

Research article

Systematic reviews of complementary therapies – an annotated bibliography. Part 3: Homeopathy

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Abstract

Background: Complementary therapies are widespread but controversial. We aim to provide a comprehensive collection and a summary of systematic reviews of clinical trials in three major complementary therapies (acupuncture, herbal medicine, homeopathy). This article is dealing with homeopathy. Potentially relevant reviews were searched through the register of the Cochrane Complementary Medicine Field, the Cochrane Library, Medline, and bibliographies of articles and books. To be included articles had to review prospective clinical trials of homeopathy; had to describe review methods explicitly; had to be published; and had to focus on treatment effects. Information on conditions, interventions, methods, results and conclusions was extracted using a pretested form and summarized descriptively.

Results: Eighteen out of 22 potentially relevant reviews preselected in the screening process met the inclusion criteria. Six reviews addressed the question whether homeopathy is effective across conditions and interventions. The majority of available trials seem to report positive results but the evidence is not convincing. For isopathic nosodes for allergic conditions, *oscillococtinum* for influenza-like syndromes and galphimia for pollinosis the evidence is promising while in other areas reviewed the results are equivocal.

Interpretation: Reviews on homeopathy often address general questions. While the evidence is promising for some topics the findings of the available reviews are unlikely to end the controversy on this therapy.

Introduction

In this third part of our series on systematic reviews in complementary therapies we report our findings on homeopathy. Homeopathy is one of the most widespread

forms of complementary medicine worldwide. According to a recent survey 3.4% of Americans have used homeopathy in the past 12 months [1]. It is even more widespread in some European countries [2], some countries

in South America, India or Pakistan [3]. This widespread use is in strong contrast with the position held by many in scientific medicine that homeopathy has no effect beyond placebo [4].

The basic principle of homeopathy is the principle of similars: A patient with a specific pattern of symptoms is best treated by a remedy which causes the same or a very similar pattern in healthy subjects. Homeopathic remedies are often prescribed in high dilutions some of which are unlikely to contain any molecules of the originally diluted agents. In consequence, homeopathic remedies – at least when applied in high dilutions – cannot act by pharmacological means. Theories for a potential mechanism of action, therefore, postulate the storage of information in the dilution process by physical means [5].

Methods

A detailed description of the methods used in this review of reviews is given in the first part of this series [6]. As a specific intervention-related inclusion criterion we required that reports reviewed prospective (not necessarily controlled) clinical trials of homeopathic medicines in humans.

Results

From a total of 22 potentially relevant reviews identified in the literature screening, 18 reviews published in 19 papers met the inclusion criteria [7–25] (see table 1). Four papers were excluded as they were only subgroup or methodological analyses of previously published papers [26–29].

Three quantitative meta-analyses addressed the general question whether homeopathy is different from placebo by pooling highly heterogeneous study samples [7–9]. Study samples and meta-analytic methods differed considerably (total number of trials covered 97). While two reviews reported significant effects of homeopathy [7,8] a third found no effect over placebo in the main analysis [9]. Several years before the publication of these studies a meta-analytic approach had already been tried in a thesis [10]. However, this review is mainly dealing with the problems encountered when trying to pool the data and cannot be interpreted meaningfully with respect to the effectiveness of homeopathy. Two older reviews included both placebo-controlled trials and comparisons with standard treatment [11,12] (total number of trials covered 107). Results were classified in a vote count as positive and negative. The majority of the studies had reported positive results. The conclusions were positive with reservations in one review and ambiguous in the other.

Two reviews focused on individualized homeopathy but were not restricted in terms of conditions investigated. A review of comparisons of individualized homeopathic and conventional treatment found that only few trials of low quality exist [13]. The other review included mainly placebo-controlled trials [14]. Overall, the results suggested that individualized homeopathy is superior to placebo but when the analysis was limited to studies of better quality the difference was no longer significant.

Four reviews focused on a single condition or a group of conditions but included a variety of homeopathic treatments [15–18]. Positive results have been reported for the treatment of postoperative ilues and asthma but definitive conclusions are not possible.

Arnica is the most often investigated homeopathic remedy. Typically it is used in conditions involving tissue trauma. Two reviews with slightly different inclusion criteria have been published [19,20] (total number of trials covered 37). While the results of the available trials seem to be contradictory the more comprehensive of the two reviews had slightly more favorable conclusions.

