

A systematic review of homoeopathy for the treatment of fibromyalgia

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Abstract Homoeopathy is often advocated for fibromyalgia (FM) and many FM patients use it. To critically evaluate all randomised clinical trials (RCTs) of homoeopathy as a treatment for FM, six electronic databases were searched to identify all relevant studies. Data extraction and the assessment of the methodological quality of all included studies were done by two independent reviewers. Four RCTs were found, including two feasibility studies. Three studies were placebo-controlled. None of the trials was without serious flaws. Invariably, their results suggested that homoeopathy was better than the control interventions in alleviating the symptoms of FM. Independent replications are missing. Even though all RCTs suggested results that favour homoeopathy, important caveats exist. Therefore, the effectiveness of homoeopathy as a symptomatic treatment for FM remains unproven.

Keywords Fibromyalgia · Homoeopathy · RCT · Systematic review

Introduction

Fibromyalgia (FM) is a chronic pain condition which can be challenging to treat with conventional medicine [1]. This

could be one reason why FM patients frequently turn to complementary and alternative medicine (CAM) [2]. Homoeopathy is one form of CAM that has become a popular treatment choice [3]. Several aspects of the treatment (e.g. long, empathetic consultation and a high degree of individualising the remedies), might make it particularly attractive to patients with FM.

The homoeopathic approach involves a largely somatically focussed assessment alongside the actual treatment (the remedy) whilst emotional symptoms are also assessed and assumed to be targeted by the remedy. Thus, homoeopathy accommodates the multidimensional nature of FM symptoms. According to the concepts of classical homoeopathy, if the optimal remedy is correctly prescribed, any co-existing emotional factors will also be alleviated in conjunction with the physical symptoms [4]. However, as the mechanism for homoeopathic action, if any, is not evident, it seems necessary to ascertain the extent that homoeopathic remedy per se is the trigger for any clinical outcome.

The aim of this systematic review was to evaluate whether homoeopathic treatments can have a therapeutic effect on the symptoms of fibromyalgia.

Methods

The following databases were searched from their inception to August 2009; MEDLINE, EMBASE and PSYCHINFO via the OVID interface, CINAHL and AMED via the EBSCO interface and CENTRAL via the Cochrane library. No restrictions were applied regarding language or time (Fig. 1). Reference lists of all full text articles were hand-searched for additional studies as were bibliographies of major reviews [5–7].

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Search Strategy MEDLINE (via OVID)

1. fibromyalgia.af.
2. fibromyal\$.af.
3. fibrositis.af.
4. fibromyositis.af.
5. chronic ADJ widespread ADJ pain.af.
6. fibromyalgia/.
7. OR/1-6
8. homeopathy.af.
9. homeopathic.af.
10. homeop\$.af.
11. homoeopathy.af.
12. homoeopathic.af.
13. homoeop\$.af.
14. homoop\$.af.
15. homeopathy/
16. OR/8-15
17. clinical trial.pt.
18. trial\$.ti,ab.
19. RCT.ti,ab.
20. random\$.ti,ab.
21. placebo.ti,ab.
22. sham.ti,ab.

Fig. 1 Search strategy MEDLINE (via OVID)

Study selection

All titles and abstracts retrieved from the searches were assessed for eligibility. All articles appearing to meet the inclusion criteria based on reading the abstract were retrieved as full documents and independently considered for inclusion by two reviewers (RP, RT). Disagreements were resolved through discussion with the third author (EE). For inclusion into the review, trials were required to meet the following pre-defined criteria: participants had to be recruited into the trial based on a diagnosis of FM with the selection criteria made transparent to the reader (e.g. self referrals/referral from specialist centre). The intervention had to be a homoeopathic medicine or homoeopathic package of care; the remedy selection could be individualised and therefore change as the treatment progressed. The remedy selection needed to be carried out by a qualified homoeopath. Placebo, no treatment, treatment as usual or waiting list control groups were permissible for the control groups. The primary outcomes had to be either: the severity of FM symptoms as measured by validated assessment tool (e.g., Fibromyalgia Impact Questionnaire; FIQ), standardised measures of pain (e.g., visual analogue

scales were acceptable), tender point count and fatigue; emotional health (as rated by patient or observer); need for medication; physical functioning; sleep quality or quality of life measure. Only studies that were described as randomised clinical trials (RCT), which evaluated the effectiveness of homoeopathy versus an appropriate comparator (as outlined above) were included. Only completed studies were included (reports of ongoing trials were excluded). Data from included studies were extracted independently by two reviewers (RP, RT) using a standardised form with pre-defined criteria. Disagreements between reviewers were resolved through discussions with the third author.

