HOMOEOPATHIC PRACTICES.

Review of Published Systematic Reviews

Dr. Craig W. Martin
W.C.B. Evidence Based Practice Group

July, 2003

Compensation and Rehabilitation Services Division
Workers' Compensation Board of BC

TABLE OF CONTENTS

Page

Review of Systematic Reviews of Homoeopathic Practices.

Background.

More and more patients are seeking treatment from complementary/alternative medicine practitioners. The American Medical Association defines complementary/alternative medicine (CAM) as diagnostic methods, treatments and therapies that appear not to confirm to standard medical practice, or are not taught at accredited medical schools[(1)]. In 1997, it was estimated that about 2.5 million patients in the US use complementary medicine[(2)]. In Europe, the number is higher. It was estimated in 2002 that one to two out of three patients use CAM and about 3.4% of those patients use homoeopathy. In a recent European wide survey, 32% of French, 31% of the Dutch and 16% of the UK population reported taking homoeopathic remedies[(3)]. In England alone, it has been estimated that there are about 470,000 recent users of homoeopathic remedies[(4)]. The number of patients using homoeopathy in the US is estimated to have increase by 500% in the last 7 years, mostly involving self-treatment with over the counter remedies. Homoeopathic remedies represent a substantial portion of over the counter market. In Europe, it was estimated that over 1.3 billion Euro was spent in 1995 on homoeopathic remedies. Some physicians use homoeopathic remedies for defined disease conditions or adopt the use of homoeopathic treatment principles for the treatment of several diseases including acute pain, diarrhea, asthma, hay fever, and migraine. However, most of the diseases treated by the homoeopathic practitioners are chronic or recurrent in nature.

Homoeopathy has been part of the NHS since its inception. Currently, there are 5 homoeopathic hospitals in the UK. Two of the largest units, in Glasgow and London, have in-patient wards. Recent survey shows that on average 30% of referrals made to homoeopathic hospitals came directly from oncologists[(5)]. Under the NHS, homoeopathic services are currently access either through GP or through referral by another primary or secondary care provider. In 1996, European Parliament issued a mandate to the European Commission to examine whether homoeopathy is beneficial. The subsequent report of the Commission's Homoeopathy Medicine Research Group recommended that homoeopathy be integrated into medical practice. In the US, homoeopathic remedies have been incorporated into the Food Drug and Cosmetic Act since its inception in 1938[(6)]. Homoeopathic products are recognized officially as drugs by the FDA. However, in the US the last homoeopathic school was closed in 1949. Currently, the World Health Organization stated that homoeopathic medicine is the second most widely used system of medicine in the world and the fastest growing.

The purpose of this paper is to provide a short description on the history and principles of homoeopathic practice and to conduct a systematic review on the reviews of homoeopathic treatment that have been published in peer reviewed journals.

Homoeopathy[(2,6,7,8,9)].

It was suggested that homoeopathy dates back to Hippocrates, approximately 2400 years ago. However, modern homoeopathy dates back to the 1796 when Samuel Hahnemann, a German physician, published 'Essay on the New Currative Principle'. It began when he was translating an herbal text from English to German when he found that

cinchona bark cured malaria because it was bitter. He thought this explanation was ridiculous and took repeated doses of cinchona to personally determine its effect. The effect was similar to malaria. He then hypothesized that one may select therapies on the basis of how closely a patient's toxicologic symptoms matched the symptoms of the patient's disease. He called this theory of similia similibus curantur or the law of similars (first principal of homoeopathic), which is an extension of Hippocrates' observation. He then gave repeated doses of many common remedies to healthy individuals and recorded the symptoms they produced. In modern homeopathy, this procedure is called a human pathogenic trial or proving. Homoeopathics attempt to select treatment for sick patients by matching these drug symptoms to symptoms in sick patients.

The second and most controversial principal in homoeopathy is called potentization or principal of dilution or infinitesimal dose. Potentization is a combination of ultradilution (dilution of the actual substance to a concentration of below Avogadro's number or $< 10^{-23}$) of the remedies and succussion (vigorous shaking of the substance). Hahnemann implemented succussion when he found that remedies that were shaken on the way to the home of the patient were more effective than those given at his office without being shaken. He was then began succussing all remedies before dosing and found an increase in therapeutic effectiveness. He claimed that this potentization process extracted the 'vital' or 'spirit like' nature of the substances. The implausibility of this claim has led many to dismiss any evidence of homoeopathic effectiveness as placebo effect.

