo response.[2] However well-designed, randomized controlled trials[3–5] have suggested that the effects cannot be entirely explained this way, and meta-analyses or systematic reviews of substantial numbers of randomized controlled trials[6–10] have further endorsed this assertion. Some recent studies[11,12] of homeopathic treatment in specific conditions have suggested a lack of efficacy, but the design of these studies has been flawed[13,14] and therefore the results cannot be regarded as reliable.

A recent paper giving an overview of current research in the field of homeopathic medicine[15] concluded that "more and better research is needed unobstructed by belief or disbelief in the system," and that "homeopathy deserves an open-minded opportunity to demonstrate its value."

Many clinicians in everyday conventional medical practice have expressed their skepticism about clinical trials and whether the results of trials transfer to clinical care. In some recent studies clinical treatment protocols using large co-

[1]Directorate of Homeopathic Medicine, United Bristol Healthcare, National Health Service Trust, Bristol, United Kingdom.
[2]University Department of Palliative Medicine, University of Bristol, Bristol, United Kingdom.

ELSEVIER

Complementary Therapies in Medicine

Volume 16, Issue 1, February 2008, Pages 15-21

Homoeopathic versus conventional treatment of children with eczema: a comparative cohort study.

T. Keil, C.M. Witt, S. Roll, W. Vance, K. Weber, K. Wegscheider, S.N. Willich,
Homoeopathic versus conventional treatment of children with eczema: A comparative cohort study,
Complementary Therapies in Medicine,
Volume 16, Issue 1, 2008, Pages 15-21,
https://doi.org/10.1016/j.ctim.2006.10.001.

Abstract

OBJECTIVES

To assess, over a period of 12 months, whether homoeopathic treatment could influence eczema signs/symptoms and quality of life (QoL) compared with conventional treatment.

DESIGN
Prospective multi-centre cohort study.
SETTING
Children with eczema aged 1-16 years were recruited from primary care practices.

INTERVENTIONS
Conventional versus homoeopathic treatment.

OUTCOME MEASURES
Patients (or parents) assessed eczema symptoms by numerical rating scales as well as disease-specific Atopie Lebensqualitaets-Fragebogen (ALF) and general quality of life (KINDL, KITA) at 0, 6 and 12 months.

RESULTS
A total of 118 children were included: 54 from homoeopathic (mean age+/-S.D. was 5.1+/-3.3 years; 56% boys) and 64 from conventional practices (6.2+/-3.8 years; 61% boys). Eczema symptoms (assessed by patients or their parents) improved from 0 to 12 months for both treatment options, but did not differ between the two groups: 3.5-2.5 versus 3.4-2.1; p=0.447 (adjusted). Disease-related quality of life improved in both groups similarly. In the subgroup of children aged 8-16 years the general quality of life showed a better trend for conventional treatment compared with homoeopathic treatment (p=0.030).

CONCLUSIONS
This observational study is the first long-term prospective investigation to compare homoeopathic and conventional treatment of eczema in children. Over a period of 12 months, both therapy groups improved similarly regarding perception of eczema symptoms (assessed by patients or parents) and disease-related quality of life.

Complementary Therapies in Medicine
Volume 11, Issue 4, December 2003, Pages 243-248

NHS patients' perspective on complementary medicine: a survey.

Sharples FM[1], van Haselen R, Fisher P.
Academic Unit, Royal London Homeopathic Hospital, UCL Hospitals NHS Trust, London , UK.
Complement Ther Med. 2003 Dec;11(4):243-8. https://doi.org/10.1016/S0965-2299(03)00107-9.

Abstract

OBJECTIVES
To examine patients' reasons for seeking complementary and alternative medicine (cam) in the national health service, including the nature and duration of the patient's main health problem, the impact of cam on this, satisfaction with clinical care, and usage of conventional prescription medication.
DESIGN
survey (n=499).
SETTING
Out-patient department, the royal London homeopathic hospital, a national health service facility dedicated to cam.
RESULTS
Five hundred and six questionnaires were returned, 499 were analysed. patients' most frequent reasons for seeking cam were that other treatment had not helped, and concerns about or experience of adverse treatment reactions. two hundred and ninety-seven patients (63%) had had their main problem for more than 5 years. musculoskeletal system problems were the most frequent diagnostic group (n=151, 32%). satisfaction with clinical care was high (443/490: 90%). three hundred and eighty patients (81%) indicated their main problem had improved very much, moderately or slightly. Of the 262 patients who had been taking prescription medicines when they first attended, 76 (29%) had stopped, and 84 (32%) had reduced their intake.
CONCLUSIONS
The results suggest that orthodox medicine is not meeting the needs of some patients and that cam may wholly or partly substitute for conventional medicines. Most patients indicated their problem had improved with cam. Implications for future research are discussed.
Zusammenfassung HRI
Eine Erhebung unter 500 Patienten am Royal London Homeopathic Hospital (RLHH) zeigte, dass viele Patienten die Einnahme schulmedizinischer Medikamente nach einer homöopathischen Behandlung verringern oder diese sogar absetzen konnten.Der Grad der Besserung variierte in Abhängigkeit von der Diagnose. Beispielsweise berichteten 72 % der Patienten mit Hautbeschwerden, sie hätten ihre schulmedizinische Medikation absetzen oder senken können; bei Krebspatienten konnte die schulmedizinische Medikation nicht reduziert werden. Die Studie zeigte zudem, dass viele Patienten sich homöopathischen Therapien zuwenden, da sie Bedenken hinsichtlich der Sicherheit einer schulmedizinischen Behandlung haben.

Homeopathy
Volume 97, Issue 3, July 2008, Pages 114-121

Towards standard setting for patient-reported outcomes in the NHS homeopathic hospitals.

Thompson EA[1], Mathie RT, Baitson ES, Barron SJ, Berkovitz SR, Brands M, Fisher P, Kirby TM, Leckridge RW, Mercer SW, Nielsen HJ, Ratsey DH, Reilly D, Roniger H, Whitmarsh TE.
1 Bristol Homeopathic Hospital, Bristol, UK. elizabeth.thompson@ubht.nhs.uk
PMID: 18657769 DOI: 10.1016/j.homp.2008.06.005
Homeopathy. 2008 Jul;97(3):114-21. doi: 10.1016/j.homp.2008.06.005.

Abstract

INTRODUCTION
We report findings from a pilot data collection study within a programme of quality assurance, improvement and development across all five homeopathic hospitals in the UK National Health Service (NHS).

AIMS
(1)To pilot the collection of clinical data in the homeopathic hospital outpatient setting, recording patient-reported outcome since first appointment; (2) to sample the range of medical complaints that secondary-care doctors treat using homeopathy, and thus identify the nature and complexity of complaints most frequently treated nationally; (3) to present a cross section of outcome scores by appointment number, including that for the most frequently treated medical complaints; (4) to explore approaches to standard setting for homeopathic practice outcome in patients treated at the homeopathic hospitals.

METHODS
A total of 51 medical practitioners took part in data collection over a 4-week period. Consecutive patient appointments were recorded under the headings: (1) date of first appointment in the current series; (2) appointment number; (3) age of patient; (4) sex of patient; (5) main medical complaint being treated; (6) whether other main medical complaint(s); (7) patient-reported change in health, using Outcome Related to Impact on Daily Living (ORIDL) and its derivative, the ORIDL Profile Score (ORIDL-PS; range, -4 to +4, where a score <or=-2 or >or=+2 indicates an effect on the quality of a patient's daily life); (8) receipt of other complementary medicine for their main medical complaint.

RESULTS
The distribution of patient age was bimodal: main peak, 49 years; secondary peak, 6 years. Male:female ratio was 1:3.5. Data were recorded on a total of 1797 individual patients: 195 first appointments, 1602 follow-ups (FUs). Size of clinical service and proportion of patients who attended more than six visits varied between hospitals. A total of 235 different medical

complaints were reported. The 30 most commonly treated complaints were (in decreasing order of frequency): eczema; chronic fatigue syndrome (CFS); menopausal disorder; osteoarthritis; depression; breast cancer; rheumatoid arthritis; asthma; anxiety; irritable bowel syndrome; multiple sclerosis; psoriasis; allergy (unspecified); fibromyalgia; migraine; premenstrual syndrome; chronic rhinitis; headache; vitiligo; seasonal allergic rhinitis; chronic intractable pain; insomnia; ulcerative colitis; acne; psoriatic arthropathy; urticaria; ovarian cancer; attention-deficit hyperactivity disorder (ADHD); epilepsy; sinusitis. The proportion of patients with important co-morbidity was higher in those seen after visit 6 (56.9%) compared with those seen up to and including that point (40.7%; P<0.001). The proportion of FU patients reporting ORIDL-PS>or=+2 (improvement affecting daily living) increased overall with appointment number: 34.5% of patients at visit 2 and 59.3% of patients at visit 6, for example. Amongst the four most frequently treated complaints, the proportion of patients that reported ORIDL-PS>or=+2 at visit numbers greater than 6 varied between 59.3% (CFS) and 73.3% (menopausal disorder).

CONCLUSIONS
We have successfully piloted a process of national clinical data collection using patient-reported outcome in homeopathic hospital outpatients, identifying a wide range and complexity of medical complaints treated in that setting. After a series of homeopathy appointments, a high proportion of patients, often representing "effectiveness gaps" for conventional medical treatment, reported improvement in health affecting their daily living. These pilot findings are informing our developing programme of standard setting for homeopathic care in the hospital outpatient context.

Zusammenfassung HRI
Eine Beobachtungsstudie am Bristol Homeopathic Hospital umfasste mehr als 6.500 konsekutive Patienten mit über 23.000 Patientenbesuchen in einem Zeitraum von sechs Jahren. 70 % der nachuntersuchten Patienten berichteten, dass sich ihr Gesundheitszustand gebessert hätte; 50 % stuften die Besserung sogar als „deutlich" ein. Am ausgeprägtesten war dies bei kindlichem Ekzem oder Asthma sowie bei entzündlichen Darmerkrankungen, Reizdarm, Wechseljahresbeschwerden und Migräne.

Complementary Therapies in Medicine
Volume 13, Issue 2, June 2005, Pages 79-86

Outcome and costs of homoeopathic and conventional treatment strategies: a comparative cohort study in patients with chronic disorders.

Witt C, Keil T, Selim D, Roll S, Vance W, Wegscheider K, Willich SN.
Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, 10098 Berlin, Germany. claudia.witt@charite.de,
Complement Ther Med. 2005 Jun;13(2):79-86.
PMID: 16036164 DOI: 10.1016/j.ctim.2005.03.005

Abstract

OBJECTIVES
To evaluate the effectiveness of homoeopathy versus conventional treatment in routine care.

DESIGN
Comparative cohort study.

SETTING
Patients with selected chronic diagnoses were enrolled in medical practice.

INTERVENTIONS
Conventional treatment or homeopathy.

OUTCOME MEASURES
Severity of symptoms assessed by patients and physicians (visual rating scale, 0-10) at baseline, 6 and 12 months and costs.

RESULTS
The analyses of 493 patients (315 adults, 178 children) indicated greater improvement in patients' assessments after homoeopathic versus conventional treatment (adults: homeopathy from 5.7 to 3.2; conventional, 5.9-4.4; p=0.002; children from 5.1 to 2.6 and from 4.5 to 3.2). Physician assessments were also more favorable for children who had received homoeopathic treatment (4.6-2.0 and 3.9-2.7; p<0.001). Overall costs showed no significant differences between both treatment groups (adults, 2155 versus 2013, p=0.856; children, 1471 versus 786, p=0.137).

CONCLUSION
Patients seeking homoeopathic treatment had a better outcome overall compared with patients on conventional treatment, whereas total costs in both groups were similar.

Homeopathy
Volume 94, Issue 1, January 2005, Pages 10-16

Patients' assessments of the effectiveness of homeopathic care in Norway: a prospective observational multicentre outcome study.

Steinsbekk A[1], Lüdtke R.
Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway. aslak.steinsbekk@ntnu.no
Homeopathy, Volume 94, Issue 1, 2005, Pages 10-16,
https://doi.org/10.1016/j.homp.2004.11.016.OBJECTIVE

OBJECTIVE
To evaluate the patient reported effects of homeopathic care 6 months after first consultations.

METHODS
Prospective uncontrolled observational multicentre outcome study. All patients visiting 80 homeopaths all over Norway for the first time in eight different time periods from 1996 to 1998 were approached. Patients wrote down their main complaint and scored its impact on daily living on a 100 mm Visual Analogue Scale (VAS) at the first consultation. Six months later they were asked to score again. The homeopaths recorded treatments given for up to two follow-up consultations.

MAIN OUTCOME MEASURE
Predefined as a reduction of at least 10 mm in the VAS score between the first consultation and follow-up.

RESULT
Patients 1097 were recruited, 654 completed the follow-up questionnaire. The main complaint improved by at least 10mm on the VAS for 71% (95% confidence interval 67-74%) of patients. The average reduction was 32mm (95% CI 30-35 mm). Fifty-one per cent (95% CI 48-55%) of the patients had an improvement in their general well being of more than 10 mm. The mean reduction in the whole group was 14mm (95% CI 12-16 mm). The proportion of patients using conventional medication reduced from 39% to 16%. Regression analysis showed that lower age and higher baseline score were predictors of better outcome.

CONCLUSION
In this study, seven out of ten patients visiting a Norwegian homeopath reported a meaningful improvement in their main complaint 6 months after the initial consultation.

Veterinärmedizin und Homöopathie

Diarrhoe (E.coli) bei Ferkeln | Dairrhoea in Piglets

In einer randomisierten, Placebo-kontrollierten, doppelblinden Studie zur Anwendung der Homöopathie bei durch das Bakterium Escherichia coli hervorgerufenem Durchfall bei Ferkeln konnte bereits 2010 gezeigt werden, dass in der homöopathischen Gruppe signifikant weniger Ferkel an durch E. coli bedingtem Durchfall erkrankten (p < 0,0024; linear model) Zudem war der Schweregrad der Erkrankung geringer und der Durchfall, sofern er auftrat, von kürzerer Dauer.

ELSEVIER

Homeopathy

Volume 99, Issue 1, January 2010, Pages 57-62

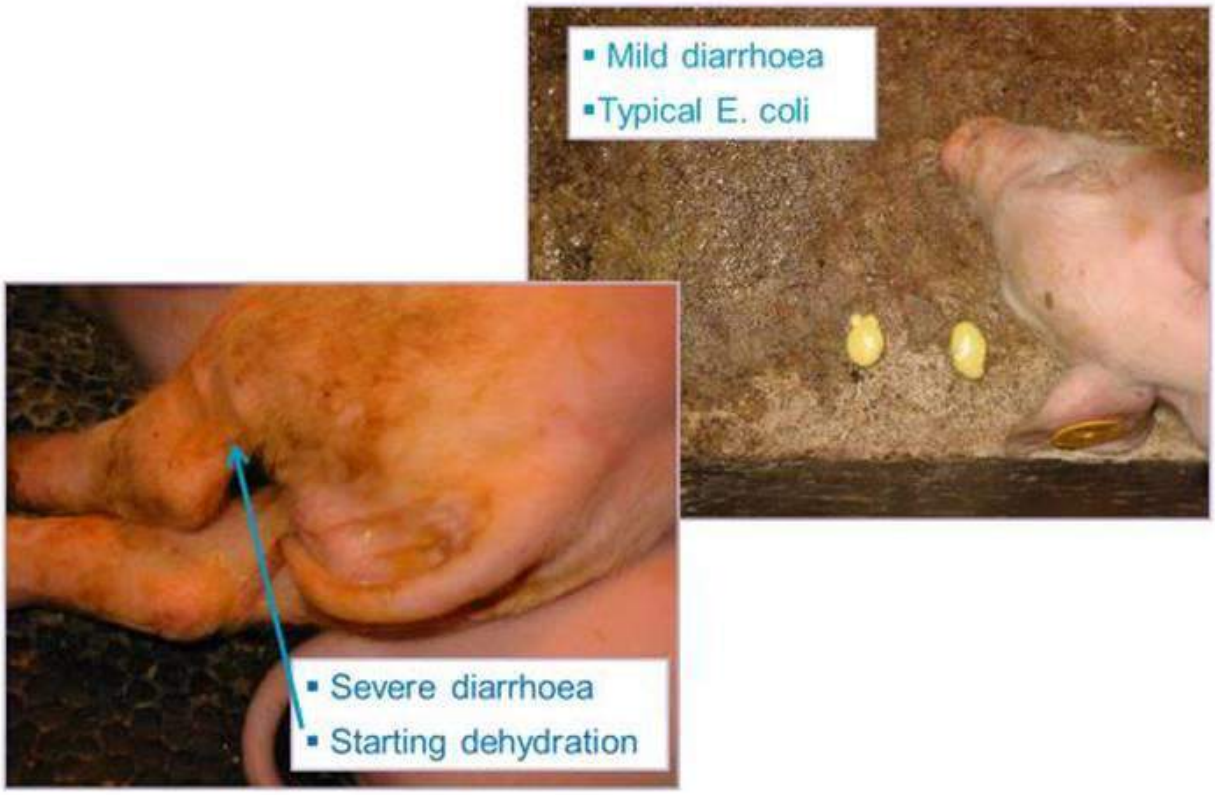
Camerlink I[1], Ellinger L, Bakker EJ, Lantinga EA.
Biological Farming Systems Group, Wageningen University, Droevendaalsesteeg 1, 6708 PB Wageningen, The Netherlands. Irene.Camarlink@wor.nl

Homeopathy as replacement to antibiotics in the case of Escherichia coli diarrhoea in neonatal piglets.

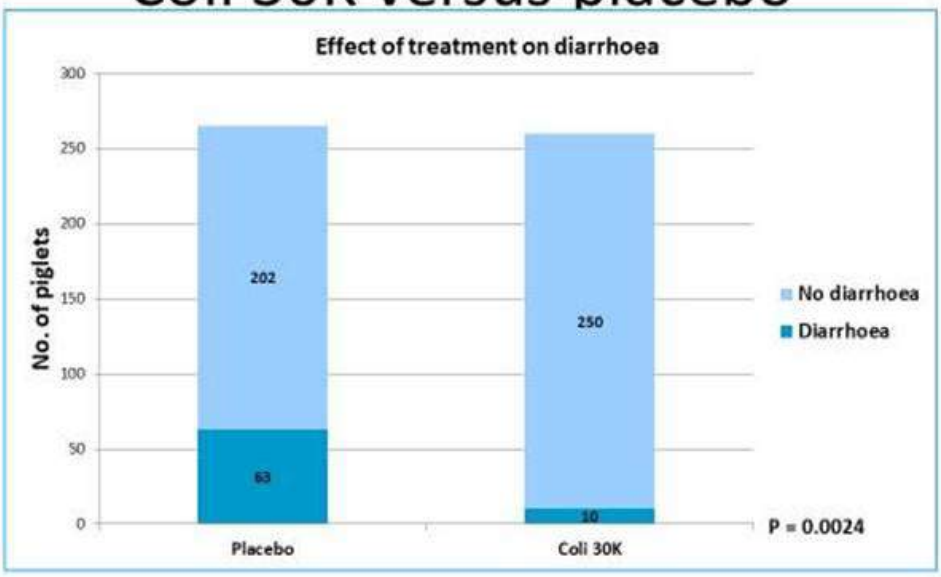
BACKGROUND
The use of antibiotics in the livestock sector is increasing to such an extent that it threatens negative consequences for human health, animal health and the environment. Homeopathy might be an alternative to antibiotics. It has therefore been tested in a randomised placebo-controlled trial to prevent Escherichia coli diarrhoea in neonatal piglets.