Quality assessment

The methodological quality of all included RCTs was evaluated independently by two researchers (RP, RT) using the Jadad score [8]. Further methodological quality data were extracted based on recommendations from the Cochrane Handbook of Systematic Reviews of Interventions (Cochrane Collaboration 2008) [9] and the Jadad Criteria for Clinical trials on Pain Management, 2000 [10].

Meta-analysis

A meta-analysis was considered but this plan had to be abandoned due to the clinical heterogeneity of the primary data.

Results

Four studies fulfilled the above criteria and are summarised in Tables 1 and 2.

Fisher [11] performed a randomised, double blind, placebo-controlled trial to compare the effectiveness of three commonly used homoeopathic remedies for FM; *Rhus toxicodendron*, *Arnica montana* or *Bryonia*. Twenty-four patients with FM were assessed in terms of sleep, pain, number of tender spots and analgesic consumption at baseline, 1, 2 and 3 months. Each patient's symptom picture was scored for goodness-of-fit to the remedy selected. The experimental group received one of the three remedies in 6c potency twice a day for 3 months. The placebo group took indistinguishable placebos during the same period of time. Analysis of the differences between groups in terms of pain and sleep measured by visual analogue scales (VAS) showed no significant effects: $p=0.19$, $p=0.078$, respectively. However, when broken down to distinguish between well-indicated remedies as opposed to poorly indicated remedies there were significant differences ($p<0.05$) in pain scores and in sleep scores (at 2 and 3 months) for those participants whose remedies were

optimal fits. There was no significant difference in tender spot counts between groups and analgesic consumption results were not reported.

In 1989, Fisher et al. [12] carried out another RCT specifically assessing the effects of *R. toxicodendron* 6c in the treatment of FM. The decision to use just this remedy was based upon the results of the previous study indicating 42% of FM patients fitted the *R. toxicodendron* picture. This study used a cross-over design. Thirty FM patients, fitting the *R. toxicodendron* picture (as established by a homoeopath), received both active treatment and placebo treatment in random order for 1 month each. The dose was two tablets three times daily. After the initial consultation, there was no further contact with the homoeopath. At the end of the treatment period, the number of tender points in the placebo group was significantly higher than in the experimental group ($p < 0.005$). Improvements in pain and sleep, measured by a combined VAS, was also significantly greater for the *rhus tox* group compared to the placebo group ($p = 0.0052$). A re-analysis of Fisher's data was published by Colquon in 1991 [13]. Distribution-free randomisation tests were applied separately to the scores of pain, sleep and tender points and no significant treatment effects after the first treatment period was found.

Bell et al. [14, 15] carried out an RCT testing the feasibility of using homoeopathic remedies in the treatment of FM. Sixty-two FM patients were included. Rather than assessing the efficacy of just one or a few homoeopathic remedies, remedy selection was kept completely open, resulting in 41 remedies being utilised in the trial. LM remedies (diluted to 1 in 50,000) in solution were used. Patients were interviewed and assessed by two homoeopaths at baseline, 2 and 4 months. They were able to change the remedy or the dosage at any time (which emulates how homoeopaths work). Primary outcome measures were collected at baseline, 3 months (and 6 months after cross-over option). After 4 months, all patients were given the option to change group for an additional 2 months. At 3-month follow-up, for treatment completers, the experimental group showed a significant greater improvement in tender point count ($p < 0.05$) and tender point pain on palpation ($p < 0.01$), appraisal of FM scores ($p < 0.05$) and global health rating ($p < 0.05$; data adjusted for anger and depression). Further analysis indicate that a significantly higher proportion of patients in the homeopathy group experienced at least a 25% improvement in tender point pain on examination (13/26) versus placebo group (four/27), (Fisher's exact test, two-tailed, $p = 0.008$). There was a trend for the homoeopathic group to improve on the affective dimension of the McGill Pain Questionnaire (MPQ), POMs depression and POMs anger-hostility (all $p < 0.10$). At 6 months [15], those who had decided to stay in the experimental group rather than switch, showed significantly greater gains in global health than the placebo-switch subgroup.