The third principal of homoeopathy is called individual specificity. Hahnemann observed that in addition to acting on acute conditions, certain remedies exerted their effects based on the constitution of individuals, such as their moral and intellectual character, their habits, their relationships, their likes and dislikes and what made them feel better or worse. Even the time of day a person's symptom appear and on what side of the body the ailment appears are taken into consideration. Thus, 2 patients with tonsillitis may receive 2 different medications. These principles are also the biggest hindrance in applying traditional medical research methodology in evaluating the effectiveness of homoeopathy. In homoeopathy assumptions that one model of treatment will fit across all therapy is most likely inapplicable. At present, there is no explanation on the biological plausibility of homoeopathic treatment[10]. However, the principal of similar and small doses are used widely in traditional medicine such as in vaccination and desensitization.

Based on these 3 principles, homoeopathic evaluation consists of the general medical examination with the standard organ and system review. The history taking is structured to provide data necessary to match a unique symptom picture of the patient with the characteristics of one of the remedies. The most important factor in the evaluation is the chief complaint and the circumstances around it. Key points of the homoeopathic anamnesa is similar to conventional medical anamnesa but with much more detail. Important elements in homoeopathic anamnesa include mental and emotional symptoms (mood, anxiety, fears), sensations with concrete examples, location (side of the body is important), direction of the symptom, concomitant symptoms, symptom modalities, symptom intensity, duration of symptoms, onset of symptom and sequence of events. After taking the list of complaints and addressing characteristics of the personality, lifestyle and reactivity to emotional and physical events, the patient's case is evaluated in its entirety.

Currently, there are at least 2 schools of thought in homoeopathy. The first one is called classic or constitutional homoeopathy and the second one is called clinical homoeopathy (homeotherapeutics). Classical homoeopathy treats the patient by prescribing a single remedy that match with the symptom. Homeotherapeutics is based on simultaneously prescribing numerous remedies that are known to help for a particular diagnostic condition in lower potencies (combination remedies).

A current survey in the US shows that patients seen by homoeopathics tend to be more affluent, more likely to be white, present more subjective symptoms and younger than patients seen by conventional family practitioners. Conventional family practitioners saw almost twice the number of patients age > 65 year old and spent less than half as much time with each patient[(11)].

Homoeopathy in Canada.

The first recorded homoeopathy practitioner in Canada was J.O. Rosenstein. He was an immigrant most likely from the Netherlands. He was recorded as practicing homoeopathy in 1845, in Montreal, Quebec. Rosenstein published what may be the first Canadian book on homoeopathy. In 1859, homoeopathy was regulated in the province of Ontario, Canada. A homoeopathic doctor required three years of training, including medical sciences, plus a clinical internship. By 1884, an estimated 80 homoeopaths were practicing in Canada. It seems, however, that from that point on, homoeopathy was declining in Canada. By 1925 only 40 homoeopaths were practicing in Canada, 32 in Ontario. It was not until the 1980's that homoeopathy returned, strongly supported by the general demand for complementary approaches in health care[(12)].

In January 1992, The International Academy of Homoeopathy (IAH) and the Toronto Homoeopathic Clinic introduced the first Homoeopathic Practitioner programme in Canada. In 1995 the Homoeopathic College of Canada (HCC) was founded as a non-profit educational institution[(12)]. Currently, there is 4 homoeopathic school in Canada (including one in Vancouver) [(13)]. In 1995, The Homoeopathic Medical Council of Canada (HMCC) was established as a self-regulatory body for the re-emerging profession. However, homoeopathy is currently unregulated in Canada and many states in the USA.

Systematic reviews on homoeopathy.

Literature searches were conducted on PubMed and the Cochrane Library in order to identify systematic reviews that have been published on homoeopathic practice. The inclusion criteria were English language systematic reviews on homeopathic medicine on which the primary trials were conducted in humans. The keywords used were (homeopathy OR homoeopathy OR homoeopathic OR homeopathic) AND (systematic review OR review OR meta analysis). The search yielded 18 published systematic reviews.