METHOD
On a commercial pig farm 52 sows of different parities, in their last month of gestation, were treated twice a week with either the homeopathic agent Coli 30K or placebo. The 525 piglets born from these sows were scored for occurrence and duration of diarrhoea.

RESULTS
Piglets of the homeopathic treated group had significantly less E. coli diarrhoea than piglets in the placebo group (P<0.0024). Especially piglets from first parity sows gave a good response to treatment with Coli 30K. The diarrhoea seemed to be less severe in the homeopathically treated litters, there was less transmission and duration appeared shorter.


▪ Mild diarrhoea
▪Typical E. coli
▪ Severe diarrhoea
▪ Starting dehydration

Coli 30K versus placebo



Complementary Medicine Research
Practice | Methods | Perspectives

Research Article / Originalarbeit

Complement Med Res 2019;26:174–181
DOI: 10.1159/000496031

Received: June 27, 2018
Accepted: December 4, 2018
Published online: 9. April 2019

Einfluss eines komplementärmedizinischen telefonischen Beratungssystems auf den Antibiotikaeinsatz bei Nutztieren in der Schweiz

Ariane Maeschli[a] Andreas Schmidt[b] Werner Ammann[c]
Priska Schurtenberger[d] Erika Maurer[e] Michael Walkenhorst[a]

[a] Forschungsinstitut für biologischen Landbau (FiBL), Frick, Schweiz; [b] Tierarztpraxis, Sirnach, Schweiz; [c] Ganterschwil, Schweiz; [d] Praxis für Tierhomöopathie, Nottwil, Schweiz; [e] Egg, Schweiz

Schlüsselwörter
Antibiotikareduktion · Komplementärmedizin · Nutztiergesundheit · Beratungsprogramm · Behandlungsinzidenz

Zusammenfassung

Hintergrund: Der Antibiotikaeinsatz bei Nutztieren fördert die Entwicklung antibiotikaresistenter Bakterien. Die Komplementärmedizin könnte einen Beitrag zur Reduktion von Antibiotika leisten, wird bisher jedoch nicht flächendeckend angeboten. Das Beratungsprogramm "Kometian" unterstützt teilnehmende Landwirte darin, ihre Tiere komplementärmedizinisch zu behandeln. ***Methoden und Resultate:*** 128 von 223 teilnehmenden Betrieben nutzten in den ersten 3 Projektjahren die telefonische Beratung von Kometian. Die Mehrheit der Landwirte hielt Milchkühe. Frühestens 1 Woche nach der Kometianberatung wurde eine telefonische Nachfrage beim Tierbesitzer hinsichtlich des Gesundheitszustandes des Tieres durchgeführt. Es konnten so 661 Beratungsfälle recherchiert werden. In 486 Fällen erfolgte keine weitere schulmedizinische Behandlung, in 373 Fällen gab der Landwirt einen Behandlungserfolg an. Von 188 angefragten und seit mindestens einem Jahr an Kometian teilnehmenden Betrieben stellten 46 ihre Behandlungsjournale zur Verfügung. Die betriebliche antibiotische Behandlungsinzidenz sank signifikant ($p < 0{,}001$) von 27 vor Beitritt auf 18 Behandlungen pro 100 Tiere im ersten Jahr. ***Schlussfolgerung:*** Es scheint, dass Kometian einen Beitrag dazu leisten konnte, den Antibiotikaeinsatz auf Betriebsebene zu reduzieren.

Influence of a Complementary and Alternative Medical Advisory Program by Telephone on the Use of Antibiotics in Livestock in Switzerland

Keywords
Reduction of antibiotics · Complementary and alternative medicine · Livestock health · Advisory program · Treatment incidence

Abstract

Background: A regular use of antibiotics in farm animals is assumed to induce antibiotic-resistant bacteria. Complementary and alternative medicine (CAM) may contribute to a reduction of antibiotic use but it is not extensively offered by Swiss veterinarians. The advisory program "Kometian" supports farmers in treating their animals with CAM. ***Methods and Results:*** 128 out of 223 participating farmers used the telephone consultations of Kometian in the first 3 years of the project. The majority of the farmers kept dairy cattle. No sooner than 1 week after such a consultation, the famer was questioned by phone about the health progress of the animal. Thus, the development of health could be verified in 661 cases (of 714). 486 cases were not treated further by conventional medicine; in 373 cases the farmer reported a positive treatment effect. Of 188 examined farms, which had participated in the advisory program for at least 1 year, 46 made their treatment records available. The incidence of antibi-

KARGER

E-Mail karger@karger.com
www.karger.com/cmr

Ariane Maeschli
Ackerstrasse 113, Postfach 219
CH–5070 Frick (Schweiz)
E-Mail ariane.maeschli@fibl.org

DE GRUYTER Open Agriculture. 2019; 4: 203–212

Research Article

Johanna Zeise*, Jürgen Fritz

Use and efficacy of homeopathy in prevention and treatment of bovine mastitis

https://doi.org/10.1515/opag-2019-0019
received September 28, 2018; accepted February 10, 2019

Abstract: Bovine mastitis is an important disease in dairy farming. As alternative therapy to antibiotics, whose use is seen as increasingly critical, farmer try to treat mastitis with homeopathy, for example. The present study examined i) whether homeopathic treatments for bovine mastitis can have positive treatment outcomes, ii) which treatments have been successful and under which conditions, iii) indications for future studies and applications for homeopathy to treat mastitis. 32 studies published to date have been evaluated. Assessment criteria and a rating score of 0 to 5 points were fixed for the appraisal. Healing and prophylaxis of mastitis were the primary focus to highlight the medication success and its framework for suitable mastitis therapy. The top eight studies of this quality ranking were subjected to differentiated evaluation. The selected studies showed a positive treatment outcome of homeopathy. Due to the homeopathic effect and the most used remedies in the selected studies, the medication should be chosen according to the homeopathic drug picture. With homeopathic drugs it was possible to reduce the antibiotic use by up to 75%. Some studies indicated that homeopathy might have a positive long-term effect. Furthermore, the results suggested a high self-healing ability in bovine mastitis.

Keywords: homeopathy, dairy cow, complementary veterinary medicine, antibiotics, clinical trials

***Corresponding author: Johanna Zeise,** University of Bonn, Agroecology and Organic Farming Group, Auf dem Hügel 6, 53121 Bonn, Germany, at present: University of Kassel, Faculty of organic agricultural sciences, Nordbahnhofstraße 1a, 37213 Witzenhausen, Germany, E-mail: johannazeise@web.de
Jürgen Fritz, University of Bonn, Agroecology and Organic Farming Group, Siegaue 16, 53773 Hennef, Germany

1 Introduction

Bovine mastitis is a common disease in dairy farming, which represents an economic, ecological and health problem (Kruif et al. 2007). Mastitis is an inflammation of the udder, which is divided into a subclinical and a clinical form. Subclinical mastitis is characterized by an increased content of somatic cells (>100,000 cells/ml) and/or pathogens in the milk. It is usually treated at the end of lactation with a combination of (long-term) antibiotics and internal teat sealer (antibiotic drying off) (DVG 2012; Wolter 2015; Molina et al. 2017). Clinical mastitis means the presence of local and general symptoms together with an increased cell count and pathogens in the milk (Winter 2009; DVG 2012). Depending on the severity of disease, clinical mastitis is treated by antibiotics either local or systemic (Hamann 2003; Tenhagen 2013). The antibiotic use is seen as increasingly critical because of the rising bacterial resistance (Wallmann 2016; Schulz-Stübner 2016). In organic and biodynamic farming, the use of antibiotics is restricted by legal requirements; therefore, the use of complementary medicine, for example homeopathy is supported (European Union 2008). Because of this, homeopathy is mainly used by ecological and biodynamic farmers in animal husbandry (León et al. 2006; Gordon et al. 2012).

Homeopathy is based on three principles: the similia principle, drug testing with healthy humans and dilution of doses, which were developed by the German doctor Samuel Hahnemann. According to Hahnemann's observations during drug testing, the simile is able to initiate a healing, which causes symptoms in the examination of healthy people, which are as similar as possible to the symptoms of the patient (*Similia similibus curentur*) (Braun 1995). Homeopathic remedies are potentiated drugs of components of plants or minerals for example, which effects are tested in drug trials on healthy people. These results are transferred to veterinary medicine, because there are rarely any homeopathic drug tests on animals (Ekert 2013). The preparation of homeopathic remedies consists of dilution and shaking or trituration of the active substance with a carrier

Metastudien und Reviews

Metastudien sollen Fragen zu einem ganzen Forschungsfeld ausleuchten.
Der Begriff Metaanalyse wurde 1976 von dem Psychologen Gene V. Glass[10] eingeführt: Er bezeichnete damit eine statistische Analyse einer großen Sammlung von Analyse-Ergebnissen mehrerer Einzelstudien, die er so zusammenführte.
Tatsächlich wurde die erste Metaanalyse jedoch bereits 1904 von Karl Pearson durchgeführt, der die *Teststärke* von Studien mit wenigen Probanden durch eine Zusammenfassung von mehreren kleinen Studien erhöhen wollte.

Eine Metaanalyse sollte ursprünglich folgendes gewährleisten:

1. **Die zusammenfassende Analyse einer großen Studienzahl zu einem Thema.**
2. **Die Erhöhung der Teststärke von kleinen Studien durch eine gemeinsame, zusammenfassende Analyse.**

Die Kritik an der Homöopathie in der wissenschaftlichen und öffentlichen Diskussion stützt sich im Wesentlichen auf eine einzige Studie von Shang et al., die 2005 im Fachjournal Lancet veröffentlicht wurde[11].
Bei ihrer Auswertung zur Studienlage vergleichen die Autoren je 110 Studien aus der konventionellen und homöopathischen Medizin. Tatsächlich werden davon allerdings nur 6 konventionelle und 8 homöopathische Studien in die vergleichende Bewertung beider Therapieformen eingeschlossen. Eine Unter-Auswahl von so wenigen Studien birgt in sich schon eine erhebliche Gefahr, dass Vorurteile – ‚Bias' der Autoren eine solche Auswahl verzerren. Die Autoren selbst legen die Kriterien dafür fest, welche Studien sie für die Vergleichsanalyse ‚zulassen' und welche nicht.

Anschließend unterziehen die Autoren diese 6 und 8 Studien zu völlig unterschiedlichen Krankheitsbildern einer Funnel-Plot Analyse. Dabei verletzen sie die wissenschaftlichen und mathematischen Mindestanforderungen für diese Methode. Siehe dazu die folgenden 4 Veröffentlichungen.

Außerdem wählen Shang und Kollegen als Referenzstudie für die Homöopathie im Funnel-Plot die größte Studie aus. Sie zeigt ein negatives Ergebnis. An ihr nahmen viele Probanden teil, die ohne jede Anamnese prophylaktisch vor einem Marathonlauf alle das gleiche Mittel einnahmen. Doch dieses Procedere entspricht keiner systematischen

[10] Gene V. Glass: *Primary, /** and Meta-Analysis of Research*. In: *Educational Researcher* 5, 1976, S. 3–8, doi:10.3102/0013189X005010003 JSTOR 1174772

[11] Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy.
Shang A, Huwiler-Müntener K, Nartey L, Jüni P, Dörig S, Sterne JA, Pewsner D, Egger M. Lancet. 2005 Aug 27-Sep 2;366(9487):726-32.

homöopathischen Verschreibung, sondern einem fachlich kaum begründbaren Konzept der Studienverantwortlichen, das sich klar außerhalb der Grundregeln einer systematischen homöopathischen Verordnung bewegt.

Dennoch wird die Shang Studie von den Verbänden der Homöopathie-Gegner und inzwischen selbst von Wissenschaftsjournalisten meist als einzige zitiert: Das angesehene Journal *Lancet* postulierte einst mit ihr das Ende, ja den Tod der Homöopathie. Die klar benannte wissenschaftliche Kritik renommierter Statistiker an einer solchen Anwendung der **Funnel-Plot Methode in Metaanalysen als potentiell stark vorurteilsfördernd** blieb bislang öffentlich unerwähnt.

Abschließend sei noch eine grundlegende Kritik an Metaanalysen als Methode in der evidenzbasierten Medizin erwähnt:
Einer der wichtigsten Begründer der modernen Epidemiologie Alvan R. Feinstein formulierte eine essentielle Kritik an der Technik jedweder Metaanalyse: Sie tauge nur bedingt als Quelle klinischer Evidenz, denn sie werde dem Problem der Heterogenität der Untersuchungsgegenstände nicht genügend gerecht. [12]

Unter der Überschrift „Evidence based medicine" wird im British Medical Journal bereits im folgenden Jahr auf die hohe Vorurteilsgefahr einer Funnel-Plot-Auswertung hingewiesen, wie sie in der Shang-Publikation angewandt wurde: In dem Artikel The case oft he misleading funnel plot fassen die Autoren ihre Analyse unter der Überschrift „Prevention of bias" wie folgt zusammen:
In conclusion, evidence based methods, including the funnel plot, should be evidence based. If treatment decisions are made on the basis of misleading methodological tests, the costs to patients and society could be high. Decisions guided by the easy assurance of a symmetrical funnel plot may overlook serious bias. Equally, it may be misleading to discredit and abandon valid evidence simply because of an asymmetrical funnel plot. The prevention of publication bias is much more desirable than any diagnostic or corrective analysis.

[12] Siehe dazu Heinrich Wilhelm Weßling: *Theorie der klinischen Evidenz.* LIT-Verlag, 2012, ISBN 978-3-643-90065-4, S. 138–147

Journal of Clinical Epidemiology
Volume 58, Issue 9, September 2005, Pages 894-901

In an empirical evaluation of the funnel plot, researchers could not visually identify publication bias.

J Clin Epidemiol. 2005 Sep;58(9):894-901.
Terrin N1, Schmid CH, Lau J.
Author information
Institute for Clinical Research and Health Policy Studies, Tufts-New England Medical Center, 750 Washington Street, Box 63, Boston, MA 02111, USA. nterrin@tufts-nemc.org

Abstract

BACKGROUND AND OBJECTIVE
Publication bias and related biases can lead to overly optimistic conclusions in systematic reviews. The funnel plot, which is frequently used to detect such biases, has not yet been subjected to empirical evaluation as a visual tool. We sought to determine whether researchers can correctly identify publication bias from visual inspection of funnel plots in typical-size systematic reviews.

METHODS
A questionnaire with funnel plots containing 10 studies each (the median number in medical meta-analyses) was completed by 41 medical researchers, including clinical research fellows in a meta-analysis class, faculty in clinical care research, and experienced systematic reviewers.

RESULTS
On average, participants correctly identified 52.5% (95% CI 50.6-54.4%) of the plots as being affected or unaffected by publication bias. The weighted mean percent correct, which adjusted for the fact that asymmetric plots are more likely to occur in the presence of publication bias, was also low (48.3 to 62.8%, depending on the presence or absence of publication bias and heterogeneous study effects).

CONCLUSION
Researchers who assess for publication bias using the funnel plot may be misled by its shape. Authors and readers of systematic reviews need to be aware of the limitations of the funnel plot.

The case of the misleading funnel plot

Evidence based medicine

The case of the misleading funnel plot

Joseph Lau, John P A Ioannidis, Norma Terrin, Christopher H Schmid, Ingram Olkin

Evidence based medicine insists on rigorous standards to appraise clinical interventions. Failure to apply the same rules to its own tools could be equally damaging

The advent of evidence based medicine has generated considerable interest in developing and applying methods that can improve the appraisal and synthesis of data from diverse studies. Some methods have become an integral part of systematic reviews and meta-analyses, with reviewers, editors, instructional handbooks, and guidelines encouraging their routine inclusion. However, the evidence for using these methods is sometimes lacking, as the reliance on funnel plots shows.

What is a funnel plot?

The funnel plot is a scatter plot of the component studies in a meta-analysis, with the treatment effect on the horizontal axis and some measure of weight, such as the inverse variance, the standard error, or the sample size, on the vertical axis. Light and Pillemer proposed in 1984: "If all studies come from a single underlying population, this graph should look like a funnel, with the effect sizes homing in on the true underlying value as n increases. [If there is publication bias] there should be a bite out of the funnel."[1] Many meta-analyses show funnel plots or perform various tests that examine whether there is asymmetry in the funnel plot and directly interpret the results as showing evidence for or against the presence of publication bias.

The plot's wide popularity followed an article published in the *BMJ* in 1997.[2] That pivotal article has already received over 800 citations (as of December 2005) in the Web of Science. With two exceptions, this is more citations than for any other paper published by the *BMJ* in the past decade. The authors were careful to state many reasons why funnel plot asymmetry may not necessarily reflect publication bias. However, apparently many readers did not go beyond the title of "Bias in meta-analysis detected by a simple, graphical test."

Details of BMJ systematic reviews mentioning funnel plots are on bmj.com

Institute for Clinical Research and Health Policy Studies, Tufts-New England Medical Center, Boston, MA 02111, USA
Joseph Lau *professor*
Norma Terrin *associate professor*
Christopher H Schmid *professor of medicine*
Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece
John P A Ioannidis *professor*

continued over

BMJ 2006;333:597–600

Authors' conclusion: Prevention of bias

In conclusion, evidence-based methods, including the funnel plot, should be evidence based. If treatment decisions are made on the basis of misleading methodological tests, the costs to patients and society could be high. Decisions guided by the easy assurance of a symmetrical funnel plot may overlook serious bias. Equally, it may be misleading to discredit and abandon valid evidence simply because of an asymmetrical funnel plot. The prevention of publication bias is much more desirable than any diagnostic or corrective analysis.

Evidence based medicine insists on rigorous standards to appraise clinical interventions. Failure to apply the same rules to its own tools could be equally damaging.

Diese empirisch hergeleitete Kritik an der Funnel-Plot Methode durch bedeutende Statistiker, setzt ein wichtiges wissenschaftliches Fragezeichen vor die nachfolgende Shang-Studie, deren Ergebnisse sich aus dieser Methode herleiten. Dennoch ist die Shang Studie in der Regel die einzige Studie, die von grundsätzlichen Gegnern der Homöopathie zitiert wird.