Systematic reviews addressing more focused questions are available for the use of isopathic nosodes (diluted allergens) in allergic conditions, *Oscillocochinum* for influenza-like syndromes, individualized homeopathy for headache and galphimia for pollinosis [21–25]. Significant differences over placebo were reported for all but the headache review.

Table 1: Systematic reviews of clinical trials of homoeopathy

Author Year	Indication	Homoeopathy/ Control	Studies	Features 1 / 2 / 3 / 4 / 5	Results	Conclusion
All homoeopathy in all conditions						
Cucherat 2000 [7]	all	all/placebo	17 RCT	y / y / y / n / y	Combined p value for an effect over placebo p = 0.000036, for best trials only p = 0.08	There is some evidence that homoeopathy is more than place- bo. Studies of high quality more likely to be negative
Linde 97 [8]	all	all/placebo	89 RCT	y / y / y / y / y	OR of all trials over placebo 2.45 (95%CI 2.05; 2.93), in better trials 1.66 (1.33; 2.08)	Results not compatible with the hypothesis that all homeo-pathy is placebo. No firm evidence for any single condition
Walach 97 [9]	all	all/placebo, conventional	41 RCT	y / p / y / y / y	Random effect size g = 0.259 (95%CI -0.319; 0.837), fixed effects 0.295 (0.223; 0.366)	The effects of homoeopathy are not different from placebo on a statis- tical level
Lutz 93 [10]	all	all/placebo, conventional	21 RCT/ CCT	? / n / y / y / p	Results of available studies contradictory	No clear conclusions drawn. (Comment: thesis mainly discuss- ing problems of meta-analysis)
Kleijnen 91 [11]	all	all/placebo, conventional	107 CCT	y / p / y / y / n	81 trials reported positive results. Most trials low quality but many exceptions	Available evidence positive but not sufficient to draw definitive conclu- sions
Hill 90 [12]	all	all/placebo, conventional	40 RCT	n / p / y / y / n	The authors of half of the studies concluded that homoeopathy was effective, further 7 promising	The results do not provide accept- able evidence that homoeopathy treat- ments are effective
Individualized homoeopathy in all conditions						
Ernst 99 [13]	all	individualized/ conventional	3 RCT, 3 CCT	y / p / n / y / n	All trials were burdened with serious methodological flaws. Results non-uniform	The relative efficacy of individual- ized homoeopathy compared to conventional treatments is not known
Linde 98 [14]	all	individualized/ placebo, convent.	32 RCT	y / y / y / y / y	Responder RR vs. placebo 1.62 (95%CI 1.17; 2.23), in better quality trials 1.12 (0.87; 1.44)	Available evidence suggests effects over placebo. Evidence not convin- cing due to shortcomings and inconsistencies
Various homoeopathic treatments in a single condition/area						
Barnes 97 [15]	postoperative ileus	various/placebo	4 RCT, 2 CCT	y / y / y / y / y	Time to first flatus in homoeopathy significantly shorter. Best trial negative	Available evidence positive but several caveats preclude definitive conclu- sions
Ernst 98 [16]	delayed- onset muscle soreness	various/placebo	8 dou- ble- blind trials (3 explicit- ly RCT)	y / y / y / y / n	Most trials with severe flaws. The 3 RCT showed no significant effects over placebo	Published evidence does not sup- port the hypothesis that homoeopathic remedies are effective for muscle

Table 1: Systematic reviews of clinical trials of homoeopathy (Continued)