A summary of these systematic reviews is presented in Table 1 and 2. With regard to issues surrounding homoeopathic practice, there are 2 basic questions that researchers try to answer i.e. the issue of whether homoeopathic has any effect over and above placebo (Table 1) and the issue of the effectiveness of homoeopathic intervention(Table 2).

Linde et al[17] first investigated the hypothesis that homoeopathic remedies were not placebos and concluded that clinical effects of homoeopathy were not completely due to placebo. However, this study was conducted across different remedies for different diseases as well as including non-randomized trials in the meta analysis. Since then several researchers[18-23] have tried to replicate and expand on Linde's research. Based on the research on this issue it can be concluded that the higher quality trials were associated with a smaller effect which in turn render the overall effect insignificant. Earlier research on similar issues (Kleijnen et al[24]) also came to this same conclusion. Thus, it can be concluded that to this date there is no evidence that homoeopathic remedies are clinically different from placebo treatment.

Systematic reviews demonstrate that homoeopathy is not effective in preventing headache or migraine[25], bruising, swelling or post-operative pain (arnica) [27], chronic asthma[29], delayed onset muscle soreness[30], rheumatic disease[31] or osteoarthritis[32]. Homoeopathic is probably effective in reducing the time course of post-operative ileus[26] and shortening the duration of influenza (as treatment, not as preventative measure) [28].

The evidence put forth from research on homoeopathy should be interpreted with caution. This is due to several problems including the quality and purpose of the primary research as well as the quality of the available systematic reviews[15,16]. Some of these concerns are noted below:

- Primary research was usually under-powered, failed to analyze using the intention to treat principal, or did not employee blinding procedure in randomized controlled trial research
- Some of the systematic reviews pooled clinically heterogenous data (with evidence of statistical heterogeneity)
- Lack of independent replications that produced conflicting results (probably due to methodological problems)
- The applicability of traditional randomized controlled trial method in assessing individualized treatment principle of homoeopathic

With regard to adverse effect/safety, serious unexpected adverse effects of homoeopathic remedies are rare[8,14]. Aggravation reaction i.e. when symptoms become acutely and transiently worse after starting homoeopathic remedies has been described. However, homoeopaths regard this phenomenon as a good prognostic factor[8]. In a systematic review of the adverse effects of homoeopathic remedies, Dantas and Rampes concluded that the mean incidence of adverse effects of homoeopathic remedies was greater than placebo in a controlled trial. However, the adverse effects were minor and transient[14]. The most common adverse effects were headache, tiredness, skin eruptions, dizziness, bowel dysfunctions and allergic reactions.

Who is paying for homoeopathic remedies?

The WCB of Alberta may pay for homoeopathic remedies if their use is recommended by the worker's physician and the WCB's medical advisor confirms they are needed as a result of the compensable injury[34]. Other WCBs in Canada do not explicitly specify or do not mention this in their payment policies or practice documents.

The insurance company Aetna specifies that they do not cover homoeopathy for allergy treatment[35].

Conclusion.

- To this date, there are > 200 clinical trials done on homoeopathic. However, most of these trials suffer from methodological errors and their results need to be interpreted with that in mind.
- Higher quality trials on homoeopathic show that the effect of homoeopathic is not different than placebo (Level 1 evidence).
- Systematic reviews on homoeopathic reveal that, with the possible exception on treating post-operative ileus and shortening the symptom duration of influenza, homoeopathic is not an effective treatment for various diseases (Level 1 evidence).

Reference:

1. American Medical Association. CSA Reports. Report 12 of the Council on Scientific Affairs (A-97). Alternative Medicine. www.ama-assn.org/ama/pub/print/article/2036-2523.html (access June 30, 2003).
2. D'Huyvetter K and Cohrssen A. Homeoptahy. Primary Care: Clinics in Office Practice. 2002;29(2):102-110.
3. European Committee for Homeopathy. A Strategy for research in homeopathy. Assessing the value of homeopathy for health care in Europe. www.homeopathyeurope.org/organisation/hmrg.html (access June 30, 2003).
4. O'Meara S, Wilson P, Bridle C et al. Homeopathy. Effectiveness Bulletin. Quality and Safety in Health Care 2002; 11: 189-194.
5. Thompson E, Kassab S. Homeopathy in cancer care. British Homeopathic Journal. 2000;89:61-62.
6. Merrel WC, Shalts E. Homeopathy. Medical Clinics of North America. Jan 2002;86(1):101-106
7. Jonas WB, Kaptchuk TJ and Linde K. Complementary and Alternative Medicine Series. A critical overview of homeopathy. Annals of Internal Medicine. 2003; 138:393-399.
8. Vickers A, Zollman C. ABC of Complementary Medicine. Homeopathy. BMJ. 1999;319:1115-1118
9. Carnall D. Website of the week. Homeopathy. BMJ. Aug 2000;321:518.
10. Widakowich J. Pharmacodynamic principles of homeopathy. Medical Hypotheses. 2000;54(5):721-722.
11. Jacobs J, Chapman E and Crothers D. Patient characteristics and practice patterns of physicians using homeopathy. Archives of Family Medicine. Nov-Dec 1998;7:537-540.
12. .Homoeopathic College of Canada. http://www.homeopathy.edu/. (access July 2, 2003).
13. . www.canadahomeopathy.com. (access July 2, 2003).
14. Dantas F, Rampes H. Do homeopathic medicines provoke adverse effects? A systematic review. British Homeopathic Journal. Jul 2000; 89(S1):S35-S38.
15. Linde K, Jonas WB, Melchart D and Willich S. The methodological quality of randomized controlled trials of homeopathy, herbal medicines and acupuncture. International Journal of Epidemiology. 2001;30:526-531.
16. Linde K, Willich SN. How objective are systematic reviews? Differences between reviews on complementary medicine. Journal of Royal Society of Medicine. Jan 2003;96(1):17-22.
17. Linde K, Claudius N, Ramirez G et al. Are the clinical effects of homoeopathy placebo effects? A meta analysis of placebo controlled trials. Lancet. Sept 20 1997;350:834-843.
18. Ernst E. Are highly dilute homoeopathic remedies placebos? Perfusion 1998; 11:291-292.

19. Linde K, Melchart D. Randomized controlled trials of individualized homeopathy: a state of the art review. Journal of Alternative and Complementary Medicine. 1998;4:388-390
20. Linde K, Scholz M, Ramirez G et al. Impact of study quality on outcome in placebo controlled trials of homeopathy. Journal of Clinical Epidemiology. 1999;52:631-636.
21. Ernst E. Classical homoeopathy versus conventional treatment. Perfusion. 1999;12:13-15.
22. Ernst E, Pittler MH. Letter. Re-analysis of previous meta analysis of clinical trials of homeopathy. Journal of Clinical Epidemiology. 2000; 53: 1188.
23. Cucherat M, Haugh MC, Gooch M et al. Evidence of clinical efficacy of homoeopathy. A meta-analysis of clinical trials. European Journal of Clinical Pharmacology. 2000;56:27-33.
24. Kleijnen J, Knipschild P, Ter Riet G. Clinical trials of homeopathy. BMJ 1991;302:316-323.
25. Ernst E. Homeopathic prophylaxis of headaches and migraine? A systematic review. Journal of Pain Symptom Management. 1999;18:353-357.
26. Barnes J, Resch KL, Ernst E. Homoeopathy for post-operative ileus?: a meta-analysis. Journal of Clinical Gastroenterology. 1997;25:628-633.
27. Ernst E, Pittler MH. Efficacy of homoeopathic arnica: a systematic review of placebo controlled clinical trials. Archives of Surgery. 1998;133:1187-1190.
28. Vickers A, Smith C. Homoeopathic oscillococcinum for preventing and treating influenza and influenza like syndromes (Cochrane Review). In: Cochrane Library, Issue 1, 2001. Oxford:Update Software.
29. Linde K, Jobst K. Homoeopathy for chronic asthma (Cochrane Review). In: Cochrane Library, Issue 1, 2001. Oxford:Update Software.
30. Ernst E, Barnes J. Are homoeopathic remedies effective for delayed onset muscle soreness? A systematic review of placebo controlled trials. Perfusion. 1998;11:4-8.
31. Jonas WB, Linde K, Ramirez G. Homoeopathy and rheumatic disease. Rheumatic Disease Clinics of North America. 2000;26:117-123.
32. Long L, Ernst E. Homoeopathic remedies for treatment of osteoarthritis: a systematic review. British Homoeopathic Journal. 2001;90:37-43.
33. .www.wcb.ab.ca (access July 1, 2003)
34. .Coverage Policy Bulletin Number:0388. Subject: Complementary and Alternative Medicine. AETNA. www.aetna.com/cpb/data/PrtCPBA0388.html. (access June 30, 2003)