THE LANCET
Volume 366, Issue 9487, 27 August–2 September 2005, Pages 726-732

Shang A1, Huwiler-Müntener K, Nartey L, Jüni P, Dörig S, Sterne JA, Pewsner D, Egger M.
Department of Social and Preventive Medicine, University of Berne, Berne, Switzerland.
Lancet. 2005 Aug 27-Sep 2;366(9487):726-32.

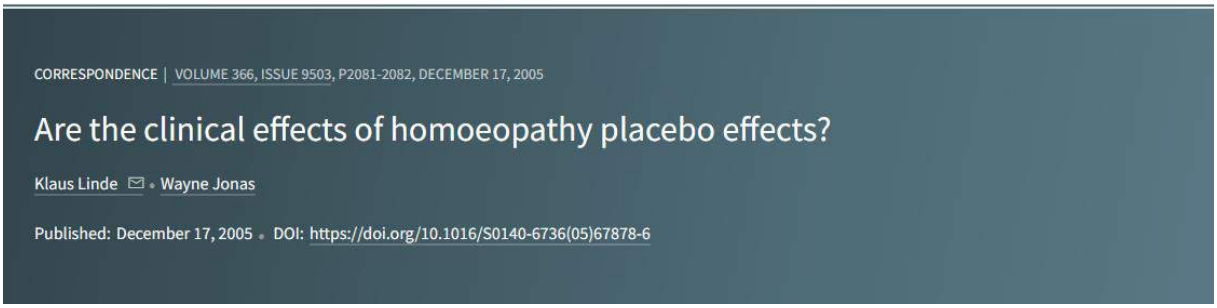
Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy.

BACKGROUND
Homoeopathy is widely used, but specific effects of homoeopathic remedies seem implausible. Bias in the conduct and reporting of trials is a possible explanation for positive findings of trials of both homoeopathy and conventional medicine. We analysed trials of homoeopathy and conventional medicine and estimated treatment effects in trials least likely to be affected by bias.

METHODS
Placebo-controlled trials of homoeopathy were identified by a comprehensive literature search, which covered 19 electronic databases, reference lists of relevant papers, and contacts with experts. Trials in conventional medicine matched to homoeopathy trials for disorder and type of outcome were randomly selected from the Cochrane Controlled Trials Register (issue 1, 2003). Data were extracted in duplicate and outcomes coded so that odds ratios below 1 indicated benefit. Trials described as double-blind, with adequate randomisation, were assumed to be of higher methodological quality. Bias effects were examined in funnel plots and meta-regression models.

FINDINGS
110 homoeopathy trials and 110 matched conventional-medicine trials were analysed. The median study size was 65 participants (range ten to 1573). 21 homoeopathy trials (19%) and nine (8%) conventional-medicine trials were of higher quality. In both groups, smaller trials and those of lower quality showed more beneficial treatment effects than larger and higher-quality trials. When the analysis was restricted to large trials of higher quality, the odds ratio was 0.88 (95% CI 0.65-1.19) for homoeopathy (eight trials) and 0.58 (0.39-0.85) for conventional medicine (six trials).

THE LANCET



CORRESPONDENCE | VOLUME 366, ISSUE 9503, P2081-2082, DECEMBER 17, 2005

Are the clinical effects of homoeopathy placebo effects?

Klaus Linde • Wayne Jonas

Published: December 17, 2005 • DOI: https://doi.org/10.1016/S0140-6736(05)67878-6

We congratulate Aijing Shang and colleagues on their meta-analysis examining the clinical effects of homoeopathy. Their methods largely reproduce those of our meta-analysis on the same topic published in *The Lancet* 8 years ago.

We agree that homoeopathy is highly implausible and that the evidence from placebo-controlled trials is not robust. However, there are major problems with the way Shang and colleagues present and discuss their results, as well as how *The Lancet* reviewed and interpreted this study. We will point out two.

First, Shang and colleagues do not follow accepted and published guidelines for reporting meta-analyses. In 1999, *The Lancet* published the QUORUM statement for improving the quality of reports of meta-analyses and the Cochrane Collaboration guidelines are listed in the instructions for authors. Shang and colleagues did not follow either of these guidelines, nor did *The Lancet* intervene. The QUORUM statement clearly requires that meta-analyses present “descriptive data for each trial” and “data needed to calculate effect sizes and confidence intervals”. Shang and colleagues do not report the trials excluded from the review, the quality assessments and odds ratios of all trials included in the review, nor which eight trials were included in the final meta-analysis. This lack of detail is unacceptable in a paper drawing a strong clinical conclusion.

Second, problems with pooling are not discussed. Pooling of data from clinical trials makes sense only if all the trials measure the same effect. In our 1997 meta-analysis, we justified the pooling of different interventions, conditions, and outcomes on the basis that, if homoeopathy is always a placebo, all trials measure, in principle, the same thing. There are major limitations associated with this assumption. If homoeopathy (or allopathy) works for some conditions and not for others (a statement for which there is some evidence), then interpretation of funnel plots and meta-regressions based on sample size is severely hampered. Since sample size is not independent of the disease, intervention, and outcome, it is impossible to separate the influence of bias from the true effect size by this method. Therefore, restricting an analysis to the largest studies risks producing a false-negative result. Furthermore, since the main analysis is based on only eight and six (probably unmatched) studies, the outcome could easily be due to chance, as is suggested by the large confidence intervals. Given these limitations, Shang and colleagues' conclusion that their findings “provide support to the notion that the clinical effects of homoeopathy are placebo effects” is a significant overstatement.

The Lancet should be embarrassed by the Editorial that accompanied the study. The conclusion that physicians should tell their patients that “homoeopathy has no benefit” and that “the time has passed for … further investment in research” is not backed at all by the data. Our 1997 meta-analysis has unfortunately been misused by homoeopaths as evidence that their therapy is proven. We now find it extremely disappointing that a major medical journal misuses a similar study in a totally uncritical and polemical manner. A subversive philosophy serves neither science nor patients.

We declare that we have no conflict of interest.

THE LANCET
Volume 350, Issue 9081, 20 September 1997, Pages 834-843

Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials.

Linde K[1], Clausius N, Ramirez G, Melchart D, Eitel F, Hedges LV, Jonas WB.
Lancet. 1997 Sep 20;350(9081):834-43. Erratum: Lancet 1998 Jan 17;351(9097):220.

BACKGROUND
Homeopathy seems scientifically implausible, but has widespread use. We aimed to assess whether the clinical effect reported in randomised controlled trials of homeopathic remedies is equivalent to that reported for placebo.

METHODS
We sought studies from computerised bibliographies and contracts with researchers, institutions, manufacturers, individual collectors, homeopathic conference proceedings, and books. We included all languages. Double-blind and/or randomised placebo-controlled trials of clinical conditions were considered. Our review of 185 trials identified 119 that met the inclusion criteria. 89 had adequate data for meta-analysis, and two sets of trial were used to assess reproducibility. Two reviewers assessed study quality with two scales and extracted data for information on clinical condition, homeopathy type, dilution, "remedy", population, and outcomes.

FINDINGS
The combined odds ratio for the 89 studies entered into the main meta-analysis was 2.45 (95% CI 2.05, 2.93) in favour of homeopathy. The odds ratio for the 26 good-quality studies was 1.66 (1.33, 2.08), and that corrected for publication bias was 1.78 (1.03, 3.10). Four studies on the effects of a single remedy on seasonal allergies had a pooled odds ratio for ocular symptoms at 4 weeks of 2.03 (1.51, 2.74). Five studies on postoperative ileus had a pooled mean effect-size-difference of -0.22 standard deviations (95% CI -0.36, -0.09) for flatus, and -0.18 SDs (-0.33, -0.03) for stool (both $p < 0.05$).

INTERPRETATION
The results of our meta-analysis are not compatible with the hypothesis that the clinical effects of homeopathy are completely due to placebo. However, we found insufficient evidence from these studies that homeopathy is clearly efficacious for any single clinical condition. Further research on homeopathy is warranted provided it is rigorous and systematic.

Mathie *et al. Systematic Reviews* 2014, **3**:142
http://www.systematicreviewsjournal.com/content/3/1/142

SYSTEMATIC REVIEWS

RESEARCH Open Access

Randomised placebo-controlled trials of individualised homeopathic treatment: systematic review and meta-analysis

Robert T Mathie[1*], Suzanne M Lloyd[2], Lynn A Legg[3], Jürgen Clausen[4], Sian Moss[5], Jonathan RT Davidson[6] and Ian Ford[2]

Abstract

Background: A rigorous and focused systematic review and meta-analysis of randomised controlled trials (RCTs) of individualised homeopathic treatment has not previously been undertaken. We tested the hypothesis that the outcome of an individualised homeopathic treatment approach using homeopathic medicines is distinguishable from that of placebos.

Methods: The review's methods, including literature search strategy, data extraction, assessment of risk of bias and statistical analysis, were strictly protocol-based. Judgment in seven assessment domains enabled a trial's risk of bias to be designated as low, unclear or high. A trial was judged to comprise 'reliable evidence' if its risk of bias was low or was unclear in one specified domain. 'Effect size' was reported as odds ratio (OR), with arithmetic transformation for continuous data carried out as required; OR > 1 signified an effect favouring homeopathy.

Results: Thirty-two eligible RCTs studied 24 different medical conditions in total. Twelve trials were classed 'uncertain risk of bias', three of which displayed relatively minor uncertainty and were designated reliable evidence; 20 trials were classed 'high risk of bias'. Twenty-two trials had extractable data and were subjected to meta-analysis; OR = 1.53 (95% confidence interval (CI) 1.22 to 1.91). For the three trials with reliable evidence, sensitivity analysis revealed OR = 1.98 (95% CI 1.16 to 3.38).

Conclusions: Medicines prescribed in individualised homeopathy may have small, specific treatment effects. Findings are consistent with sub-group data available in a previous 'global' systematic review. The low or unclear overall quality of the evidence prompts caution in interpreting the findings. New high-quality RCT research is necessary to enable more decisive interpretation.

Keywords: Individualised homeopathy, Meta-analysis, Randomised controlled trials, Systematic review

Background

The nature of the research evidence in homeopathy is a matter of ongoing scientific debate. Homeopathy's advocates tend to deny the worth of randomised controlled trials (RCTs) [1] or over-interpret their findings, whilst its critics dispute the therapy's scientific rationale and the existence of any positive findings in the research literature [2]. There is a need to temper these divergent opinions by considering the existing RCT evidence from an objective, rigorous and transparent assessment of the research, reflecting its particular nature and intrinsic methodological quality.

Five systematic reviews have examined the RCT research literature on homeopathy as a whole, including the broad spectrum of medical conditions that have been researched and by all forms of homeopathy: four of these 'global' systematic reviews reached the conclusion that, with important caveats [3], the homeopathic intervention probably differs from placebo [4-7]. By contrast, the most recent global systematic review, by Shang et al., concluded there was "weak evidence for a specific effect of homeopathic remedies...compatible with the notion

* Correspondence: rmathie@britishhomeopathic.org
[1]British Homeopathic Association, Luton, UK
Full list of author information is available at the end of the article

Forschende Komplementärmedizin
Wissenschaft · Praxis · Perspektiven

Review Article · Übersichtsarbeit

Forsch Komplementmed 2013;20:376–381
DOI: 10.1159/000355916

Published online: October 17, 2013

Homeopathy: Meta-Analyses of Pooled Clinical Data

Robert G. Hahn[a,b]

[a] Research Unit, Södertälje Hospital, Södertälje,
[b] Department of Anesthesiology, Linköping University, Linköping, Sweden

Keywords
Homeopathy · Study quality · Meta-analysis · Randomized controlled trials

Summary
In the first decade of the evidence-based era, which began in the mid-1990s, meta-analyses were used to scrutinize homeopathy for evidence of beneficial effects in medical conditions. In this review, meta-analyses including pooled data from placebo-controlled clinical trials of homeopathy and the aftermath in the form of debate articles were analyzed. In 1997 Klaus Linde and co-workers identified 89 clinical trials that showed an overall odds ratio of 2.45 in favor of homeopathy over placebo. There was a trend toward smaller benefit from studies of the highest quality, but the 10 trials with the highest Jadad score still showed homeopathy had a statistically significant effect. These results challenged academics to perform alternative analyses that, to demonstrate the lack of effect, relied on extensive exclusion of studies, often to the degree that conclusions were based on only 5–10% of the material, or on virtual data. The ultimate argument against homeopathy is the 'funnel plot' published by Aijing Shang's research group in 2005. However, the funnel plot is flawed when applied to a mixture of diseases, because studies with expected strong treatments effects are, for ethical reasons, powered lower than studies with expected weak or unclear treatment effects. To conclude that homeopathy lacks clinical effect, more than 90% of the available clinical trials had to be disregarded. Alternatively, flawed statistical methods had to be applied. Future meta-analyses should focus on the use of homeopathy in specific diseases or groups of diseases instead of pooling data from all clinical trials.

Schlüsselwörter
Homöopathie · Studienqualität · Metaanalyse · Randomisierte kontrollierte Studien

Zusammenfassung
Im ersten Jahrzehnt der evidenzbasierten Ära, die in der Mitte der 1990er Jahre begann, wurden Metaanalysen durchgeführt, um den Nachweis der Wirksamkeit von Homöopathie unter medizinischen Bedingungen zu prüfen. In diesem Beitrag wurden Metaanalysen einschließlich der gepoolten Daten aus Placebo-kontrollierten klinischen Homöopathie-Studien sowie entsprechende Debatten in Form von Artikeln untersucht, die infolge der Studien publiziert wurden. 1997 konnten Klaus Linde und Mitarbeiter 89 klinische Studien identifizieren, die insgesamt eine Odds Ratio von 2,45 zugunsten der Homöopathie gegenüber Placebo gezeigt hatten. Dabei zeigte sich ein Trend hinsichtlich einer geringeren Wirkung in Studien höchster Qualität; dennoch zeigten die 10 Studien, die den höchsten Jadad-Score aufwiesen, dass Homöopathie einen statistisch signifikanten Effekt hatte. Diese Ergebnisse forderten Akademiker heraus, alternative Analysen durchzuführen, die zum Zwecke des Nachweises einer mangelnden Wirkung von Homöopathie auf der Grundlage eines großflächigen Ausschlusses relevanter Studien durchgeführt wurden. Das Kernargument, das gegen die Homöopathie angeführt wurde, ist der «Funnel Plot», der 2005 von Aijing Shangs Forschungsgruppe veröffentlich wurde. Allerdings erweist sich er Funnel Plot als fehlerhaft, wenn er auf diverse Krankheiten angewendet wird, da Studien mit erwarteten starken Behandlungseffekten aus ethischen Gründen im Vergleich zu Studien, mit erwarteten schwachen oder unklaren Behandlungseffekten eine geringere Teststärke aufweisen. Um den Schluss ziehen zu können, dass Homöopathie einer klinischen Wirkung entbehrt, müssten 90% der vorhandenen klinischen Studien außer Acht gelassen werden. Alternativ müssten fehlerhafte statistische Methoden angewendet werden. Zukünftige Metaanalysen sollten den Einsatz von Homöopathie bei spezifischen Krankheiten oder Erkrankungsgruppen untersuchen, anstatt Daten aus allen klinischen Studien zu poolen.

KARGER
Fax +49 761 452 07 14
Information@Karger.com
www.karger.com

1661-4119/13/0205-0376$38.00/0

Accessible online at:
www.karger.com/fok

Robert G. Hahn M.D., Ph.D
Research Unit
Södertälje Hospital
152 86 Södertälje, Sweden
r.hahn@telia.com

Introduction

Homeopathy has a long tradition in European medicine but remains controversial due the unknown mechanism of action. Although the lack of such knowledge is not unique for treatments used in the clinic, the skepticism expressed by academic scientists in this case is fueled by the difficulty perceiving a biologically reasonable explanation for why homeopathy would be effective [1].

A new era in the dispute between believers and non-believers began in the mid-1990s when evidence-based medicine was first popularized. A mechanism of action no longer needed to be proved as long as it could be demonstrated statistically that the therapy was effective. What 'worked' could be shown with large randomized double-blind trials but, more commonly, by systematic reviews and meta-analyses.

Methodology

Evidence-based medicine initiated a decade of struggle between believers and non-believers in which meta-analyses were used as the tool of analysis. All of them were based on virtually the same material, but authors arrived at different conclusions. The aim of the present re-appraisal of this period was to scrutinize the arguments used and to illustrate what non-believers rely on to advocate abandoning homeopathy in the evidence-based era.

Results

Linde and Colleagues' Meta-Analysis

In 1997 Klaus Linde and co-workers in Munich received much attention after publishing a meta-analysis of homeopathy clinical trials in *The Lancet* [2]. The researchers had searched for homeopathy studies in a wide selection of databases. Out of 186 trials, the group identified 119 that were randomized placebo-controlled studies of clinical conditions. Of these studies, 89 provided data that were adequate for a meta-analysis.

When all data were pooled, the odds ratio and 95% confidence interval (CI) were 2.45 (2.05–2.93) in favor of homeopathy. After correction for publication bias, the odds ratio decreased to 1.78 (1.03–3.10). When only the 26 studies of highest quality were included, the benefit was somewhat weaker but still statistically significant, 1.66 (1.33–2.08).

The study by Linde and co-workers [2] demonstrated, with a likelihood of more than 95% CI, that homeopathy is overall a more effective remedy than placebo. The path was then opened for the unusual approach of pooling all published studies of one type of treatment regardless of disease and specific remedy used for the cure.

Study Quality

The earliest criticism of Linde et al.'s meta-analysis [2] focused on the fact that high-quality studies seemed to show weaker effects than studies of lower quality. In 1999, Linde's group re-assessed this issue [3]. They divided the studies into subgroups instead of using a weighting system to consider differences in quality. Naturally, the use of subgroups reduced the capacity of the available clinical trials to demonstrate differences between treatment and placebo.

The 89 clinical trials were grouped according to the Jadad score, which describes the quality of clinical trials on a scale ranging from 0 to 5. Linde et al. [3] found that the strength of a meta-analysis became gradually poorer when dealing with studies of higher quality, but the relationship was not linear; the 10 studies with the highest quality score (Jadad 5) had greater strength in favor of homeopathy than those with Jadad 3 (19 studies) and Jadad 4 (11 studies). For all 6 Jadad score levels, homeopathy was still statistically superior compared to placebo.

Linde et al. [3] also divided the studies into 12 subgroups according to the group's own Internal Validity Scale, in which the capacity to disclose statistically significant differences at each step was further reduced. Here, homeopathy was statistically superior to placebo at all quality levels except the highest, where 5 clinical trials yielded an odds ratio of 1.55 (0.77–3.10). However, the best estimate of the odds ratio did not differ from previous evaluations, and the lack of statistical significance is explained by the fact that the calculation is based on only a few studies.