Rather than assessing the specific effects of the homoeopathic remedy in isolation, Relton [16] compared a homoeopathic package of care as an adjunct to usual care with usual care alone in a pilot, feasibility study. Forty-seven FM patients were recruited and assessed at baseline and 22 weeks on a number of outcome measures. The primary outcome measure was the FIQ total score. Intent to treat between groups analysis found a significantly greater reduction in the FIQ total scores ($p < 0.01$) for the homoeopathic package of care being observed, but no significant difference in FIQ pain scores was found. In the completers' sample between-groups change score analysis, there were significantly greater reductions in the McGill pain scores, McGill Affective Scores, McGill Affective and Sensory Scores, the FIQ fatigue and the tiredness upon waking scores in the homoeopathic care group than the usual care group (all $p < 0.05$). In addition, the number of days felt good ($p < 0.05$) was significantly greater in the homoeopathy group. There were no significant differences in tender point count, EuroQol, MYMOPS or HADS between the groups.

Discussion

All four RCTs included in this systematic review reported evidence supporting the effectiveness of homoeopathy compared to placebo or to usual care. However, none of them is free from flaws.

The first study by Fisher suggested no effect of the homoeopathic treatments for the total group of patients but a significant result in favour of homoeopathy when broken down into well-indicated remedies. The fact that the authors individualised the remedies to some degree indicates a more realistic approach to homoeopathic practice, although total individualisation of remedy selection would have been more in keeping with concepts of classical homoeopathy. The main points of critique are the very small sample size and the short duration of treatment. The paucity of details given on the randomisation process means that it is impossible to assess its appropriateness. The lack of demographic information on the patients limits interpretation of the study findings.

In 1989, Fisher et al suggested that a homoeopathic remedy can lead to improvements greater than those of a placebo. A repeated measures design was used with no washout period between active and placebo. As homoeopathic remedies are claimed to continue having an effect long after the remedy has been administered, the possibility that the data were confounded by carryover treatment effects cannot be discounted. Further problems with the study were the small sample size, insufficient information relating to the randomisation procedure and no demograph-