Table 1. Is homoeopathic effect a placebo effect? Systematic review (Level 1 evidence)

Reference	Result	Conclusion
Linde et al, 1997[17]	186 trials (2588 patients). Of 89 trials that could be included in the meta analysis OR=2.45; 26 good quality trials OR=1.66 in favour of homoeopathy	Homoeopathy is not completely placebo. However, this review included different remedies, conditions and nonrandomized trials
Ernst, 1998 [18]	Trials from Linde's[17] review with score 90/100 (5 trials, 587 patients). OR = 1.0	Homoeopathy is the same with placebo
Linde et al, 1998[19]	Only classical homoeopathic remedies from Linde[17]. 32 trials (1778 patients). 19 trials included in meta-analysis, OR=1.62. However, when analysis was limited to good quality trials OR=1	Classical homoeopathy has an effect over placebo, however, the evidence is weak
Linde et al, 1999[20]	All trial from Linde[17] which fulfill criteria for meta-analysis (89 trials). The mean OR of the best study does not favour homoeopathy	There is evidence that better quality studies tend to yield negative results
Ernst, 1999[21]	6 trials on classical homoeopathy vs. traditional treatment. The results were evenly distributed between superiority of classical homoeopathy, traditional treatment and no difference between the 2 treatment methods. All trials have serious methodological flaws.	The relative value of individualized homoeopathic over traditional treatment is still unknown
Ernst el al, 2000[22]	All trials on Linde(17) who received Jadad score 1-4 (77 trials). There is a strong linear correlation between OR and Jadad score.	Homeopathic remedies are placebo
Cucherat et al, 2000[23]	16 trials, 65% showed statistically significant results in favour of homoeopathy. Low methodological quality of trials. Studies on high quality trials were more likely to be negative	Weak evidence that homoeopathy is more effective than placebo
Kleijnen et al, 1991[24]	105 interpretable trials. 77% in favour of homoeopathy. Positive results were more likely among lower methodological quality trials	The evidence on clinical effectiveness of homoeopathy is inconclusive due to the role of publication bias

Table 2. Systematic reviews on the effectiveness of homoeopathic (Level 1 evidence)

Reference	Disease/condition	Result	Conclusion
Ernst E, 1999[25]	headache & migraine	4 trials (284 patients). 1 trial found significant improvement, 3 no significant improvement	Homoeopathy was not effective in the prophylaxis of migraine or headache beyond placebo effect
Barnes et al, 1997[27]	post-op ileus	6 trials (776 patients). Weighted mean difference was -7.4 hrs in favour of homoeopathy.	Homoeopathy could reduce duration of post-op ileus. However, the best methodological trial was negative
Ernst et al, 1998[28]	arnica	8 trials (338 patients). No trend in favour of homoeopathy.	The effect of arnica was not different than placebo
Vickers et al, 2001[29]	influenza	7 trials (3459 patients). Treatment reduced length of illness significantly by 0.28 days	However, the authors stated that the data were not strong enough to give general recommendation
Linde et al, 2001[30]	chronic asthma	3 trials (154 patients). Severity symptoms lessen in 1 trial, improved lung function and medication use in 1 trial, no different between groups in 1 trial. Poor methodology.	Treatment in these trials were not representative of common homoeopathic practice. The authors concluded that there was not enough evidence to assess the role of homoeopathy in asthma
Ernst et al, 1998[31]	DOMS*	8 trials (311 patients). All trials were negative.	No evidence that homoeopathic was better than placebo
Jonas et al, 2000[32]	rheumatic diseases	6 trials (392 patients). Combined for rheumatoid arthritis (3 trials) osteoarthritis (1 trial), fibromyalgia (1 trial), myalgia (1 trial). Pooled OR 2.19 (1.55-3.11)	Need very high caution due to pooling of heterogenous clinical data
Long et al, 2001[33]	osteoarthritis	4 high quality trials (406 patients). Mixed of hips and knees OA. Inconsistent findings across trials. Standardised treatment (not likely occur in common homoeopathic practice)	Not enough evidence in the effectiveness of homoeopathy in treating OA. Standardized treatment being used did not reflect common homoeopathic practice

*DOMS = delayed onset muscle soreness