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, oscillococcinum 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. Homoeopathic remedies are often prescribed in high dilutions some of which are unlikely to contain any molecules of the originally diluted agents. In consequence, homoeopathic 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 homoeopathic 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 homoeopathic 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 homoeopathic 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, Oscillococcinum 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 | Features | Studies | Results | Conclusion |
|-------------|------|------------|---------------------|----------|---------|---------|------------|
| **All homoeopathy in all conditions** |      |            |                     |          |         |         |            |
| Cucherat    | 2000 | all        | all/placebo         | 17 RCT   | y / 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 placebo. Studies of high quality more likely to be negative |
| Linde 97    | [8]  | all        | all/placebo         | 89 RCT   | 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 homoeopathy is placebo. No firm evidence for any single condition. |
| Walach 97   | [9]  | all        | all/placebo         | 41 RCT   | y / y / | Random effect size $g = 0.259$ | The effects of homoeopathy are not different from placebo on a statistical level. |
| Lutz 93     | [10] | all        | all/placebo,        | 21 RCT/C | y / p / | Results of available studies | No clear conclusions drawn. (Comment: thesis mainly discussing problems of meta-analysis) |
| Kleijnen    | 91   | all        | all/placebo         | 107 CCT  | y / p / | 81 trials reported positive results. | Available evidence positive but not sufficient to draw definitive conclusions. |
| Hill 90     | [12] | all        | all/placebo,        | 40 RCT   | n / p / | The authors of half of the studies concluded that homoeopathy was effective, further 7 promising are effective. | The results do not provide acceptable evidence that homoeopathy treatments are effective. |
| **Individualized homoeopathy in all conditions** |      |            |                     |          |         |         |            |
| Ernst 99    | [13] | all        | individualized/     | 3 RCT, 3 | y / p / | All trials were burdened with serious methodological flaws. Results non-uniform | The relative efficacy of individualized homoeopathy compared to conventional treatments is not known. |
| Linde 98    | [14] | all        | individualized/     | 32 RCT   | 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 convincing due to shortcomings and inconsistencies. |
| **Various homoeopathic treatments in a single condition/area** |      |            |                     |          |         |         |            |
| Barnes 97   | [15] | postoperative | various/placebo     | 4 RCT, 2 | y / y / | Time to first flatus in homoeopathy significantly shorter. Best trial negative. Most trials with severe flaws. The published evidence does not support the hypothesis that homoeopathic remedies are effective for muscle soreness. | Available evidence positive but several caveats preclude definitive conclusions. |
| Ernst 98    | [16] | delayed-   | various/placebo     | 8 double-blind trials | y / y / | 3 RCT showed no significant effects over placebo | Published evidence does not support... |

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**Features**

- 1: All trials or all trials except those comparing two different interventions
- 2: Homoeopathy trials only
- 3: Placebo trials only
- 4: RCT
- 5: CCT

**Notes**

- RCT: Randomized Controlled Trial
- CCT: Controlled Clinical Trial
- y: Yes
- n: No
- n.y: Not known.
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 *Oscillococcinum* 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

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

| Reviewer | Condition | Intervention | Design | Positive/Negative/Neutral | Outcome |
|----------|-----------|--------------|--------|---------------------------|---------|
| Jacobs 91 | Rheumatic diseases | Various/placebo | 4 CCT | y/y/n | 3 of 4 trials positive. Quality poor |
| Linde 98 | Asthma | Various/placebo | 3 RCT | y/y/y | Trials highly heterogeneous. Two reports statistically significant effects |
| Lüdtke 99 | Arnica in various conditions (mainly various tissue traumata) | All | 23 RCT, 14 CCT | y/y/y | Quality often low. 13 of 35 studies |
| Linde 98 | Asthma | Various/placebo | 3 RCT | y/y/y | Trials highly heterogeneous. Two trials positive, 2 trials positive |
| Arnica in various conditions (mainly various tissue traumata) | All | Arnica/placebo, no treatment | 23 RCT, 14 CCT | y/y/y | Available evidence suggests that arnica can be efficacious. Further rigorous trials needed |
| Ernst 98 | Trauma | Conventional | 4 RCT, 4 CCT | y/n | Trend. Most studies with severe flaws |
| Similar homoeopathic treatments in one condition/a group of conditions | Taylor | Allergic | 4 RCT | n/n/n | Available evidence suggests that isopathic nosodes were different from placebo on both subjective and objective measures |
| Vickers | Influenza-like syndrome | Oscillococcinum/placebo | 7 RCT | y/y/y | No evidence for preventative effects |
| 2000 ** | Conditions | Nosodes/placebo | 4 RCT | y/y | Pooled analysis of 100 mm visual analogue scores 9.8 (95%CI 4.2;15.4) better with isopathy |
| Wiesenauer | Pollinosis | Galphimia/placebo | 8 RCT, 1 CS, 2 UCS | p/n/n | Responder RR galphimia vs. placebo 1.25 (95%CI 1.09; 1.43) |
| 96 ** | [24,25] | | | | |

*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
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 homoeopathy 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 homoeopaths.

Competing interest
KL, AV, GT 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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