In a subanalysis of 32 trials of individualized homeopathic treatment, Linde and Melchart [4] found an overall odds ratio of 1.62 (1.17–2.23) in favor of homeopathy. Based on the study with the best quality, the odds ratio was 1.12 (0.87–1.44), which is not statistically significant.

Edzard Ernst

Since 1997, attempts to invalidate Linde et al.'s [2–4] results have followed the path of excluding most of the clinical trials or, for various reasons, focused on smaller subgroups of studies. The first claim was made by the German-British physician Edzard Ernst, a former professor of complementary medicine in UK. In 1998, he selected 5 studies using highly diluted remedies from the original 89 and concluded that homeopathy has no effect [5].

In 2000, Ernst and Pittler [6] sought to invalidate the statistically significant superiority of homeopathy over placebo in the 10 studies with the highest Jadad score. The odds ratio, as presented by Linde et al. in 1999 [3], was 2.00 (1.37–2.91). The new argument was that the Jadad score and odds ratio in favor of homeopathy seemed to follow a straight line (in fact, it is asymptotic at both ends). Hence, Ernst and Pittler [6] claimed that the highest Jadad scores should theoretically show zero effect. This reasoning argued that the assumed data are more correct than the real data.

Two years later, Ernst [7] summarized the systematic reviews of homeopathy published in the wake of Linde's first meta-analysis [2]. To support the view that homeopathy lacks effect, Ernst cited his own publications from 1998 and 2000 [5, 6]. He also presented Linde's 2 follow-up reports [3, 4] as being further evidence that homeopathy equals placebo. Moreover, Ernst cited a book chapter [8] that will be commented upon later.

Cucherat and Colleagues

Another meta-analysis of pooled clinical data on homeopathy was authored by Cucherat et al. [9]. The group identified 118 randomized controlled clinical trials as being potentially evaluable, but excluded all except 17 (hence, 86% were disregarded). The most common reason for exclusion was that the primary end point was judged to be unclear. Prevention trials and those evaluating only biological effects were also excluded.

The patient outcomes were not pooled which is an uncommon approach in meta-analyses. Instead, the significance values (p) from the different studies were combined to arrive at an overall grand p. Out of 7 ways to combine such significance values the authors chose the one that was least prone to show a favorable outcome for homeopathy. The overall treatment effect in the 17 studies was still highly statistically significant in favor of homeopathy, $p < 0.000036$ (risk is less than 3.6 out of 100,000 that the difference can be explained by chance). The clarity of this result was diluted by the subsequent removal of studies according to quality. Not much strength was lost when studies were removed that were open instead of blinded. When the 9 studies included that were randomized and double-blinded but had lost less than 10% of patients on follow-up, the p value was still 0.0084 (risk is less than 8.4 out of 1,000 that the effect is due to chance). Finally, when only the significance values for the 5 studies with less than 5% loss during follow-up were pooled, the difference between homeopathy and placebo was only close enough to be statistically significant ($p = 0.082$, risk of 8.2 in 100 that the superiority of homeopathy over placebo is explained by chance). Cucherat et al. [9] remained skeptical about homeopathy although their data, even after most of the statistical power was removed by excluding 86% of the clinical trials, showed that the therapy is superior to placebo. Their impression was that the studies were of poor quality, a view not shared by others [2, 10]. Cucherat et al. [9] provided odds ratios along with the exclusion exercise, which is honest. However, the reasons for exclusion and the subsequent loss of analyzing power are unbalanced. For example, there is little reason to exclude half of the material (from 9 to 5 studies) just because the dropout incidence is reduced from <10 to <5%. In fact, a dropout incidence much higher than 10% would normally be acceptable in a clinical trial and can be handled by statistical methods.

Shang and Colleagues

The meta-analysis published by Shang et al. in 2005 [10] identified essentially the same set of clinical trials as Linde et al., although some recently published material was added. The purpose was to compare homeopathic remedies with conventional medical therapy, although the aftermath focused entirely on the clinical efficacy of homeopathy. The group identified 165 publications and excluded 60 for various reasons, one being that an appropriate match with a conventional medical treatment study could not be found. The authors also excluded cross-over studies. The final material consisted of 110 homeopathic trials and 110 using conventional medications.

No odds ratio was presented for the effect of homeopathy versus placebo in these 110 studies, although the authors mentioned that it was in favor of homeopathy. Instead, all except 21 studies were excluded, based on quality measures. Again, no statistics were provided. The authors then created a second set of exclusions, down to 8 studies, without clearly explaining why. Their final claim, after having disregarded 95% of the available clinical trials, was that the inverse odds ratio for homeopathy was 0.88 (0.65–1.19), which is not statistically significant. This means that the best estimate of the treatment effect is 1/0.88, i.e. homeopathy is 13% more effective than placebo.

Shang et al. [10] used the 'funnel plot' in the same way as the senior author (M. Egger) applied to Linde's work in a book chapter 4 years earlier [8]. This is a scatter plot of the odds ratios versus the standard errors for a group of studies. Small studies are more likely to be published when they show a positive result, while such publication bias is more unlikely to occur when a study sample is large. As larger studies usually have smaller standard errors, the overall 'true' odds ratio is the one indicated when the regression line in the funnel plot approaches a standard error of zero. This means that the positive results of smaller studies are disregarded as they are assumed to be balanced by negative outcomes in studies that never came to press. By relying on a funnel plot for interpretation, conclusions are based on the existence of data we believe exist, although we do not know for sure.

The funnel plot is a hopeless research tool when making conclusions about treatment effects in a mixed set of medical conditions, because studies are powered according to expected treatment effects. For example, new studies of homeopathy in allergic and rheumatic diseases cannot, for ethical reasons, include a large sample due to the positive effects reported in previous publications [7, 11, 12]. In contrast, studies of conditions where the treatment effect is expected to be low or uncertain have to have a larger sample to reach adequate 'power.' Therefore, when applied to a mixture of diseases, it is impossible to alter the shape of the funnel plot shown by Shang et al., regardless of how effective homeopathy might be in allergic and rheumatic diseases. Treatment effects will always be poorer in the largest studies if we power them according to previous works in the field.

These calculations made by Shang et al. [10] have been widely used by academics and skeptics as well as by the Editor of *The Lancet* to claim that homeopathy lacks clinical effect. A critical discussion about this conclusion followed in a later issue of the journal [13–15].

Discussion

Meta-Analysis as a Research Tool

Many researchers are skeptical to the placebo-controlled randomized clinical trial (RCT) as the optimal tool to evaluate methods in complementary medicine. The RCT provides highly valid information about the efficacy of clearly defined treatments but is poorly suited to evaluate the efficiency of more complex interventions [16]. However, one cannot disregard the fact that the placebo-controlled RCT and the subsequent pooling of data in the form of meta-analyses are highly ranked scientific methods in school medicine. Their results will continue to have a strong impact in society's opinion about the usefulness of complementary medicine. However, meta-analyses can arrive at different conclusions despite being based on virtually the same material. They are not performed according to strict methodology and are, to a variable extent, guided by creativity, interpretation, and personal bias. This is why everyone can find arguments for and against homeopathy in the meta-analyses of the pooled clinical data. The heterogeneity encourages critical reading including personal reflections about why the various authors have chosen to present their analysis in the way they do.

Extensive Exclusion of Data

Our considerations should include the fact that some studies rely on extensively excluding data. There must always be a sound balance between the scientific gain made by excluding studies and the limitations imposed by the associated loss of statistical power. Some of the works reviewed here, and in particular works by authors who are negative about homeopathy, reach their conclusions after having excluded 90–95% of the available trials. This is done with reference to quite small differences in quality, such as whether the dropout frequency is <10 or <5%, or with no reference at all. Little attention is given to the fact that the statistics then become based on much smaller groups of patients, which rapidly hampers the possibility of disclosing true differences between homeopathic and placebo treatments. Extensive exclusion exercises are normally excused by academic rigor but also constitute a tempting way for the non-believer to ruin any evidence there might be. The challenge for the researcher is to evaluate the available data and not to exclude virtually all of them. Studies of very poor quality and those that do not contain necessary data must always be excluded, but the remainder should be allowed to contribute to the conclusion, possibly after having been given graded importance depending on how well the studies have been conducted.

Another drawback of excluding a large number of studies is that the composition of the finally analyzed mix of conditions becomes very important to the conclusion. Here, one must remember that the overall conclusion made in these meta-analyses relates to the overall efficacy of a heterogeneous group of treatments for a heterogeneous group of diseases. One example of this problem is that the nonsignificant odds ratio for the effectiveness of homeopathy versus placebo presented by Shang et al. [10] seems to be due to a single study of muscle soreness in 400 long-distance runners [17]. Without this study, the result would have shown the statistically significant superiority of homeopathy over placebo. Moreover, Shang et al. [10] excluded all except 21 studies based on quality, and providing the results from all of them would have demonstrated the statistically significant benefit of homeopathy over placebo [13]. Why the number was further reduced from 21 to 8 was not explained beyond that the latter were 'large'. Critical readers suspect that the authors played around with the study selection until eventually they found the desired result. Strong conclusions made about the usefulness of homeopathy made in a previous report [7] and in public [14] could fuel such behavior.

In the following debate Shang's study was criticized for lack of transparency and the highly selected nature of the finally evaluated studies [13–15, 17].

Evidence versus Recommendation

Therapies should be evaluated in 2 steps. The first one is objective and summarizes the evidence for the efficacy of the therapy. The second step is to make recommendations for use. The clinical value of a treatment is then judged more subjectively with reference not only to evidence but also to scientific, ethical, economic, and practical perspectives.

Authorities often ask different persons to do these parts when formulating clinical recommendations or guidelines. The reason is that an objective evaluation of existing evidence should be carried out regardless of what the consequences might be. If the same individual performs both evaluations it is tempting to distort the evidence when other considerations disagree with the evidence. This author believes that overlap between these 2 roles has been common in the meta-analyses of the pooled clinical data about homeopathy. That is also why the conclusions are vastly different and the debate about the evidence contains a certain degree of emotion.

Distortion of the evidence is also common in society. The present review is based on a series of blog articles published in 2011 as a reaction to a summer campaign against homeopathy organized by skeptics in Sweden. One claim was that homeopathy is poorly studied. This is not true as the number of RCTs in this area is quite large. Many therapies used in clinical medicine are based on much less data. Another widespread argument, which was even adopted by politicians, is that not a single study on homeopathy shows a positive treatment effect. In reality, the majority of RCTs on homeopathy shows positive effects. A third claim was that the studies are of low quality, which does not receive support from researchers who have specifically evaluated this issue [2, 10]. A fourth point spread to newspapers by a professional academic was that the analyses by Ernst [7] and Shang et al. [10] demonstrate beyond a doubt that homeopathy is fraud and humbug. As we have seen, these publications represent a biased selection of the literature.

Ideology Plays a Part

The reader of this literature must be aware that ideology plays a part in these meta-analyses. For example, Ernst [7] makes conclusions based on assumed data [6] when the true data are at hand [3]. Ernst [7] invalidates a study by Jonas et al. [18] that shows an odds ratio of 2.19 (1.55–3.11) in favor of homeopathy for rheumatic conditions, using the notion that there are not sufficient data for the treatment of any specific condition [6]. However, his review deals with the overall efficacy of homeopathy and not with specific conditions. Ernst [7] still adds this statistically significant result in favor of homeopathy over placebo to his list of arguments of why homeopathy does not work. Such argumentation must be reviewed carefully before being accepted by the reader.

The most believable of the meta-analyses is still Linde et al.'s work from 1997 [2] along with the associated consideration of study quality [3] as the authors appear to maintain a reasonable balance between exclusion and statistical power. The follow-up analyses by Cucherat et al. [9] and Shang et al. [10] rest on such extensive exclusion of data that the conclusions are based on only a tiny fraction of the published studies. These meta-analyses are good examples of how the same data can yield results that are statistically in favor and not in favor of homeopathy, and having a negative result is most likely when making conclusions based on as little material as possible. Applying funnel plots to a heterogeneous mix of remedies and diseases is another example of playing around with data. If this approach is statistically correct, all further clinical trials would have to include the same number of patients regardless of the expected clinical effect. Alternatively, all treatments must exert the same effect. If not, the funnel plot is flawed.

The Way Forward

Meta-analyses of pooled data from the treatment of many conditions are difficult to interpret. From a clinical point of view, such analyses are warranted only if the same effect is measured [14]. They also provide many opportunities for those who strive to reach a predetermined conclusion to choose selectively. Further meta-analyses should focus on areas where homeopathy tends to be effective instead of diluting the results with data from diseases in which an effect is unlikely. Socioscientific issues are also relevant to discuss [19]. In the meantime, the issue continues to be a struggle between believers and non-believers, guided by plausibility bias [20].

Homeopathy is not a very strong remedy but seems to show better effects than placebo particularly in conditions that either are known or can be assumed to arise from the immunologic system. A guide was given in Linde et al.'s study [2] in which good clinical effects were to be found in allergic rhinitis, rheumatology, dermatology (except warts), and certain neurological disorders, such as seasickness and migraine. Benefit was more uncertain or absent in asthma, surgery, gastrointestinal disorders, anesthesiology, and gynecology [2].

As already stated, it can be argued that evidence-based approaches including the RCT are not the best forms of evaluating the efficacy of homeopathic remedies, as well as the efficiency of more complex interventions in complementary medicine. Traditional therapy might be a better comparator than placebo due to the fact that complementary therapies often show a large nonspecific effect ('efficacy paradox') [13, 16]. Recently, Mathie et al. [21] collected all current 263 high-standard RCTs of homeopathy in humans to enable future systematic reviews based on specific traits, such as the type of condition and whether placebo or other treatments serve as controls. Until alternative methods of evaluation have gained widespread acceptance, homeopaths have a lot to gain by aligning their therapeutic ambitions to the areas and treatments in which placebo-controlled studies have shown a better outcome than placebo. In reality, homeopathic treatments are usually individualized while most of the performed clinical trials are nonindividualized [13, 22]. Therefore, the practice is not evidence-based, regardless of the results of all the trials.

Conclusion

Clinical trials of homeopathic remedies show that they are most often superior to placebo. Researchers claiming the opposite rely on extensive invalidation of studies, adoption of virtual data, or on inappropriate statistical methods. Further work with meta-analyses should abandon the concept of summarizing all available clinical trials and focus on the effects of homeopathy versus placebo or other treatments in specific diseases or groups of diseases. One way to reduce future emotional-driven distortion of evidence by investigators and skeptics would be to separate the evidence-seeking process from the formulation of clinical guidelines more clearly.

Note

The author has never practiced, received, or studied homeopathy, but has worked in clinical medicine and performed traditional medical research in anesthesiology and surgery for the past 30 years.

Disclosure Statement

There was no financial support, thus there is no conflict of interest concerning this paper.

Rachel Roberts1 and Dr Alexander Tournier1
Homeopathy Research Institute, International House, 142 Cromwell Road, London SW7 4EF Correspondence: Rachel Roberts, rachelroberts@hri-research.org; Dr Alexander Tournier, alextournier@hri-research.org

The best studies show individualised homeopathic treatment has beneficial effects beyond placebo

Several systematic reviews and meta-analyses of homeopathy have been performed. However, none had looked solely at placebo-controlled trials of individualised homeopathic treatment as delivered by homeopaths in practice. The research team of Mathie et al. 1 have now performed such an analysis and found that homeopathic medicines, when prescribed during individualized treatment, are 1,5 – 2-timesmore likely to have a beneficial effect than placebo. Use of a rigorous and transparent methodology, including a sensitivity analysis, gives credibility to these findings, which fundamentally challenge claims that homeopathy is purely a placebo effect.

INTRODUCTION

To date, many of the systematic reviews of clinical studies on homeopathy have analysed studies on all forms of homeopathic treatment together, in an attempt to answer the general question, "Is homeopathy better than placebo?". However, homeopathy takes several forms. 'Individualised homeopathic treatment', consisting of a consultation plus personalised prescription, is considered to be usual care as provided by homeopaths in real world clinics. In contrast, 'non-individualised homeopathy' involves the same remedy being used by all patients, based on a clinical diagnosis only (e.g. over-the-counter homeopathic preparations containing multiple remedies for conditions such as hay fever or travel sickness). There is no reason to assume that different homeopathic treatment approaches are equally effective or ineffective. It is therefore not surprising that studies combining the results of all homeopathy trials, with little or no attempt to disentangle the different types of treatment involved, have led to some negative studies and reports2,3 and ensuing heated debate. In Mathie et al.'s study, placebo-controlled trials of individualised homeopathy have been analysed in isolation1, allowing us to explore the key question - do homeopathic medicines, when prescribed during individualised homeopathic treatment (IHT) have an effect beyond placebo?

META-ANALYSIS OF INDIVIDUALISED HOMEOPATHIC TREATMENT (IHT)

Mathie et al.identified 22 eligible clinical trials comparing Individualised Homeopathic Treatment (IHT) to placebo for a range of clinical conditions. To ensure that the results would be recognised by the wider academic world, Mathie's team used state-of-the-art methods for analysing a large body of clinical trial data, namely a systematic review and meta-analysis (see Definition box).

All 22 trials were assessed for quality using the wellrecognised Cochrane collaboration's assessment tool4 and given an overall "reliability" rating of A, B or C. Three of the 22 trials met the strict criteria set by Mathie et al. to be designated as the most "reliable" evidence (i.e. rated B1 and above); a meta-analysis of these three top trials found that IHT is more beneficial than placebo. It is important to note that this definition of "reliable" is more stringent than that used in previous meta-analyses of homeopathy performed by other groups (e.g. Shang et al 2). Also, this method of classifying study quality and "reliability" should not be misinterpreted as suggesting that the remaining 19 trials are not meaningful: rather, they are simply lower down the scale of relative reliability

KEY FINDINGS

Overall, IHT had a positive effect that was statistically different from placebo. Specifically, individually prescribed homeopathic medicines were found to be 1.5- to 2- times more likely to have a beneficial effect than placebo. The size of the treatment effect was measured by the 'Odds Ratio' (OR); if an OR is

greater than 1.0, the effect of the intervention is positive, and the greater the OR, the greater the size of that positive effect.

The treatment effect seen in the 3 trials designated as most "reliable" was calculated to be OR=1.98 (95% CI [1.16 - 3.38]; p = 0.013.) As these results were based on only 3 studies, Mathie et al. performed a 'sensitivity analysis' to check that they were robust i.e. the choice of trials analysed was changed in multiple ways according to their quality rating to see whether this caused the final result to alter (see Figure 1).