Jacobs 91* [17]	rheumatic diseases	various/placebo	4 CCT	p / y / n / y / n	3 of 4 trials positive. Quality poor	soreness No specific conclusion on homoeopathy (generally: no convincing evidence for alternative therapies in rheumat.)
Linde 98 [18]	asthma	various/placebo	3 RCT	y / y / y / y / n	Trials highly heterogeneous. Two report statistically significant effects	Currently available evidence insufficient to assess the possible role of homoeopathy in the treatment of asthma
Arnica in various conditions (mainly various tissue traumata)						
Lüdtke 99 [19]	all	arnica/placebo, no treatment	23 RCT, 14 CCT	y / y / y / n / n	Quality often low. 13 of 35 studies vs. placebo with significant results, 10 with trend	Available evidence suggests that arnica can be efficacious. Further rigorous trials needed
Ernst 98 [20]	all (mainly trauma)	arnica/placebo, conventional	4 RCT, 4 CCT	y / y / y / y / n	2 trials positive, 2 trials positive trend. Most studies with severe flaws	Claims that homoeopathic arnica is efficacious are not supported by rigorous trials
Similar homoeopathic treatments in one condition/a group of conditions						
Taylor 2000** [21]	allergic conditions	isopathic nosodes/placebo	4 RCT	n / n / n / y / y	Pooled analysis of 100 mm visual analogue scores 9.8 (95%CI 4.2;15.4) mm better with isopathy	Isopathic nosodes were different from placebo on both subjective and objective measures
Vickers 2000 [22]	influenza-like syndrome	oscillococinum/ placebo	7 RCT	y / y / y / y / y	No evidence for preventative effect (3 trials) but reduction of length of illness in treatment trials	Oscillococinum probably reduces the duration of influenza-like syndromes. Further trials needed
Ernst 99 [23]	headache prophylaxis	individualized/ placebo	4 RCT	y / p / y / y / n	one trial positive, one partially positive, 2 negative	The trial data do not suggest an effect over placebo in the prophylaxis of migraine or headache
Wiesenaue 96** [24,25]	pollinosis	galphimia/placebo	8 RCT, 1 CS, 2 UCS	p / n / n / y / y	Responder RR galphimia vs. placebo from 7 trials 1.25 (95%CI 1.09; 1.43)	Galphimia is significantly more effective than placebo

*Disease-focused review on a variety of complementary medicine interventions including homoeopathy; **Meta-analytic overviews of researchers of their own trials on the topic Features: 1 = comprehensive search, 2 = explicit inclusion criteria, 3 = formal quality assessment, 4 = summary of results for each included study, 5 = meta-analysis; y = yes, p = partly, n = no, - = not applicable, ? = unclear RCT = randomized controlled trials, CCT = non-randomized controlled trials, CS = cohort study, UCS = uncontrolled study; OR = odds ratio, RR = rate ratio

Discussion

Systematic reviews on homeopathy address, more often than in other areas of complementary medicine, general questions such as "is it more than placebo?" or "is it effective?" This is probably due to the fact that any effect of homeopathy over placebo is considered scientifically implausible. In consequence, the discussion does not primarily focus on specific clinical problems but on whether there is a real effect at all. While many overviews report that the majority of trial results are positive conclusions of reviewers are contradictory.

With few exceptions such as arnica for trauma or individualized homeopathy for headache, the reviews (and probably the primary research) do not cover conditions and treatment approaches which are relevant in homoeopathic practice. Self-medication with *Oscillococinum* for influenza-like syndromes is popular in several countries but cannot be considered representative practice.

We want to emphasize again that it was not our primary objective to assess the effectiveness of homeopathy and the other therapies included in our series but to provide

an annotated bibliography of the available systematic reviews. This provides an overall picture of the evidence but for an in-depth review readers must go back to the original reviews.

In conclusion, the available systematic reviews on homeopathy provide little guidance for patients and doctors. They rather reflect the ongoing fundamental controversy on this therapy and strengthen the perception that, on one side, positive evidence from clinical trials will not convince skeptics, and that on the other side negative results from trials not representing actual practice will not have any impact on homeopaths.

Competing interest

KL, AV, GtR and DM have been involved in some of the reviews analyzed. These were extracted and assessed by other members of the team.