Table 1 Results table

First author (date)	Sample size	Participant groups	Treatment schedules	Assessment schedule for most relevant outcome	Type of analysis and measure	Main results
Fisher [11]	N=24	Intervention N=12 <i>arnica</i> 6c (n=5) or <i>bryonia</i> 6c (n=2) or <i>rhus tox</i> 6c (n=5) 2x/day Control N=12	2 active or placebo tablets /day for 3 months	Baseline, 1, 2, 3 months	VAS for pain and sleep whole treatment period. TSC (Mann-Whitney U test)	Overall, n/s difference between groups for pain but, when remedy well indicated ^a , sig less pain in intervention group $p=0.046$ (AUC). N/s when poorly indicated ^b $p=0.81$ Overall, n/s difference between groups for sleep, but when remedy well indicated ^a sig improvement in sleep in intervention group $p=0.018$ (AUC). Sleep measures were significantly different ($p<0.05$) at specific times points (2 and 3 months) but n/s when poorly indicated ^b $p=1.00$ Overall, TSC: n/s differences between groups for TSC ^c
Fisher [12]	N=30	<i>arnica</i> placebo N=3 <i>bryonia</i> placebo n=4 <i>rhus tox</i> placebo n=5 2x/day Intervention N=30	Participants received both active and placebo treatment for one month each in random sequence	Comparison made at end of active and placebo treatments	TPC (Wilcoxon), VAS for combined pain and sleep (Paired <i>t</i> test) randomisation tests	Significant difference between number of tender points after intervention treatment = 10.6 and after placebo treatment = 14.1 ($p<0.005$). Number of patients with improved pain or sleep after intervention N=53 and after placebo N=27 ($p=0.0052$) Overall assessment showed a non-significant preference for the active treatment. Re-analysis for the first period only indicates no effect of treatment
Re-analysis by Colquhoun [13]		Control N=30 Placebo 2 tablets 3x/day				
Bell [14, 15]	N=62	Intervention N=30 Overall number of remedies given = 41 Given as LM potencies Control N=32 Placebo	LM1 daily dose of individual remedy, increasing to LM 2, LM3 as necessary, or placebo (remedy-free solvent)	Baseline, 3 months, (plus 6 months— 2 months after crossover)	TPC TPP on palp Appraisal of FM Global Health Rating MPQ POMs (ANOVA adjusted for baseline)	Main outcomes at 3 months (N=53, 85.4%): When adjusted for baseline POMs depression and POMs anger/hostility scores, a significant reduction in tender point count -1.9 (-3.5 to -0.24) $p<0.05$, tender point pain on palpation -22.6 (-38.3 to -6.9) $p<0.01$ in homeopathic group. Appraisal of FM scores improved significantly -2.1 (-4.0 to -0.28) $p<0.05$, as did global health rating 1.5 (0.14 to 2.8) $p<0.05$ after receiving homeopathic treatment compared to placebo.

<p>Trends in favour of homoeopathic treatment were found on MPQ affective dimension, POMs depression and POMs anger hostility ($p < 0.10$)</p> <p>No significant difference in MPQ sensory pain or POMs fatigue between the groups.</p> <p>Change in outcome scores: Significant greater reduction in the FIQ total score in the homoeopathic care group -6.53 (15.03) compared to usual care 1.74 (12.85) $p < 0.01$. N/s difference in FIQ pain score.</p>	<p>Relton [16]</p> <p>$N = 47$</p> <p>Intervention (homoeopathic care) $N = 23$</p> <p>Usual care plus 1 h in-depth interview with homoeopath followed by 4x 30 min interviews (4–6 weeks apart). Individually tailored homoeopathic remedies were given</p>	<p>1 h baseline interview for remedy selection, then 4 x 30 min follow up interviews where remedy choice and potency could be assessed and changed</p>	<p>Baseline, 22 weeks</p> <p>Intent to treat sample</p>	<p>Change scores for FIQ total score and FIQ pain score (ANCOVA, adjusted for baseline differences between groups)</p> <p>Treatment completers ($n = 36$, 76.6%)</p> <p>MPQ (ANCOVA, adjusted for baseline differences between groups)</p> <p>Change in outcome scores: McGill Affective scores -0.55 (3.62) $p < 0.05$ and affective and sensory scores -3.50 (10.56) $p < 0.05$ were significantly improved in the homoeopathic group compared to usual care group. FIQ sub-scores showed a significant reduction in fatigue -1.3 (2.11) $p < 0.05$ and tiredness upon waking -1.30 (2.09) $p < 0.05$ in the homoeopathic care group compared to usual care.</p> <p>Outcome measures scores: significant differences at 22 weeks for FIQ number of days felt good (usual care 1.88 (1.86), homoeopathy 3.25 (1.97) $p < 0.05$), FIQ tiredness on waking (usual care 8.6 (1.8), homoeopathy 7.1 (2.1), $p < 0.05$), FIQ stiffness (usual care 8.4 (1.7), homoeopathy 6.6 (2.7) $p < 0.05$) and McGill pain score VAS usual care 78.1 (19.7), homoeopathy 64.1 (24.3) $p < 0.05$ were found.</p> <p>There were no significant differences in TPC, EuroQol, MYMOPS or HADS scores between the groups</p>
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^a well indicated (score 2)—patient has three or more symptoms characteristic of the remedy prescribed