When analysing the 12 trials rated as B6 and above, the OR did not change significantly: OR=1.63 (95% CI [1.24 - 2.14]; p < 0.001) (Fig. 1. Remove C1.0 studies); and when all 22 trials were analysed together, regardless of quality, the result was again not significantly different: OR=1.53 (CI [1.22 - 1.91]; p < 0.001) (Fig. 1. All studies). This sensitivity analysis demonstrates that Mathie et al.'s findings are robust. It is also important to note that there is no evidence of larger treatment effects being found in lower-quality trials, contradicting the notion that only poor quality studies on homeopathy show positive results.

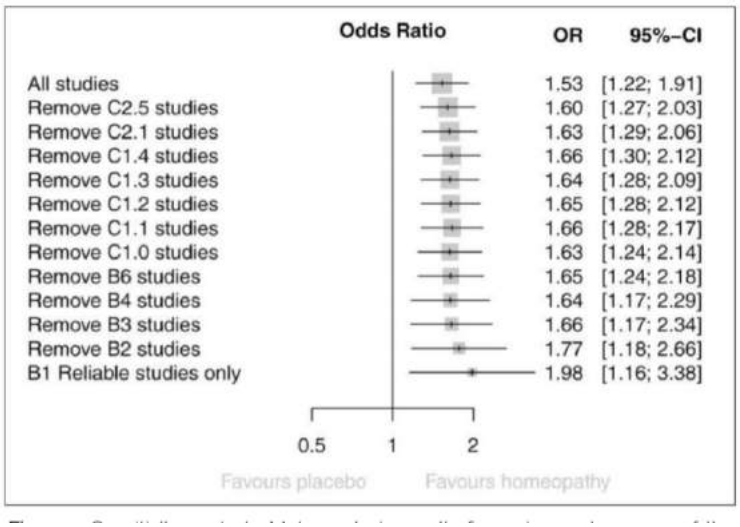


Figure 1: Sensitivity analysis. Meta-analysis results for various sub-groups of the 22 eligible trials. Each line represents a different sub-group of trials according to their quality/reliability rating (C2.5 being the lowest and B1 the highest). The top line ("All studies") represents the odds ratio (OR) results from all 22 studies pooled together. Successive lines from top to bottom represent the results after step-wise removal of trials with the next reliability rating. The bottom line ("B1 Reliable studies only") represents the results when analysing the three 'best' trials only. (Figure reproduced with permission from Mathie et al.1).

When testing the efficacy of IHT for several different clinical conditions, one might expect the results to vary depending on the condition being treated, making it more difficult to detect a specific effect when all conditions are pooled: interestingly this was not the case. Additionally, two of the three most "reliable" trials used homeopathic remedies that were diluted beyond the Avogadro limit, yet a significant specific effect was still detected. This is a striking finding considering that many detractors of homeopathy argue that this is either scientifically implausible or simply impossible.

While the effect of individually prescribed homeopathic medicines was greater than placebo, the clinical 'effect size' detected was "small". To put this into context, conventional drugs with a similar effect size include sumatripan for migraine, fluoxetine for major depressive disorder and cholinesterase inhibitors for dementia.

COMPARISON WITH OTHER STUDIES

Two previous systematic reviews of IHT have been performed. Ernst et al. (published in 1999) located 3 randomised controlled trials comparing IHT to conventional medicine and the low trial quality prevented any conclusions from being drawn7. In 1998 Linde et al's study looked at 32 trials of IHT versus placebo and found a positive, but unconvincing, trend. Mathie et al. added an extra level of significance to these previous systematic reviews performing a state-of-the-art meta-analysis.

When the meta-analysis of Mathie et al. is directly compared with perhaps the most often cited meta-analysis of "global" homeopathy performed by Shang et a l .2, which reached negative conclusions, key differences between the two studies become clear:

- the criteria for reliability of the clinical trials used by Mathie et al. were more stringent
- the trials used by Mathie et al. were more up-to-date (14 of the 22 trials identified were not included in Shang et al., published in 2005)
- the positive results of this study are based on trials which test individualised homeopathic care; Shang et al. final conclusion that homeopathy does not have an effect beyond placebo was beses only on trials of non-individualised homeopathy
- Mathie et al. performed a rigorous sensitivity analysis to confirm that despite basing their main conclusion on only 3 of 22 available studies, the findings are reliable. Shang et al. did not perform such an analysis on their data, but other authors have shown that their results (based on only 8 of 110 available studies) fail a rigorous sensitivity analysis and are therefore unreliable.

IMPACT OF THE STUDY

In summary, Mathie et al. have taken the three most reliable, high quality studies of individualised homeopathic treatment available and found that when the results are analysed together, the result is positive, showing a beneficial effect of homeopathic medicines beyond placebo. The input from two highly respected, independent biostatisticians from the University of Glasgow as co-authors gives further credibility to the findings.

Although the authors remain only cautiously optimistic about their findings, the meta-analysis by Mathie et al, is well constructed and methodologically sound, providing a strong argument in favour of the existence of specific effects beyond placebo in real-world homeopathic treatment. The results of this meta-analysis challenge the commonly repeated argument, 'the best studies show homeopathy doesn't work', and provide strong evidence that the opposite is actually correct, i.e. the best studies show homeopathy works.

Definition box

A **systematic review** is a highly structured scientific method used to locate, collate, critically assess and evaluate all research studies available that address a particular question. The highest quality evidence is then used to synthesise a final position and draw conclusions.

A **meta-analysis** is a statistical method used to assess overall trends in the combined data extracted from multiple individual studies identified through systematic review. A meta-analysis assigns a level of statistical significance to the combined results (i.e. how likely it is that the result is 'real' and not simply due to chance).

Grundlagenforschung

Die Grundlagenforschung zeigt einen klaren Trend:
Die Qualität der Grundlagenstudien nimmt seit der Jahrtausendwende deutlich zu - siehe den Review von Klein, Würtenberger, Wolf, Baumgartner und Tournier.
Ergebnis dieser Forschung sind klare Hinweise auf eine biologische oder physikalische Wirkung potenzierter, also sukzessive verdünnter und dabei verschüttelter Substanzen.
Diese beiden Schritte[13] - verschütteln und verdünnen - müssen offenbar kombiniert werden, da dann eine signifikante Wirkung in doppelblinden, placebokontrollierten Versuchen an Pflanzen, Tieren oder in Kristallisationsprozessen messbar wird.
Besonders interessante Ergebnisse zeigen die rein physikalischen Untersuchungen von potenzierten Substanzen durch Spektroskopie, in Kristallisationsprozessen, sowie in den NMR-Messungen potenzierter homöopathischer Substanzen von Demangeat.

Fazit

Die Qualität der klinischen Forschung und der Grundlagenforschung in der Homöopathie nimmt eindeutig zu. Sie zeigt in ganz verschiedenen hochwertigen Studien beim Menschen, aber auch bei Pflanzen und Tieren und in Kristallisationsprozessen eine signifikant erhöhte Wirkung gegenüber Placebo. Diese Forschung im Sinne der Bürger auszubauen, bedarf der ausreichenden Forschungs-Finanzierung. Nur so lassen sich schrittweise auch die Wirkmechanismen selbst erforschen.

Wichtig wird der wissenschaftliche Austausch mit anderen Forschungsfeldern

Alle medizinischen Wirkstoffe leisten einen Informationstransfer, sobald sie in Körpern wirken. Aber können nur Atome physikalisch-chemisch wirken? Dann müssten wir ab sofort GPS-Navigation und Smartphone abschalten, weil die Geräte mit der Information, die sie für uns abrufen und senden, kein Atom mit den zugehörigen Satelliten austauschen, sondern physikalische Felder generieren und nutzen. Gerade weil sie keine trägen Atome, sondern Feldwirkungen im Datentransfer einsetzen, sind sie so schnell und weitreichend.
In der Biologischen Forschung liefert die neu entstehende Quantenbiologie interessante Hinweise, dass in lebenden Organismen ebenfalls nicht atomare Prozesse[14] zum schnellen und weitreichenden Informationstransfer genutzt werden.

---

[13] Homeopathy (2017) 106, 47e54 _ 2016 The Faculty of Homeopathy. Published by Elsevier, Lucietta Betti,*, Grazia Trebbi, Maria Olga Kokornaczyk, Daniele Nani, Maurizio Peruzzi, Giovanni Dinelli, Paolo Bellavite, Maurizio Brizzi, Number of succussion strokes affects effectiveness of ultra-high-diluted arsenic on in vitro wheat germination and polycrystalline structures obtained by droplet evaporation method.

[14] - Klinman JP, Kohen A. 2013 Hydrogen tunneling links protein dynamics to enzyme catalysis. *Annu. Rev. Biochem.* 82, 471–496.
- Narth C, Gillet N, Cailliez F, Lévy B, de la Lande A. 2015 Electron transfer, decoherence, and protein dynamics: Insights from atomistic simulations. *Acc. Chem. Res.* 48, 1090–1097.
-Brookes JC, Hartoutsiou F, Horsfield AP, Stoneham AM. 2007 Could humans recognize odor by phonon assisted tunneling? *Phys. Rev. Lett.* 98, 38101.

Published online: 2019-08-27

14 Original Research Article

Homeopathic Potencies May Possess an Electric Field(-like) Component: Evidence from the Use of Encapsulated Solvatochromic Dyes

Steven J. Cartwright[1]

[1] DiagnOx Laboratory, Cherwell Innovation Centre, Upper Heyford, Oxon, United Kingdom

Homeopathy 2020;109:14–22.

Address for correspondence Steven J. Cartwright, PhD, DiagnOx Laboratory, Cherwell Innovation Centre, Upper Heyford, Oxon, OX25 5HD, United Kingdom
(e-mail: steven.cartwright@oxford-homeopathy.org.uk).

Abstract

Background Homeopathic potencies have been shown to interact with a range of solvatochromic dyes to produce spectroscopic changes in the visible region of the electromagnetic spectrum. Furthermore, the nature of the changes observed under different experimental conditions is beginning to limit the number of possible hypotheses that can be put forward regarding the fundamental identity of potencies.
Aims and Methods The present study uses β-cyclodextrins to encapsulate solvatochromic dyes of widely varying structures. The purpose of this approach is to de-couple the primary dye–potency interaction from any subsequent aggregation effects.
Results Despite large differences in molecular structure between dyes, results show that potencies affect all dyes according to the same fundamental principles. Specifically, positively and negatively solvatochromic dyes collectively respond in opposite and complementary ways to potencies in accordance with the differential stabilisation of their excited and ground electronic states. Under the conditions of encapsulation, positively solvatochromic dyes display a bathochromic shift of, on average, 0.4 nm with a 2% absorbance change, and negatively solvatochromic dyes display a hypsochromic shift of, on average, 0.2 nm with a 1% absorbance change. This behaviour is only ever seen in two situations—where solvent becomes more polar or where an electric field is applied to solutions of dyes.
Conclusions The conditions used in this and previous studies to investigate the interaction of potencies with solvatochromic dyes preclude increased polarity of solvent as being responsible for the observed effects and that an explanation in which potencies carry an electric field (or electric field-like) component is by far the more likely. From the magnitude of the spectral changes induced in the dye Brooker's merocyanine by *Arsenicum* 10M, an estimate of the strength of the postulated electric field of 1.16×10^7 V/m can be made, which is comparable with the potential difference across cell membranes.

Keywords
- solvatochromic dyes
- β-cyclodextrin
- *Arsenicum* 10M
- electric field
- metastable state

Introduction

Several studies have shown that homeopathic potencies interact with a large range of π-conjugated push-pull, or solvatochromic, molecular systems.[1–4] This interaction produces changes in the dyes' visible spectrum, which can be monitored over time and provides information about potencies at an existential level.

'What are homeopathic potencies?' and 'how do they act to produce clinical effects?' are probably the two most important questions that can be asked in the field of homeopathy. The

received
May 1, 2019
accepted after revision
May 30, 2019
published online
August 27, 2019

DOI https://doi.org/10.1055/s-0039-1693985.
ISSN 1475-4916.

THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 24, Number 5, 2018, pp. 409–421
Mary Ann Liebert, Inc.
DOI: 10.1089/acm.2017.0249

JACM

REVIEW ARTICLE

Physicochemical Investigations of Homeopathic Preparations: A Systematic Review and Bibliometric Analysis—Part 1

Sabine D. Klein, PhD,[1] Sandra Würtenberger, MSc,[2] Ursula Wolf, MD,[1] Stephan Baumgartner, PhD,[1,3,4] and Alexander Tournier, PhD[1,5]

Abstract

Objectives: The last systematic review of physicochemical research performed on homeopathic preparations was published in 2003. The aim of the study is to update and expand the current state of knowledge in the area of physicochemical properties of homeopathic preparations. In part 1 of the study, we aim to present an overview of the literature with respect to publication quality and methods used. In part 2, we aim to identify the most interesting experimental techniques. With this, we aim to be in a position to generate meaningful hypotheses regarding a possible mode of action of homeopathic preparations.

Methods: A two-step procedure was adopted: (1) an extensive literature search, followed by a bibliometric and quality analysis on the level of publications and (2) a thorough qualitative analysis of the individual physicochemical investigations found. In this publication, we report on step (1). We searched major scientific databases to find publications reporting physicochemical investigations of homeopathy from its origin to the end of 2015. Publications were assessed using a scoring scheme, the Manuscript Information Score (MIS). Information regarding country of origin of the research and experimental techniques used was extracted.

Results: We identified 183 publications (compared to 44 in the last review), 122 of which had an MIS ≥5. The rate of publication in the field was ~2 per year from the 1970s until 2000. Afterward, it increased to over 5.5 publications per year. The quality of publications was seen to increase sharply from 2000 onward, whereas before 2000, only 12 (13%) publications were rated as "high quality" (MIS ≥7.5); 44 (48%) publications were rated as "high quality" from 2000 onward. Countries with most publications were Germany ($n=42$, 23%), France ($n=29$, 16%), India ($n=27$, 15%), and Italy ($n=26$, 14%). Techniques most frequently used were electrical impedance (26%), analytical methods (20%), spectroscopy (20%), and nuclear magnetic resonance (19%).

Conclusions: Physicochemical research into homeopathic preparations is increasing both in terms of quantity and quality of the publications.

Keywords: systematic review, homeopathy, physics, very high dilutions, serially diluted and agitated solutions, ultrahigh aqueous dilutions

[1]Institute of Complementary Medicine, University of Bern, Bern, Switzerland.
[2]Scientific & Regulatory Affairs, Hevert-Arzneimittel GmbH & Co. KG, Nussbaum, Germany.
[3]Society for Cancer Research, Arlesheim, Switzerland.
[4]Institute of Integrative Medicine, University of Witten/Herdecke, Witten, Germany.
[5]Homeopathy Research Institute, London, United Kingdom.

THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 25, Number 9, 2019, pp. 890–901
Mary Ann Liebert, Inc.
DOI: 10.1089/acm.2019.0064

JACM

Physicochemical Investigations of Homeopathic Preparations: A Systematic Review and Bibliometric Analysis—Part 2

Alexander Tournier, PhD,[1,2] Sabine D. Klein, PhD,[1] Sandra Würtenberger, MSc,[3] Ursula Wolf, MD,[1] and Stephan Baumgartner, PhD[1,4,5]

Abstract

Objectives: In Part 1 of the review of physicochemical research performed on homeopathic preparations the authors identified relevant publications of sufficient reporting quality for further in-depth analysis. In this article, the authors analyze these publications to identify any empirical evidence for specific physicochemical properties of homeopathic preparations and to identify most promising experimental techniques for future studies.

Methods: After an update of the literature search up to 2018, the authors analyzed all publications in terms of individual experiments. They extracted information regarding methodological criteria such as blinding, randomization, statistics, controls, sample preparation, and replications, as well as regarding experimental design and measurement methods applied. Scores were developed to identify experimental techniques with most reliable outcomes.

Results: The publications analyzed described 203 experiments. Less than 25% used blinding and/or randomization, and about one third used adequate controls to identify specific effects of homeopathic preparations. The most promising techniques used so far are nuclear magnetic resonance (NMR) relaxation, optical spectroscopy, and electrical impedance measurements. In these three areas, several sets of replicated high-quality experiments provide evidence for specific physicochemical properties of homeopathic preparations.

Conclusions: The authors uncovered a number of promising experimental techniques that warrant replication to assess the reported physicochemical properties of homeopathic preparations compared with controls. They further discuss a range of experimental aspects that highlight the many factors that need to be taken into consideration when performing basic research into homeopathic potentization. For future experiments, the authors generally recommend using successed (vigorously shaken) controls, or comparing different homeopathic preparations with each other to reliably identify any specific physicochemical properties.

Keywords: physics, very high dilutions, serially diluted and agitated solutions, ultrahigh aqueous dilutions

Introduction

Homeopathy is a very popular complementary medicine worldwide.[1] Scientific interest into therapeutic efficacy of homeopathic remedies is reflected in the growing number of studies and meta-analyses in clinical research.[2] However, specific efficacy and the mode of action of homeopathic remedies—especially in high dilution—is still the subject of scientific debate.

A major challenge of homeopathic basic research is to decode any physicochemical mode of action. The aim of this review project was to contribute to this effort through a

[1]Institute of Complementary and Integrative Medicine, Faculty of Medicine, University of Bern, Bern, Switzerland.
[2]Water Research Lab, Heidelberg, Germany.
[3]Scientific and Regulatory Affairs, Hevert-Arzneimittel GmbH & Co. KG, Nussbaum, Germany.
[4]Society for Cancer Research, Arlesheim, Switzerland.
[5]Institute of Integrative Medicine, Faculty of Health, University of Witten/Herdecke, Witten, Germany.