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References

- Eisenberg DM, Davis RB, Ettner SL, et al: **Trends in alternative medicine use in the United States, 1990-1997. Results of follow-up national survey** *JAMA* 1998, **280**:1569-1575
- Fisher P, Ward A: **Complementary medicine in Europe** *BMJ* 1994, **309**:101-111
- Malik IA, Khan NA, Khan W: **Use of unconventional methods of therapy by cancer patients in Pakistan** *Eur J Epidemiol* 2000, **16**:155-160
- Vandenbroucke JP: **Homeopathy trials going nowhere** *Lancet* 1997, **350**:824
- Schulte J: **Effects of potentization in aqueous solutions** *Br Hom J* 1999, **88**:155-160
- Linde K, Vickers A, Hondras M, et al: **Systematic reviews of complementary therapies – an annotated bibliography Part 1: acupuncture.** *BMC Complementary and Alternative Medicine* 2001, **1**:3
- Cucherat M, Haugh MC, Gooch M, Boissel JP: **Evidence of clinical efficacy of homeopathy. A meta-analysis of clinical trials** *Eur J Clin Pharmacol* 2000, **56**:27-33
- Linde K, Clausius N, Ramirez G, et al: **Are the clinical effects of homeopathy placebo effects? A meta-analysis of randomized placebo-controlled trials** *Lancet* 1997, **350**:834-843
- Walach H: **Unspezifische Therapie-Effekte. Das Beispiel Homöopathie** *PhD thesis, Psychologisches Institut, Albert-Ludwigs-Universität Freiburg*, 1997
- Lutz C: **Quantitative Meta-Analyse empirischer Ergebnisse der Homöopathieforschung** *Diplomarbeit, Psychologisches Institut, Albert-Ludwigs-Universität Freiburg*, 1993
- Kleijnen J, Knipschild P, ter Riet G: **Clinical trials of homeopathy** *BMJ* 1991, **302**:316-323
- Hill C, Doyon F: **Review of randomized trials of homeopathy** *Rev Epidém et Santé Publ* 1990, **38**:139-147
- Ernst E: **Classical homeopathy versus conventional treatments: a systematic review** *Perfusion* 1999, **12**:13-15
- Linde K, Melchart D: **Randomized controlled trials of individualized homeopathy: a state-of-the art review** *J Alt Complement Ther* 1998, **4**:371-388
- Barnes J, Resch KL, Ernst E: **Homeopathy for post-operative ileus: a meta-analysis** *J Clin Gastroenterol* 1997, **25**:628-633
- Ernst E, Barnes J: **Are homeopathic remedies effective for delayed-onset muscle soreness? A systematic review of placebo-controlled trials** *Perfusion* 1998, **11**:4-8
- Jacobs JW, Rasker JJ, van Riel PL, Gribnau FW, van de Putte LBA: **Alternatieve behandelingswijzen by reumatische aandoeningen; een literatuuronderzoek** *Ned Tijdschr Geneesk* 1991, **135**:317-322
- Linde K, Jobst K: **Homeopathy for asthma (Cochrane Review)** *In: The Cochrane Library, Issue 4, 1998. Oxford: Update Software.*
- Lüdtke R, Wilkens J: **Klinische Wirksamkeitsstudien zu Arnica in homöopathischen Zubereitungen** *In: Karl und Veronica Carstens-Stiftung, Jahrbuch Band 5 (1998). Edited by Albrecht H, Frühwald M. Essen: KVC Verlag 1999* 97-112
- Ernst E, Pittler MH: **Efficacy of homeopathic Arnica. A systematic review of placebo-controlled clinical trials** *Arch Surg* 1998, **133**:1187-1190
- Taylor MA, Reilly D, Llewellyn-Jones RH, McSharry C, Aitchison TC: **Randomised controlled trials of homeopathy versus placebo in perennial allergic rhinitis with overview of four trial series** *BMJ* 2000, **321**:471-476
- Vickers AJ, Smith C: **Homeopathic Oscillocochinum for preventing influenza and influenza-like syndromes (Cochrane Review)** *In: The Cochrane Library, Issue 1, 2000. Oxford: Update Software.*
- Ernst E: **Homeopathic prophylaxis of headaches and migraine? A systematic review** *J Pain Symptom Manag* 1999, **18**:353-357
- Wiesnauer M, Lüdtke R: **A meta-analysis of the homeopathic treatment of pollinosis with Galphimia glauca** *Forsch Komplementärmed* 1996, **3**:230-236
- Lüdtke R, Wiesnauer M: **Eine Metaanalyse der homöopathischen Behandlung der Pollinosis mit Galphimia glauca** *Wien Klin Wochenschr* 1997, **147**:323-327
- Ernst E, Resch KL: **Clinical trials of homeopathy: a re-analysis of a published review** *Forsch Komplementärmed* 1996, **3**:85-90
- Ernst E: **Are highly dilute homeopathic remedies placebos?** *Perfusion* 1998, **11**:291-292
- Jonas WB, Linde K: **Homeopathy and rheumatic disease** *Rheum Dis Clin North America* 2000, **26**:117-123
- Linde K, Scholz M, Ramirez G, Clausius N, Melchart D, Jonas WB: **Impact of study quality on outcome in placebo-controlled trials of homeopathy** *J Clin Epidemiol* 1999, **52**:631-636

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