^b poorly indicated (score 0 or 1)—patient has one or two characteristic symptoms or 0 no definitive prescribing symptoms

^c tender spot count—inter-group matching is very poor so that comparison was not possible

N number of participants, VAS visual analogue scale, AUC area under curve, n/s not significant, TSC tender spot count, TPC tender point count, TPP on palp tender point pain on palpation, LM LM dilutions are 1 in 50,000 dilution factor, MPQ McGill Pain Questionnaire, FIQ Fibromyalgia Impact Questionnaire, POM profile of mood states, HAD hospital anxiety and depression scale, EuroQol European Quality of Life Scale

Table 2 Methodological quality of trials

Authors and date	Was the treatment allocation randomised?	Was the randomization procedure described and was it appropriate?	Was the treatment allocation concealed?	Were groups similar at baseline on prognostic indicators?	Were blind outcome assessments conducted?	Was the number of withdrawals/dropouts in each group mentioned?	In addition to stating the number of withdrawals/dropouts, were reasons given for each group?	Was an analysis conducted on the intention-to-treat sample?	Was an a priori power calculation described?	What was the experience level of the homoeopath?	Were co-morbidities avoided/controlled for?	Was the therapeutic time equivalent between groups/conditions?	Jadad score (maximum score = 5)
Fisher [11]	Yes	Not described	NR	NR	Yes	No	No	NR – but assumed as no drop outs	No	NR	NR	Yes	3
Fisher [12]	Yes	Not described	Yes	N/A	Yes	No	No	NR	No	NR	NR	Yes	3
Bell [14]	Yes	Yes it was computer generated	Yes	No: active group had more tender pain points on examination and used more anti-histamine and expectory drugs	Yes	Yes 14.5% in total	Yes but not by group	Yes— carried out but findings not reported	Yes	Minimum 5 yrs in practice	Yes	Yes	4
Relton [16]	Yes	SPSS random number generator and block randomisation — opaque sealed envelopes containing group assignment	No	Yes	No but tender point count was conducted by blinded assessor	Yes	No	Yes	Yes	NR	Yes	No	2

NR not reported

ic data of the patients. The re-analysis by Colquhoun [13] suggested that there was no evidence for the efficacy of homoeopathic treatment when distribution-free randomisation tests were employed. He criticised Fisher for combining pain and sleep scores thus invalidating the results.

The feasibility study by Bell et al. [14] was a well-constructed RCT (albeit slightly underpowered) which scored highly on methodological quality (Jadad score 4), only failing to obtain the highest Jadad score of 5 because reasons for drop out were reported for all of the participants rather than by group. The randomisation process was transparent and appropriate (computer generated with treatment allocation concealed), and an indistinguishable placebo was used. A detailed description of participants was disclosed to enable assessment of generalisability. Bell et al. individualised the remedy selection and allowed for changes to remedy and dosage (as in real homoeopathic prescribing). There was no restriction on remedy chosen except that it had to be given as an LM potency. They included a large number of outcome measures which generated large amounts of data. In terms of the crossover part of the trial [15], it has been argued that a longer washout period is needed between receiving the active and placebo solution; estimating a 1 month per year of the suffering [17]. Interpretation of the results obtained during the crossover period is more problematic as it is difficult to establish whether the lack of washout period had confounded the data obtained from active-switch group. Nonetheless, interesting differences between groups were observed which suggests that homoeopathic remedies were affecting FM symptoms over and above the non-specific placebo effects.

One proposed mechanism for homoeopathy is time-dependant sensitisation (“*the progressive, persistent amplification of responses within a susceptible individual from repeated, intermittent exposures to an environmental factor, pharmacological or non-pharmacological in nature*” [18]). In addition to the primary paper, Bell et al published further articles [18] on this study examining possible sensitisation-related changes in electroencephalography (EEG) relative alpha magnitude in order to test the hypothesis that repeated administration of individualised homoeopathic remedies will produce measurable increases in EEG alpha responses over time. In line with their hypothesis, the authors reported significant patterns of progressive increases in alpha (1 and 2) magnitudes during the sniff tests in the active group, whereas the placebo group’s declined between the initial and 3-month sessions. Baseline measures of alpha did not differ which indicates it is the homoeopathic remedy that brings about the effect. Over the whole sample at the end of the 6-month study, increased alpha magnitudes correlated significantly with total amount of time on active remedy

treatment either due to randomised assignment or optional crossover decision which is consistent with the time dependant sensitisation (TDS) hypothesis that it is amount of time on the remedy rather than dosage. Although not a clinical outcome, the investigation of the physiological differences in neurological responses between conditions is an important development in homoeopathic research.