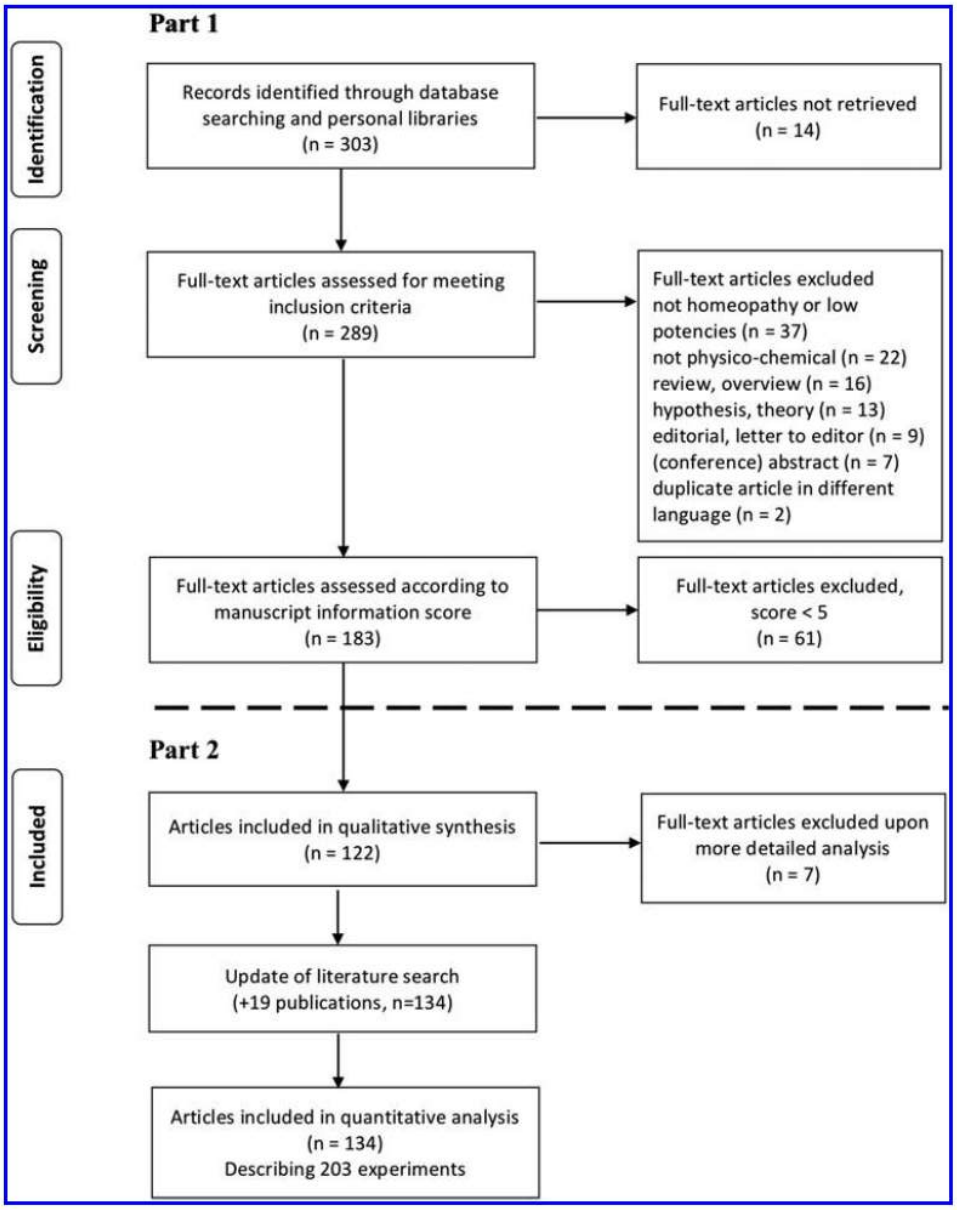


FIG. 1. PRISMA flow diagram describing the process of paper inclusion through Part 1 and Part 2 of the review to arrive at the 203 experiments being described. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

generally that the effects of homeopathy are the result of as yet unknown water characteristic, only 24% of experiments used ultrapure water as the medium for the dilution/succussion process. Most experiments (35%) used ethanol at different concentrations. Of interest, 20% of experiments used specifically prepared water-based mediums such as solutions of sodium bicarbonate, silicic acid, sodium chloride, and lithium chloride.

TABLE 1. PHYSICOCHEMICAL EXPERIMENTS REPORTING DIFFERENCES BETWEEN HOMEOPATHIC PREPARATIONS AND CONTROLS

Findings	*Count*	*%*
Differences reported	147	72
No differences reported	35	17
Mixed results	2	1
NA	19	9

A total of 192 different substances were investigated. The most used potentized substance was *Natrium muriaticum* (sodium chloride), followed by 2.4-dichlorophenoxyacetic acid, *Arnica montana*, sulfur, *Nux vomica*, and *Silicea* (Table 4).

The most frequently used measurement techniques were electrical impedance, spectroscopy followed by nuclear magnetic resonance (NMR) (Table 5). From the breakdown per method we see that blinding and randomization was used most often in NMR, although still less than half of the experiments used them. Use of inferential statistics was generally low except for NMR where they were used often (77%). In terms of the use of succussed controls, these were used less than half of the time except for NMR (63%). The use of independent production lots was generally very low except for NMR (33%) and chromatography (100%). According to the methodological score applied (MFI score, see Materials and Methods section), NMR comes out as the method with the most reliable empirical evidence for specific properties of homeopathic preparations

TABLE 2. CONTROLS, BIAS PREVENTION AND STATISTICS USED IN PHYSICOCHEMICAL EXPERIMENTS

	Count	*%*
Controls[a]		
Potentized medium	57	28
Succussed medium	18	9
Dilution without succussion	24	12
Unsuccussed medium	109	54
Other	50	25
Unknown	15	7
Blinding		
Yes	46	23
No	22	11
Not described	135	67
Randomization		
Yes	43	21
No	20	10
Not described	140	69
Independent production lots		
Unique production lot	43	21
Multiple production lots	31	15
Unknown	129	64
Statistics		
Inferential	56	28
Descriptive	27	13
None	120	59

Types of controls used in experiments, and information on whether sample blinding and randomization was used, whether experiments used independent production lots (i.e., how many times the homeopathic preparations were produced from the original substance) and whether statistics were used and what type.
[a]Experiments often used several controls.

(MFI score of 15.8), followed by spectroscopy techniques (MFI score of 10.2), analytical methods (6.2), and electrical impedance (MFI score of 6.0).

If we look at the best experiments, defined as those that used blinding, randomization, and inferential statistics, we find overall 24 experiments, of which 79% reported differences between homeopathic preparations and controls (Table 6). Of those, 10 fulfilled a further two methodological criteria (use of succussed controls and use of independent lot production), 80% of which reported differences between homeopathic preparations and controls.

Replications

For the purposes of this review, we define a replication as an experiment that used the same investigative technique to measure the same physicochemical properties of homeopathic potencies made of the same substances. Note that this is different from a reproduction where the same instrument and potencies would have to be used, along with the same statistical analysis, experiment protocol, and materials.

We extracted the replication data for all research techniques. The data tables summarizing these replications for each of the 11 experimental methods are given in the Supplementary Tables S1–S11. A synthesis of the replication data is given in Table 7. To score the different replications, we defined the Experimental Replication (ER) score as the number of replications times the average methodological score of these replications times the percentage of experiments reporting differences. This score enables to determine

TABLE 3. HOMEOPATHIC SAMPLE PREPARATION

	Count	*%*
Potentizing method		
Multiple tube (Hahnemann)	124	61
Single tube (Korsakov)	11	5
Mixed	25	12
Unknown	43	21
Succussion method		
Hand	56	28
Machine	81	40
Mixed	10	5
Unknown	56	28
Production		
Self-made	119	59
Specific external	40	20
Off the shelf	27	13
Mixed	17	8
Potencies		
<12c, 24x	17	8
≥12c, 24x	42	21
Mixed	141	69
Unknown	3	1
Composition of potentization medium		
Ethanol high concentration (>50%)	56	28
Ethanol low concentration	15	7
Ultrapure water	49	24
Water-based inorganic solutions	40	20
Mixed	13	6
D_2O	3	1
Unknown	27	13

Methods that were employed in the production of the samples: potentizing method (multiple- or single-vessel method), succussion method (hand, machine), production location (in-house or outsourced), and dilution level (below or above the inverse Avogadro number, i.e., whether any of the original substance could be expected to remain in the sample).

TABLE 4. SUBSTANCES POTENTIZED MOST USED IN EXPERIMENTS

Remedies	*Usage*
Natrium muriaticum	28
2,4-dichlorophenoxyacetic acid	24
Arnica montana	24
Sulfur	21
Nux vomica	17
Silicea	15
Argentum nitricum	12
Arsenicum album	12
Argentum metallicum	11
Cuprum sulfuricum	10
Magnesium muriaticum	10
Arsenicum sulphuratum rubrum	9
Plumbum nitricum	7
Aurum muriaticum	7
Lycopodium clavatum	6
Aurum metallicum	6
Zincum metallicum	6
Histaminum	5
Zincum oxidatum	5
Alcoholus (ethanol)	5
Bryonia	5

Usage in number of experiments.

TABLE 5. EXPERIMENTAL METHODS USED

Methods	*Count*	*Blinding (%)*	*Randomization (%)*	*Statistics (%)*	*Successed controls (%)*	*Independent production lots (%)*	*MFI score*	*Differences reported (%)*
NMR	30	40	50	77	63	33	15.8	73
Spectroscopy	39	31	21	31	38	10	10.2	79
Analytical methods[a]	22	27	32	14	45	23	6.2	18
Electrical impedance	41	12	12	12	22	15	6.0	80
Imaging methods	16	25	25	38	50	6	4.6	69
Surface tension/ various physical	9	33	22	22	56	11	2.6	56
Luminescence	11	18	18	27	36	9	2.4	100
Calorimetry	16	0	0	13	13	0	0.8	94
Raman spectroscopy	7	29	0	0	29	0	0.8	86
Chromatography	3	0	0	0	0	100	0.6	100
Electrochemistry	9	0	0	0	11	0	0.2	89

Ordered by MFI score (see the Materials and Methods section). Count, number of experiments per method. Blinding, randomization, inferential statistics, successed controls, and independent production lots, frequency of use. Differences between homeopathic preparations and controls as reported in publication: frequency.

[a]The low level of reported differences in the Analytical Methods group is because of the fact that many experiments used analytical methods to control sample purity, not as a technique to compare samples.

MFI, Methodological and Frequency of Investigation.

which replications have most reliably reported differences between homeopathic preparations and controls and should therefore be replicated further to confirm (or not) their results.

We see that the seven replications investigating T1 and T2 NMR relaxation times of potentized silica have high methodological scores and that all seven experiments reported differences between homeopathic preparations and controls, leading to a high ER score of 31.0. Similarly, NMR relaxation time investigations of potentized histamine have a high score of 17.0 with 5/5 replications reporting differences.

In spectroscopy, we have two sets of ultraviolet (UV) measurements (*Cuprum sulfuricum*, sulfur potencies) with high ER scores. In electrical impedance, the two replications of the REDEM experiments (black box measurements) stand out as having high methodological scores, and both replication lines reported differences between homeopathic preparations and controls leading to a decent ER. We also see the three studies of thermoluminescence using homeopathic preparations of *Lithium muriaticum*.

Discussion

Appropriate controls for potentized preparations

A major question that came up during this review is how to define the most appropriate controls for homeopathic preparations in physicochemical measurements. We can distinguish two main classes of controls: (1) plain (unsuccussed) solvent or diluted (but not succussed) homeopathic samples and (2) potentized or succussed (vigorously shaken) solvent. It is quite evident that succussion of a fluid in ambient air leads to a number of effects such as formation of air bubbles of different size with differential lifetimes, increased dissolution of air components (N_2, O_2, CO_2) in the fluid, increased dissolution of potentization vessel wall material (Si, B, Na, K etc.), and maybe cavitation effects.[144] These processes may lead to further consequences such as increased oxidative processes (because of O_2 dissolution), changes in pH (because of CO_2 dissolution and acid formation), changes in nuclear magnetic relaxation (O_2 as relaxation agent), increased silica-hydrogel formation (because of

TABLE 6. HIGH-QUALITY EXPERIMENTS

Method	*Experiments fulfilling three criteria*	*Reported differences (%)*	*Experiments fulfilling five criteria*	*Reported differences (%)*
NMR	10	90	6	100
Spectroscopy	7	86	1	100
Imaging methods	4	75	1	0
Analytical methods	2	0	0	—
Surface tension/various physical	2	100	2	50
Electrical impedance	2	50	0	—
Luminescence	2	100	0	—
Grand total	29	79	10	80

Number of experiments fulfilling three quality criteria (blinding, randomization, and inferential statistics) along with percentage of experiments reporting differences, number of experiments fulfilling an additional two quality criteria (successed controls and independent series production) along with corresponding percentages of experiments reporting differences.

NMR, nuclear magnetic resonance.

TABLE 7. REPLICATED EXPERIMENTS

Technique	*Replication series*	*No. of replications*	*Average MFI score*	*No. of reported differences (%)*	*ER score*
NMR	T1, T2: *Silicea*	7	4.4	100	31.0
NMR	T1, T2: Histamine	5	3.4	100	17.0
Spectroscopy	UV: Sulfur	4	4.0	100	16.0
Spectroscopy	UV: *Cuprum sulfuricum*	3	4.3	100	13.0
NMR	T1, T2: Sulfur	9	2.1	44	8.4
Electrical impedance	REDEM: *Argentum nitricum*	2	4	100	8.0
Electrical impedance	REDEM: *Aurum*	2	4	100	8.0
NMR	T1, T2: *Nux vomica*	3	2.3	100	7.0
Luminescence	Thermo: *Lithium muriaticum*	3	2.0	100	6.0
Imaging methods	GDV: *Natrium muriaticum*	2	2.5	100	5.0
Spectroscopy	UV: *Aconitum napellus*	3	1.7	100	5.0

Number of replications of a given experiment, showing average methodological (MFI) score of experiments within a replication, how often differences between homeopathic preparations and controls were reported and associated ER score. Replications with ER score ≥5 sorted according to ER score.

ER, Experimental replication; GDV, gas discharge visualization; MFI, Methodological and Frequency of Investigation; NMR, nuclear magnetic resonance; UV, ultraviolet.

increased Si dissolution), radical formation (because of cavitation), and potentially other effects.

When investigating the hypothesis that potentization of a given material leads to remedies with specific effects, it is evident that any such specific effects have to be different from pure succussion effects that are unspecific in the sense that they are not related to the substance potentized. From this point of view, only succussed or potentized controls are valid controls for demonstrating any evidence for specific (remedy-related) properties of potentized preparations.

Considering the hypothesis that succussion leads to some information transfer of the substance potentized to the potentization medium, the question arises what happens when pure medium is potentized as control sample (e.g., potentized water). One could speculate that the potentization process is amplifying some random information. This would lead to a situation where samples with specific information (homeopathic preparations) would be compared with samples with random information (potentized water as control). In this sense potentized medium (and by extension succussed medium too) might not to be the best controls possible as they could introduce a random element.

On the contrary, one can argue that it would not be wise to compare homeopathic preparations with each other in case the measurement method used is not able to distinguish the putative homeopathic structures. Because the nature of the homeopathic structures is not known yet, it cannot be decided at present if a given measurement method is able or not to distinguish the presumed structures.

We therefore recommend in future investigations the use of two types of controls: (1) potentized solvent and (2) other homeopathic preparation(s). The use of several homeopathic samples increases the probability to identify different structures. Furthermore, if possible, we recommend the additional use of (3) unsuccussed and (4) succussed control samples that would allow determining the effect of pure succussion. A study of the effect of succussion on the observed physicochemical activities would be a welcome endeavor as it is currently lacking, in particular investigating the effect of the number of succussions would be very interesting. Such a study would complement the work by Betti et al., which used wheat germination assays and the droplet evaporation method to explore this topic, showing a sigmoidal type behavior as a function of the number of succussions.[145]

As mentioned previously, certain experimental methods might be more suitable to investigating the presence/absence of such structures rather than distinguishing between such structures. The issue here is in conceiving appropriate controls that would not suffer from confounding factors such as gas dissolution for example. Such an approach is being pioneered by the group of Prof. Elia in their conductivity measurement experiments; they used trace analytics methods to levels of sodium in their samples and are thereby able to calculate the theoretical conductivity of the sample (sodium being the most relevant element for conductivity in their setup) to obtain the so-called "excess conductivity" as the difference between the measured conductivity and the theoretical prediction. This technique is interesting as in principle it probes directly for the presence of structures with unexplained properties (here in terms of conductivity). However, the technique does not currently control for other elements and gases originating from the succussion process that could also play a role.

Bias prevention and statistics

Most of the studies neither used blinding nor randomization. This is not entirely unusual in physicochemical research where one usually does not expect experimenter effects. Most of conventional research does not invoke blinding on such experiments for that very reason. Giving the history and heated debate surrounding homeopathy, we recommend implementing blinding and randomization protocols in future investigations to ensure that experimenters do not have any effect on the results.

Rather worrying is the lack of use of proper statistical tools. Part of the problem here is that many of the studies are quite dated and statistical tools were often not used at that time. Another effect is that many experiments such as in spectroscopy have been rather descriptive and therefore did

not use statistical tools. Now, again given the controversy in the field, there is a great need for proper statistical methods to be implemented, so as to quantify the degree of uncertainty in the results and to avoid Type I and Type II errors.

We recommend the implementation of systematic negative control (SNC) experiments on a regular basis. SNC experiments are full experiments with identical design and evaluation as experiments with homeopathic preparations, but all samples are either from the same source material (e.g., plain potentization medium) or consist of potentized medium, prepared analogously as the homeopathic samples.[146] Depending on the design of the experiments, systematic positive control (SPC) experiments may also be a valid approach, consisting of the same sample (either a positive control or a homeopathic preparation), independently prepared in the number of samples assessed in the "true" experiments. SNC and SPC experiments are excellent scientific tools to evaluate the stability of a given experimental system, to identify any systematic error, and to assess applicability of statistical models. In this review, only one investigation implemented SNC experiments.[97]

Another aspect that needs to be addressed in the future is the inherent variability present in physicochemical studies of homeopathic remedies. It is quite clear that there is a high degree of variability in the experimental measurements,[139] which cannot be solely attributed to instrumental error and are because of the high variability inherent in water itself.[147] SNC and SPC experiments are well suited to address these issues. In addition, adapted statistical models may be necessary to address variability in itself.

Most promising techniques

Looking at the results gathered in this review a number of experiments emerge as deserving further replication and exploration. First of all, NMR relaxation studies of potentized silica and histamine preparations have shown the most methodological rigor and the most promising results, demonstrating the ability to distinguish between potentized silica or histamine, and potentized controls. Of interest, potentized sulfur seems to be harder to distinguish from corresponding controls.

Based on the available data, UV spectroscopy seems to be the second most interesting technique. With this experimental approach only, a formal meta-analysis over three independent experimental series yielded statistically significant differences between potencies of copper sulfate and succussed medium.

Thermoluminescence on potentized lithium chloride seems to be the third promising technique, although it requires quite sophisticated and expensive equipment.

In contrast, both NMR relaxation and UV spectroscopy can be performed with desktop instruments, and can additionally be equipped with autosamplers to allow a high number of samples to be measured. From a pragmatic point of view, these two methods therefore seem to be most promising to be recommended for further replication studies.

Of interest, two unconventional experimental methods (so-called REDEM spectroscopy and gas discharge visualization) also seem to have a potential to distinguish between potentized preparations (silver nitrate, gold, sodium chloride) and controls. The disadvantage of these approaches is that the exact measurement process is only partially understood, and cannot be scientifically interpreted in a straightforward way.

Limitations

The search criteria defined homeopathic preparations as having undergone succussion steps, as such a number of publications from the field of water research and of high-dilutions research were not included. In particular the work of Pollack on "Exclusion Zone" (EZ) water, which is often cited as a possible line of enquiry for explaining homeopathy, did not fulfill the criteria and was not retained (for a overview of this field, the reader is referred to the book by Pollack: "The Fourth Phase of Water"[148]). Similarly, the work of Konovalov and Ryzhkina on structures terms "Nanoassociates" at ultralow dilutions, did not meet the criteria and was not retained (for more details the reader is referred to the review of the field by Konovalov and Ryzhkina[149]). It is quite clear that the homeopathic remedy production process with iterative dilution and succussion steps raises fundamental questions in the realm of physics and chemistry that go far beyond the field of homeopathy research. A review on water structures and water/ethanol structures and on physicochemical effects of succussion would be a very valuable complementary approach for homeopathic basic research.

Conclusions

We reviewed 134 publications describing 203 experiments in the area of physicochemical research into homeopathically potentized preparations, which we analyzed in detail with the aim of extracting relevant information about what has been learned in the field and which experiments to undertake in the future.

To conclude, the most promising techniques used so far are NMR relaxation, optical spectroscopy, and electrical impedance measurements. In these three areas, several sets of replicated high-quality experiments provide evidence for specific physicochemical properties of homeopathic preparations.

For future experiments, we recommend using succussed controls, or comparing different homeopathic preparations with each other to reliably identify any specific physicochemical properties. We also recommend the use of systematic positive and negative control experiments as a way of measuring the inherent variability in an experimental setup.

Further in-depth analysis of the experiments published is warranted to extract hypotheses regarding a possible mode of action of potentized remedies; such an analysis will be published as Part 3 of this review.

Author Disclosure Statement

S.W. was an employee of Hevert-Arzneimittel GmbH & Co. KG, Germany; however, none of the publications included in this review used Hevert products. All other authors have no competing financial interests.

Supplementary Material

Supplementary Data

THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 27, Number 1, 2021, pp. 45–57
Mary Ann Liebert, Inc.
DOI: 10.1089/acm.2020.0243

JACM

Physicochemical Investigations of Homeopathic Preparations: A Systematic Review and Bibliometric Analysis—Part 3

Alexander Tournier, PhD,[1,2] Sandra Würtenberger, MSc,[3] Sabine D. Klein, PhD,[1] and Stephan Baumgartner, PhD[1,4,5]

Abstract

Objectives: In parts I and II of our review of physicochemical research performed on homeopathic preparations, we identified relevant publications and analyzed the data in terms of individual experiments, looking for the most promising techniques that were used in the past. In this third part, we analyze the results of the experiments seeking to extract information about the possible modes of action underpinning homeopathic preparations.

Methods: We summarized the results from the 11 experimental areas previously introduced, extracting the general findings and trends. We also summarized the results in terms of specific research topics: aging, medium used for potentization, sample volume, temperature, material of potentization vessel, and, finally, the use of molecules to probe homeopathic samples.

Results: We identified a number of effects that appear consistently throughout the data: Differences to controls seem to increase with: time, moderate temperature, small samples volume, and in ionic medium, whereas high temperatures seem to abolish differences to controls. Based on the present analysis, there is no consistent evidence to date for the nanoparticle hypothesis to explain specific homeopathic treatment effects. However, the quantum coherence domain hypothesis, the dynamic water cluster hypothesis, and the weak quantum theory are still contenders and need to be further assessed experimentally.

Conclusions: The field requires further targeted experimentation to validate past findings reporting differences between homeopathic dilutions and controls, and to expand these findings by specifically testing the three main working hypotheses that are currently at hand.

Keywords: physics, very high dilutions, serially diluted and agitated solutions, ultrahigh aqueous dilutions

Introduction

In the previous two parts of this review, we found promising experimental evidence supporting the idea that homeopathic dilutions have physicochemical properties different than appropriate controls.[1,2] However, not knowing the mode of action through which homeopathy might work leads to a big stumbling block for research into this medical treatment method.

Several hypotheses have been suggested to explain the preclinical and clinical effects of homeopathic preparations; however, consistent experimental evidence to back those

[1]Institute of Complementary and Integrative Medicine, Faculty of Medicine, University of Bern, Bern, Switzerland.
[2]Water Research Lab, Heidelberg, Germany.
[3]Scientific & Regulatory Affairs, Hevert-Arzneimittel GmbH & Co. KG, Nussbaum, Germany.
[4]Society for Cancer Research, Arlesheim, Switzerland.
[5]Institute of Integrative Medicine, University of Witten/Herdecke, Witten, Germany.

Grundlagenforschung – Einzelne Abstracts wichtiger Untersuchungen:

CRIMSON PUBLISHERS
Wings to the Research

Advances in Complementary & Alternative medicine

ISSN 2637-7802

Review Article

Towards a Rational Insight into the Paradox of Homeopathy

Jean Louis Demangeat*

Department of Nuclear Medicine, General Hospital, France

***Corresponding author:** Jean Louis Demangeat, MD, PhD, Department of Nuclear Medicine, General Hospital, Haguenau, France

Submission: : March 09, 2018; **Published:** April 10, 2018

Abstract

Biological efficacy of infinitesimally diluted substances is still controversial. However, homeopathic remedies are manufactured through an iterative dilution/dynamization procedure which induces collateral phenomena, especially nanobubbles and release of silica from the glass container. Our own NMR studies and a review of the literature show that dilutions could contain much more molecules than expected, moreover in nanoparticulate forms which increase with dilution. Dilution/dynamization beyond a threshold of 10^{-6}-10^{-8} generates superstructures associated with the solute, which grow at each step by affixing layers of nanobubbles and silica, or by self-assembly. Sizes from 1-2nm to hundreds of nanometers could be demonstrated by electron microscopy. Dynamization appears crucial, by producing specific superstructures (distinguishable according to the dissolved substance), and inducing paradoxical biological effects. Superstructures are neither observed without dynamization nor at low dilution, where even a paradoxical chaotropic effect on the solvent is observed by NMR. Thus, a dual structure of the homeopathic medicine is highlighted. We postulate that dynamization and nanobubbles ensure formation, stereospecificity, growth and transfer of superstructures across dilutions. The sampling tip may play a major role by catching the superstructures and conveying the encaged remedy across the successive dilutions. Some studies managed to show the presence of the remedy source, as a non-zero asymptote, in ultrahigh dilutions, far beyond the Avogadro's limit. Owing to this physical duality, low dilutions would act on organ receptors through ligand-receptor interactions, and high dilutions on systemic size-dependent targets, due to peculiar properties of nanoparticles, able, as a function of size, to cross physiological barriers, stimulate endocrine and immune systems or enter nerves to directly reach the brain. Inverse effects, observed within the 10^{-3}-10^{-6} range, might correspond to the onset of the nanoparticulate form. The number of dynamizations could be the true factor for biological activity, rather than the rate of dilution.

Keywords: Homeopathy; Ultrahigh dilutions; NMR relaxation; Dynamization; Nanobubbles; Nanostructures; Homeopathic remedy as nanomedicine; Hormesis; Hypotheses about biological effects

Abbreviations: NMR: Nuclear Magnetic Resonance; NS: Nanostructure; NB(s): Nanobubble(s); NP(s): Nanoparticle(s); DLS: Dynamic Light Scattering; R/B: Rayleigh/Brillouin; (T)EM: (Transmission) Electron Microscopy; AFM: Atomic Force Microscopy; BBB: Blood-Brain-Barrier; OB: Olfactory Bulb

Introduction

Today, despite non-recognition and even opposition by scientific and medical institutions, homeopathy is the most widely used form of alternative medicine in the world. According to the World Health Organization, approximately 500 million people worldwide are treated by homeopathy. It is also used widely by veterinarians. Its origin goes back to Hahnemann [1] over 200 years ago. It is based on the "law of similia": a substance that elicits symptoms in a healthy organism is able to cure similar symptoms in a diseased organism. Despite positive meta-analyses of hundreds of studies-clinical [2-6], biological [7,8] and physicochemical [9]- its efficacy remains a subject of controversy due to trials judged to be insufficiently reliable [10-14]. Yet a recent review established the good quality of the physicochemical research in this field [15]. But the main reason for mistrusting homeopathy is ignorance concerning its mode of action, especially incredulity towards the action of infinitesimally diluted substances. In accordance with the pharmacopoeia, homeopathic remedies are prepared following a specific iterative centesimal dilution/agitation procedure-also called dilution/dynamization, dilution/succussion or potency- (with C1 corresponding to a 10^{2}-fold dilution, and Cn to a 10^{2n}-fold dilution), so that the initial solute is virtually no longer present beyond C12 (Avogadro=$6x10^{23}$).

Yet ultramolecular dilutions, such as C15 and C30, are regularly prescribed in France and much more highly diluted solutions (C100, C200,...) are prescribed in other parts of the world. The stumbling block is here: a theoretical implausibility that legitimately leads to its being considered a placebo. Moreover, the target of the remedy differs according to the level of the dilution.

Homeopathy (2016) 105, 55–65

http://dx.doi.org/10.1016/j.homp.2015.08.002, available online at http://www.sciencedirect.com

ORIGINAL PAPER

Solvatochromic dyes detect the presence of homeopathic potencies

Steven J Cartwright*

DiagnOx Laboratory, Cherwell Innovation Centre, Upper Heyford, Oxon, OX25 5HD, UK

A systematic approach to the design of simple, chemical systems for investigating the nature of homeopathic medicines has led to the development of an experimental protocol in which solvatochromic dyes are used as molecular probes of serially diluted and agitated solutions. Electronic spectroscopy has been used to follow changes in the absorbance of this class of dyes across the visible spectrum in the presence of homeopathic potencies.

Evidence is presented using six different solvatochromic dyes in three different solvent systems. In all cases homeopathic potencies produce consistent and reproducible changes in the spectra of the dyes.

Results suggest that potencies influence the supramolecular chemistry of solvatochromic dyes, enhancing either dye aggregation or disaggregation, depending upon dye structure. Comparable dyes lacking the intramolecular charge transfer feature of solvatochromic dyes are unaffected by homeopathic potencies, suggesting potencies require the oscillating dipole of solvatochromic dyes for effective interaction.

The implications of the results presented, both for an eventual understanding of the nature of homeopathic medicines and their mode of action, together with future directions for research in this area, are discussed. *Homeopathy* (2016) **105**, 55–65.

Keywords: Homeopathic potencies; Solvatochromism; Aggregachromism; Solvatochromic dyes; Intramolecular charge transfer; Supramolecular chemistry; Dye aggregation and disaggregation

Introduction

There is no doubt that a plausible and testable hypothesis for the mode of action of homeopathy and, by implication, an understanding of the physico-chemical nature of homeopathic potencies, would profoundly enhance homeopathy, both as an area of legitimate scientific study and as an effective medical approach.

Research at the molecular level has the advantage over other approaches in that it can ask the kinds of searching and detailed questions necessary to arrive at fully testable hypotheses as to the *modus operandi* of homeopathy.

*Correspondence: Steven J Cartwright, DiagnOx Laboratory, Cherwell Innovation Centre, Upper Heyford, Oxon, OX25 5HD, UK.
E-mail: steven.cartwright@oxford-homeopathy.org.uk
Received 12 March 2015; revised 18 June 2015; accepted 12 August 2015

With this view in mind a programme of investigation aimed at developing well-defined chemical systems capable of detecting consistent and replicable effects of serially diluted and agitated solutions has been initiated. Specifically, a simple chemical system utilising environment sensitive solvatochromic dyes[1] has been developed. Solvatochromic dyes are sensitive to, and can be used to follow, a range of solution dynamics through changes in their absorbance spectra which, conveniently, occur in the visible portion of the electromagnetic spectrum.

The system described below demonstrates not only that homeopathic potencies have *in vitro* effects which can be measured, but also because the system is both simple and versatile, very specific questions can be asked about what molecular effects potencies are having in solution and what their ultimate nature might be.

Whilst a range of chemical and physical systems have been employed in the past in the study of homeopathic medicines, including UV-spectroscopy,[2] nuclear magnetic resonance spectroscopy,[3] thermoluminescence,[4] high

Characterization of *Antimonium crudum* Activity Using Solvatochromic Dyes

Leoni Villano Bonamin[1] Renata Rossettini Palombro Pedro[1] Hannah Maureen G. Mota[1] Michelle S. Correia Aguiar[1] Sandra A. G. Pinto[1] Jefferson de Souza[1] Larissa Helen Silva de Oliveira[1] Ana Carla Aparicio[1] Giovani B. Peres[1] Ivana Suffredini[1] Maristela Dutra-Correa[1] Steven J. Cartwright[2]

[1] Universidade Paulista, UNIP, Graduation Program in Environmental and Experimental Pathology, São Paulo, Brazil
[2] DiagnOx Laboratory, Cherwell Innovation Centre, Upper Heyford, Oxon, United Kingdom

Homeopathy 2020;109:79–86.

Address for correspondence Leoni V. Bonamin, DVM, PhD, Universidade Paulista, UNIP, Graduation Program in Environmental and Experimental Pathology, Rua Dr Bacelar, 1212. 4th Floor, CEP 04026-002, São Paulo, Brazil (e-mail: leoni.bonamin@docente.unip.br; leonibonamin@gmail.com).

Abstract

Background The mechanism by which highly diluted and agitated solutions have their effect is still unknown, but the development in recent years of new methods identifying changes in water and solute dipole moments is providing insights into potential modes of action.

Objective The objective of the current study was to compare the biological effects of *Antimonium crudum* (AC) previously obtained by our group and already described in the literature with now measurable physico-chemical effects on solvatochromic dyes.

Methods Different dilutions of AC and succussed water have been characterized with respect to their effect on the visible spectra of the solvatochromic dyes methylene violet (MV), a pyridinium phenolate (ET33), and a dimethylamino naphthalenone (BDN) compared with in-vitro action against *Leishmania amazonensis*-infected macrophages.

Results Dye responses varied according to the dye used and the level of AC dilution and results were found to corroborate previously published in-vivo and in-vitro effects of AC. In addition, a very significant enhancement in the absorbance increase of MV was seen using the supernatant from AC 200cH-treated cells (15%; $p < 0.0001$) over that seen with AC 200cH itself (4%; $p = 0.034$), suggesting the amplification of ultra-high dilution effects by biological systems. Furthermore, supernatants from AC-treated cells increased the range of dilutions of AC that were capable of producing effects on the spectra of MV. The effect of AC dilutions on dye ET33 was eliminated by a weak electric current passed through potency solutions.

Conclusion The data confirm a correspondence between the biological effects of dilutions of AC in-vitro and physico-chemical effects on solvatochromic dyes as measured by changes in their visible spectra. Results also indicate high dilutions of AC are sensitive to exposure to electric currents and biological systems.

Keywords
- *Antimonium crudum*
- *Leishmania amazonensis*
- solvatochromic dyes
- macrophages
- electric current

Introduction

The therapeutic effects of ultra-diluted homeopathic medicines have been demonstrated in several experimental studies.[1–7] The pharmaco-technical process used for their production, called "dynamization", is based on a Hahnemannian centesimal (1:100, designated C or cH) or decimal (1:10, designated D or dH) serial dilution process, followed at each dilution step by manual or mechanical vertical and rhythmic

received
March 28, 2019
accepted after revision
July 4, 2019
published online
October 11, 2019

DOI https://doi.org/10.1055/s-0039-1697000.
ISSN 1475-4916.

Bio-Crystallization

Homeopathy
Volume 105, Issue 1, February 2016, Pages 12-13

Replication of specific effects of a *Stannum metallicum* 30x preparation in a cress seedling/biocrystallization test system

P Doesburg J.-O Anderse C Scherr S Baumgartner

One of the aims of basic homeopathic research is to reveal any specific mode of action of potentized preparations. This requires stable and reliable preclinical tests measuring either specific physicochemical properties or biological effects of homeopathic preparations.
Within a precursor project, we developed a bio-assay which yielded highly significant evidence for specific effects of an ultra-molecular *Stannum metallicum* 30x preparation relative to *Water* 30x, based on 15 independent randomized and blinded experiments performed at two independent laboratories.

The test system is based on cress seed germination, biocrystallization and subsequent computerised image analysis of the biocrystallization patterns. The biocrystallization method is based on the phenomenon that self-organizing, additive-specific crystallization patterns emerge when a $CuCl_2.2H_2O$ solution with additives is crystallized on a glass plate. The method acts as an indicator for systemic properties of the applied additive.

In the present project we investigated the reproducibility of the effects found in repeated experiments based on improved methodology towards:

(i) optimization of the laboratory procedures to avoid any processing order effects,
(ii) full implementation of blinded systematic negative control (SNC) experiments, and
(iii) *Water* 30x was replaced by *Lactose* 30x to control for the trituration of *Stannum metallicum*. In total 10 + 10 independent randomized, coded experiments were performed in two independent laboratories. In addition, 10 + 10 SNCs were performed to control experimental stability.

Meta-analysis of the data revealed the same data structure in both projects, i.e. a reproduction of the significant differences between the two homeopathic preparations. The SNCs showed no significant intra-day, inter-day or inter-lab differences, indicative of a robust and reproducible test system.
We were thus able to establish a test system yielding reproducible biological effects of an ultra-molecular homeopathic preparation. These ground-breaking results point to a promising potential of the method to contribute to basic homeopathic research.

Contents lists available at ScienceDirect

European Journal of Pharmaceutical Sciences

journal homepage: www.elsevier.com/locate/ejps

Empirical investigation of preparations produced according to the European Pharmacopoeia monograph 1038

P. Doesburg[a,b,*], J.-O. Andersen[c], C. Scherr[d], S. Baumgartner[a,e]

[a] Institute for Integrative Medicine, University of Witten/Herdecke, Gerhard-Kienle-Weg 4, 58313 Herdecke, Germany
[b] Crystal Lab, Landgoed Roepaen, Kleefseweg 9, 6595 NK Ottersum, the Netherlands
[c] Biodynamic Research Association Denmark, Landsbyvaenget 7, Herskind, 8464 Galten, Denmark
[d] Verein für Krebsforschung, Kirschweg 9, 4144 Arlesheim, Switzerland
[e] Institute of Complementary and Integrative Medicine, University of Bern, Fabrikstrasse 8, 3012 Bern, Switzerland

ARTICLE INFO

Keywords:
European Pharmacopoeia
Praeparationes homoeopathicae
Meta-analysis
$CuCl_2$ crystallization
Bio-assay
Systematic negative control experiments

ABSTRACT

According to the European Pharmacopoeia monograph 1038 (*Praeparationes homoeopathicae*), homeopathic preparations are produced by successive dilution and succussion steps. Dilution levels beyond Avogadro's limit, however, render specific effects implausible according to standard scientific knowledge. Accordingly, we were interested in a critical empirical investigation of preparations produced according to this monograph.