Bell et al. [19] also looked at EEG cordance in relation to responses to homoeopathic treatment. This is a measure derived from absolute and relative scalp EEG power which has been found to correlate with patterns of brain blood flow and metabolic functional neuro-imaging studies. Based on evidence from prior depression studies [20, 21] they hypothesised that there would be differences in EEG cordance between exceptional and non-exceptional responders to homoeopathic treatment. When EEG cordance was analysed, the six “exceptional responders” had more negative initial EEG cordance difference scores in the prefrontal cortex (FP1 and FP2). Right prefrontal cordance correlated significantly with reduced local pain and trait absorption (ability to focus attention selectively and fully). The authors also reported a significant finding at the 10% level in improvement in global health.

Although the findings of the study were interesting, they need replication before any firm conclusions can be drawn, both the EEG and cordance studies provide some indication that homoeopathic remedies might lead to physiological responses which differ from non-specific or placebo responses to homoeopathic intervention. Both studies highlight the need to consider differences in individual characteristics which may correlate with or predict trial outcomes.

Relton et al. [16] also reported favourable results. The design of this study did not control for placebo effects, although the authors make it clear that they did not set out to test whether homoeopathic remedies work better than placebo. They aimed at testing the feasibility of using a homoeopathic package of care in addition to usual care. Arguably, the results would have been more meaningful if Relton had compared the homoeopathic package of care with the same package of care where patients saw a homoeopath for an equal length of time but did not receive an active treatment, instead a placebo sugar pill. This would have controlled for the non-specific effects of the therapeutic setting that may have brought about the positive effects found in this study. A systematic review of trials adopting this design has shown that such studies will always generate a positive result, even if the experimental treatment has no specific therapeutic effects [22]. In addition, a high drop-out rate in the usual care group was observed in Relton et al’s study (eight/24) which reduced the power of the study. The between-group analyses from the trial completers look favourable for homoeopathy but

with such a large drop-out in the usual care group, it is difficult to relate to the homeopathic treatment alone. The only significant result from the intent-to-treat sample was a greater reduction in the FIQ total score in the homeopathic care group -6.53 (15.03) $p < 0.01$ than usual care. This study, however, does not tell us much about homeopathy per se.

When evaluating the evidence for or against homeopathy one should briefly comment on the plausibility of this treatment. Homeopathy is based on two main principles [4]. The Law of Similars claims that, if a substance causes symptoms in healthy volunteers, it can be used to treat these symptoms effectively when they occur in patients. The law of the infinitesimal dose holds that, if a substance is serially diluted in the homeopathic way, it becomes not weaker but stronger, even if the dilution is beyond Avogadro's number. Currently, there is little scientific evidence to support these theoretical principles. It is therefore difficult to accept that homeopathy is biologically plausible [23]. Bell et al's [18] research into TDS, however, does provide an alternative methodology for investigation physiological changes in response to homeopathic remedies.

Our review has a number of limitations. Even though our searches were thorough, we cannot be sure that all relevant RCTs were located. Negative studies tend to remain unpublished [24]. This bias could therefore have distorted the overall picture. All the four RCTs tested different homeopathic treatments or approaches; this means that no independent replication of any of the tested approaches exists. The paucity and, at times, disappointing quality of the available RCTs render firm conclusions problematic.

In summary, the findings of the four existing RCTs all favour homeopathy over controls. Yet none of the studies is sufficiently rigorous to provide a definitive answer. Future studies should minimise bias more effectively than did the trials available so far.

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