Within a precursor study we developed a bioassay based on a fingerprint metabolomic analysis of *Lepidium sativum* seeds germinated in vitro in either homeopathic preparations or controls in a blinded and randomized assignment. Results of the precursor study were not consistent with the hypothesis that the effects of a *Stannum metallicum* 30x preparation are identical to placebo.

In the present study we investigated the reproducibility of these effects after scrutinizing and optimizing experimental procedures. Ten independent experiments were performed in a blinded and randomized assignment in two independent laboratories. Additionally, 10 systematic negative water control experiments were performed in both laboratories to critically assess the stability of the experimental set-up.

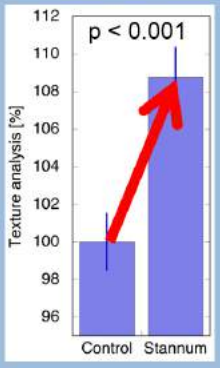
The effects of the *Stannum metallicum* 30x treatment were reproduced. The systematic negative control experiments did not yield false-positive results, indicating a stable experimental set-up.

We thus repeatedly observed biological effects conflicting with the assumption that *Stannum metallicum* 30x is identical to placebo. We therefore wish to discuss whether these findings are to be considered a scientific anomaly or whether they might stimulate further investigations to clarify whether application of the European Pharmacopoeia monograph 1038 may result in pharmaceutical preparations with specific effects.

Homeopathy and Traditional Medicine: From Zero Molecules to Macromolecules

Effects of potentised *Stannum met.* 30x in a bioassay with *Lepidium sativum*

- Treatment of *L. sativum* with *Stannum met.* 30x or Water/Lactose 30x, growth for 4 days *in vitro*
- 35 independent randomized blinded experiments in 3 laboratories (n=15 1st series, n=20 2nd series)
- Pre-metabolomic analysis (crystallization patterns of *L. sativum* extract with $CuCl_2$ added, analysis by computerized texture analysis)
- Experimental stability verified by independent internal biological replicates (15 exp.) or full Systematic Negative Control experiments (20 exp.)
- Texture analysis: $p < 0.001$ for *Stannum metallicum* 30x compared to Water/Lactose 30x



Doesburg et al. 2019 Eur J Pharm Sci

Complementary Therapies in Medicine (2014) 22, 333–340

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevierhealth.com/journals/ctim

Droplet evaporation method as a new potential approach for highlighting the effectiveness of ultra high dilutions

Maria Olga Kokornaczyk[a,*], Grazia Trebbi[a], Giovanni Dinelli[a], Ilaria Marotti[a], Valeria Bregola[a], Daniele Nani[b], Francesco Borghini[c], Lucietta Betti[a,*]

[a] *Department of Agricultural Sciences, University of Bologna, Viale Fanin 42, 40127 Bologna, Italy*
[b] *Italian National Health System, Lombardy District, ASL, Corso Italia 19, 20122 Milan, Italy*
[c] *Department of Medical Therapy, Faculty of Medicine, Chieti University, Via dei Vestini 31, 66013 Chieti, Italy*

Available online 24 February 2014

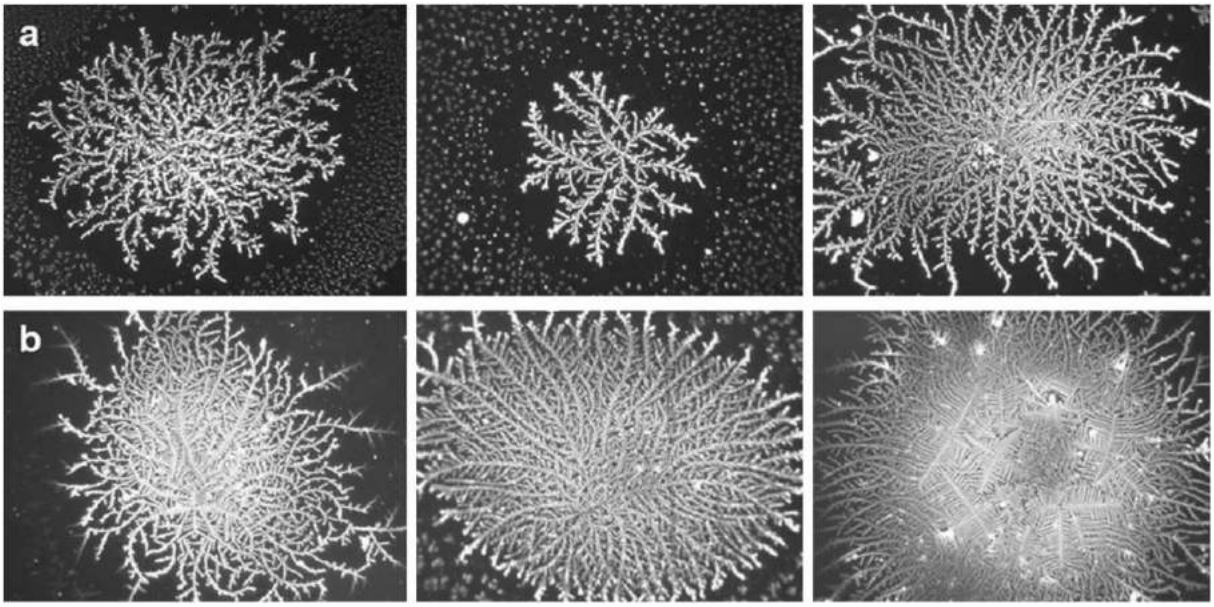
KEYWORDS
Droplet evaporation method;
Fractal dimension;
Fluctuating asymmetry;
Wheat seedling growth;
Arsenic trioxide;
Ultra high dilutions;
Polycrystalline structures

Summary
Objective: This study sought to verify whether the droplet evaporation method (DEM) can be applied to assess the effectiveness of ultra-high dilutions (UHDs). We studied the shape characteristics of the polycrystalline structures formed during droplet evaporation of wheat seed leakages.
Methods: The experimental protocol tested both unstressed seeds and seeds stressed with arsenic trioxide 5 mM, treated with either ultra-high dilutions of the same stressor substance, or with water as a control. The experimental groups were analyzed by DEM and *in vitro* growth tests. DEM patterns were evaluated for their local connected fractal dimension (measure of complexity) and fluctuating asymmetry (measure of symmetry exactness).
Results: Treatment with arsenic at UHD of both stressed and non-stressed seeds increased the local connected fractal dimension levels and bilateral symmetry exactness values in the polycrystalline structures, as compared to the water treatment. The results of *in vitro* growth tests revealed a stimulating effect of arsenic at UHD *vs.* control, and a correlation between the changes in growth rate and the crystallographic values of the polycrystalline structures was observed.
Conclusions: The results indicate that polycrystalline structures are sensitive to UHDs, and so for the first time provide grounds for the use of DEM as a new tool for testing UHD effectiveness. DEM could find application as a treatment pre-selection tool, or to monitor sample conditions during treatment. Moreover, when applied to biological liquids (such as saliva, blood, blood serum, *etc.*), DEM might provide information about UHD effectiveness on human and animal health.

* Corresponding authors. Tel.: +39 051 2096734; fax: +39 051 2096770.
E-mail addresses: maria.kokornaczyk@unibo.it (M.O. Kokornaczyk), lucietta.betti@unibo.it (L. Betti).

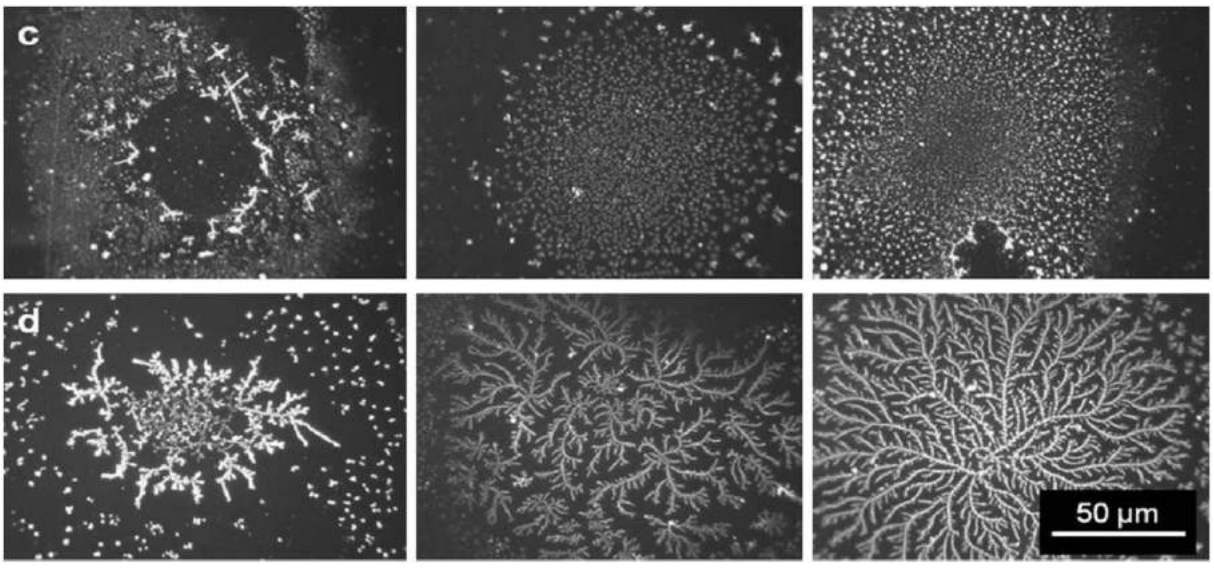
http://dx.doi.org/10.1016/j.ctim.2014.02.005
0965-2299/

Für diese Versuche wurden für jede der 4 Anordnungen 5 intakte Weizenkeime ausgesucht, möglichst uniform nach Farbe, Größe und Form.



- Die beiden Chargen für Versuch a) und b) wurden für 1 Stunde in destilliertem Wasser inkubiert,
- Die beiden Chargen für Versuch c) und d) wurden zeitgleich in einer wässrigen Lösung des Zellgifts Arsen (5 millimolar) inkubiert.

Anschließend wurden aus allen Chargen Flüssigkeitüberstände entnommen und auf einen sauberen Objektträger getropft und bei 25 Grad in einem Wärmeofen getrocknet. Während dieses Trocknungsprozesses bildet der wässrige Überstand von gesunden Weizenkeimen regelmäßige Kristallisationsmuster, die das bloße Auge ähnlich einer Pflanzenformation wahrnimmt (Abb a), die jedoch zur objektiven Messung eine computergesteuerte Strukturanalyse durchlaufen.
Der Überstand aus den mit Arsen geschädigten Keimen löst diese Strukturbildung nicht mehr aus (Abb c).
Anschließend wurden beide Weizenkeim-Chargen a) und c) mit einer homöopathisch potenzierten Verdünnung von Arsen (D 45, jenseits der Avogadro Konstante) imprägniert. Daraufhin zeigten die anschließend entnommenen Flüssigkeitschargen bei den gesunden b) wie bei den mit Arsen geschädigten Chargen d) diesmal beide eine Kristallisationsbildung. Die Versuche wurden an insgesamt 4 Tagen 3x repliziert.



Evidenz und evidenzbasierte Medizin

Evidenz bezeichnet ursprünglich das dem Auge unbezweifelbar Erkennbare oder die unmittelbare, mit einem besonderen Wahrheitsanspruch auftretende vollständige Erkenntnis.

Immanuel Kant hat für die geistige Bewegung der Aufklärung formuliert, dass wir ein „Ding an sich" nicht erfassen können, sondern nur eine durch unsere Sinne vermittelte indirekte Anschauung der Dinge wahrnehmen können. Messgeräte können die Anschauung unserer Sinne erweitern, doch das Ding an sich erfassen sie ebenfalls nicht.
Er hat sodann Evidenz als eine anschauende Gewissheit definiert. Innerhalb der Evidenz definiert er apodiktische Aussagen genau wie Aristoteles als diejenigen, deren Wahrheitswert vollkommen unstrittig ist[15]. Dieses so sagt Kant, ist im strengen Sinne nur in der Mathematik gegeben.

Evidenzbasierte Medizin
Herkunft:
Der schottische Arzt George Fordyce veröffentlicht bereits 1793 eine Schrift *An Attempt to Improve the Evidence of Medicine*.

Einführung in die moderne Medizin:
Die Bezeichnung evidence-based Medicine wurde in den 90er Jahren von Gordon Guyatt eingeführt. Die beste Übersetzung wäre: **Nachweisorientierte Medizin**

Die moderne evidenzbasierte Medizin basiert bisher auf *drei Säulen*[16].

1. **Die Erfahrung und die Erkenntnis des Therapeuten**
2. **Die Werte und Wünsche und die Erfahrung des Erkrankten**
3. **Der aktuelle Stand der Wissenschaft und des medizinisch Wissbaren**

[15] siehe dazu Immanuel Kant, Die *Kritik der reinen Vernunft*
[16] Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS.
Evidence based medicine: what it is and what it isn't.
BMJ. 1996 Jan 13;312(7023):71-2. doi: 10.1136/bmj.312.7023.71.

Fazit

- In der klinischen Forschung und in der Versorgungsforschung finden sich in zahlreichen Studien **deutliche Hinweise auf die Wirksamkeit einer homöopathischen Therapie.**

- Eine Reihe von Grundlagenuntersuchungen - wie die von Baumgartner, Cartwright und Demangeat etc. - zeigen eindeutig, dass homöopathische Zubereitungen **reproduzierbar messbare Effekte auf biologische und physikalische Systeme haben,** die signifikant über einer Placebo-Wirkung liegen.

- WIE genau und WARUM es zu diesen Effekten kommt, ist **bisher noch nicht schlüssig erklärbar.**

- Genau das ist der idealtypische Fall für ein forschungswürdiges Feld: **Es wird ein Naturphänomen wiederholt beobachtet, das man mit bisherigen Modellen nicht erklären kann.**

- Exakt hier muss Forschung ansetzen und **genau hier weist die Natur die Richtung zu neuen Erkenntnisebenen.**

Eine vierte Säule der Evidenz ist sinnvoll

Wir möchten abschließend anregen, dass die Auswirkung von Bias, also von Vorurteilen innerhalb der ersten, interkollegialen und der zweiten, patientenbasierten sowie der dritten, wissenschaftlich begründeten Säule ein ausdrücklich gefördertes, neues Forschungsfeld wird. So kann mit einer vierten, tragfähigen Säule durch die Vorurteilsforschung eine besser evidenzbasierte Medizin entstehen.

Die Akademie

Die Akademie Wissenschaftliche Homöopathie fördert die

- Integrative Kooperation von internationalen Forscherteams
- Kooperation mit den bestehenden seriösen Verbänden und Institutionen im Bereich der Homöopathie, der Komplementärmedizin, der Psychotherapie sowie der Schulmedizin und mit Patientenverbänden
- Internationale Vernetzung exzellenter, wissenschaftlicher Teams
- Entwicklung von traditionsorientierter zu evidenzbasierter Homöopathie
  An die Homöopathen stellt sich aus Sicht der Wissenschaft die zukunftsorientierte Anforderung, ihr Fachgebiet aus einem historisierenden Kontext zu befreien und forschend weiter zu entwickeln.

Die Akademie Wissenschaftliche Homöopathie stärkt die internationale Forschung zu

- den charakteristischen Merkmalen von Krankheit, Gesundheit und Heilung
- der Wirkweise des Simileprinzips und der Homöopathie
- der Methodenqualität in der Homöopathie
- der Optimierung einer Integrativen Versorgung.

Die Internationale Akademie für Integrative Wissenschaftlich Orientierte Homöopathie vertritt keine einzelnen Interessengruppen, denn sie ist gemeinnützig. Sie ist der Erkenntnis verpflichtet und dient der wissenschaftlich geprägten fairen Kooperation. Die Akademie fördert die Integrative Homöopathische Forschung und die Information der Bürger.

Postadresse
Internationale Akademie für Integrative Wissenschaftlich Orientierte Homöopathie e. V.
Bertha-von-Suttner-Str. 8a
77654 Offenburg

E-Mail: request@akademie-wissenschaftliche-homoeopathie.org
Homepage: www.akademie-wissenschaftliche-homoeopathie.org

Weitere Forschungsdaten finden Sie unter:
www.wisshom.de
www.hri-research.org www.hri-research.de

AKADEMIE WISSENSCHAFTLICHE

HOMÖOPATHIE

Vorstand

Dr. med. Irene Schlingensiepen
Vorsitzende der Akademie, forschte in der Neurobiologie, Tagungsleitung „Science meets Homeopathy", ärztliche Dozentin

Dr. med. Knut Werner
Zweiter Vorsitzender
FA für Allgemeinmedizin und Homöopathie

Karl-Heinz Gormanns
Dritter Vorsitzender
Steuerberater, Wirtschaftsprüfer

Beirat

Priv. Doz. Dr. sc. nat. Stephan Baumgartner,
Physiker, Mathematiker, Astronom Universität Bern, Schweiz

Professor Dr. Leoni Bonamin,
Veterinärmedizinerin, Universität Paulista – UNIP, Brasilien

Mark-Alexander Brysch
Autor

Dr. med. Jaume Costa
FA für Allgemeinmedizin, Master of Public Health Irland, war Berater der WHO und EU

Dr. vet. Liesbeth Ellinger
Studienleiterin in der Veterinärmedizin, Niederlande

Universitäts-Professor Dr. med. Michael Frass
FA für Innere Medizin u. Internistische Intensivmedizin, Wien, Österreich

Dr. med. Heiner Frei
FA für Pädiatrie, Studienleiter Homöopathie bei ADHS mit der Universität Bern, Schweiz

Professor Dr. Carla Holandino
Pharmakologin, Associate Professor, Federal University of Rio de Janeiro, Brasilien

MD Jean Pierre Jansen
FA Homöopathie und Neuraltherapie, ECH Komitee Provings, Niederlande

Professor Dr. Harald Matthes
Charité, Berlin
Onkologie, Gastroenterologie
Ärztlicher Leiter
Klinikum Havelhöhe, Berlin

Dr. med. Menachem Oberbaum
Leiter des Zentrums für Integrative Komplementämedizin Jerusalem, Universität Shaare Zedek Medical Center

Dr. Harald Noack
Rechtsanwalt
Leitete den Rechtsausschuss des Niedersächsischen Landtags

Professor Ashley Ross
entwickelte den Masterstudiengang Homöopathie in Südafrika

Dr. med. Carola Schröder
Fachärztin für Psychiatrie und Psychotherapie

Professor Dr. med. Dr. rer. nat. Diana Steinmann
Geschäftsführende Oberärztin Klinik für Strahlentherapie, Universität Hannover