Efficacy of multicomponent treatment in fibromyalgia syndrome: a meta-analysis of randomized controlled clinical trials

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CRD summary
The review concluded there was strong evidence that multicomponent treatment had beneficial short-term effects on the key symptoms of fibromyalgia syndrome including pain, fatigue and depressive mood, and of improved self-efficacy and physical fitness post-treatment. The authors’ conclusions appeared reasonable, but it should be borne in mind that results of some outcomes were based on a small number of trials.

Authors’ objectives
To evaluate the efficacy of multicomponent treatment of fibromyalgia syndrome.

Searching
MEDLINE, PsycINFO, Scopus and the Cochrane Library were searched without language restriction to December 2007. Search terms were reported. Reference lists of retrieved articles, reviews and evidence-based guidelines were also searched for additional papers. European experts in the field were contacted for additional studies. Only studies published as full reports in paper format were included; abstracts were excluded from the review.

Study selection
Randomised controlled trials (RCTs) evaluating multicomponent treatment of fibromyalgia syndrome compared with no treatment, care as usual or other treatment with a lower intensity than multicomponent therapy were eligible for inclusion. To be included trials had to include at least two non-pharmacologic therapies (e.g. at least one educational or other psychological therapy and at least one exercise therapy); diagnosis of fibromyalgia syndrome must have been based on recognised criteria; data had to be suitable for meta-analysis.

Outcomes were required to be symptom-specific of the key symptoms of fibromyalgia syndrome including pain, fatigue, sleep disturbance, depressive symptoms, health-related quality of life, relevant pain-related psychological domains (e.g. self-efficacy pain), and/or objective tests of physical fitness.

Included trials compared multicomponent therapy with education, relaxation, waiting list, and treatment as usual. Multicomponent therapy included various combinations of swimming, relaxation, exercise, Tai Chi, self-management techniques, cognitive behavioural therapy, or massage. Most of the trials were conducted in Europe; the remainder were conducted in the USA or Canada. Duration of treatment ranged from 18 to 46 hours over a period of six to 25 weeks. The proportion of women in the included trials was 96%; the median mean age was 44.7 years (range 44 to 50 years). Some trials excluded patients with somatic disease or with mental disorders. Outcomes assessed included pain, fatigue, sleep, depressive symptoms and health-related quality of life.

Two reviewers independently screened papers for inclusion. The authors did not state how disagreements were resolved.

Assessment of study quality
 Validity was assessed using the van Tulder Score, with a maximum possible total of 11 points. RCTs scoring 8 to 11 points were classified as high quality, those scoring 5 to 7 points as moderate quality and those scoring between 1 and 4 points as low quality.

The authors did not state how many reviewers assessed validity.

Data extraction
Data on mean value and standard deviation (SD) or mean changes were extracted for the relevant outcomes from each trial. These were used to calculate the weighted mean difference (WMD) where the same instrument was used for the
outcome measure or the standardised mean difference (SMD) where outcomes were assessed by different instruments. Trial authors were contacted for missing data, and trial with any remaining missing data were excluded from the meta-analysis.

Two reviewers independently extracted data using standardised forms. Disagreements were resolved through discussion.

**Methods of synthesis**

Data were pooled using a fixed-effect model, except when there was evidence of significant heterogeneity where a random-effects model was used. Heterogeneity was assessed using the $I^2$ statistic. Sensitivity analyses were conducted to determine whether the duration of treatment (less than 30 hours compared to 30 hours or more) and methodological quality of each trial had a significant effect on the results. Where more than one outcome measure was assessed a predefined order of preference was used for entry into the meta-analysis. Analysis was conducted on an intention-to-treat basis (ITT) where possible.

Modified levels of evidence descriptors were used to classify results of the meta-analysis data as: strong (consistent findings in at least two moderate quality RCTs); moderate (consistent findings in at least two low quality RCTs or one moderate-quality RCT); limited (findings in one low quality RCT); conflicting (inconsistent findings among multiple RCTs); and no evidence (findings in no RCTs). Publication bias was assessed using visual inspection of funnel plots and the file-drawer test. Follow-up ranged from one month to 15 months post-treatment.

**Results of the review**

Nine RCTs ($n=1,119$) were included in the review. Six RCTs were of moderate quality and three RCTs were low quality.

**Post-treatment:** There was strong evidence to show that compared to control, multicomponent treatment reduced: post-treatment pain (SMD -0.37, 95% CI -0.62 to -0.13; five RCTs); fatigue (WMD -0.85, 95% CI -1.50 to -0.20; three RCTs); depressive symptoms (SMD -0.67, 95% CI -1.08 to -0.26; four RCTs); limitations in health-related quality of life (SMD -0.59, 95% CI -0.90 to -0.27; three RCTs). There was also strong evidence that multicomponent treatment improved self-efficacy pain (SMD 0.54, 95% CI 0.26 to 0.82) and physical fitness (SMD 0.30, 95% CI 0.02 to 0.57; four RCTs) post-treatment compared to control. There was no evidence of statistical heterogeneity for these analyses.

**Three to four months follow-up:** There was strong evidence that multicomponent therapy improved self-efficacy pain (SMD 0.47, 95% CI 0.14 to 0.80; two RCTs) at three to four month follow-up, but no evidence of efficacy on pain, sleep disturbances, depressive symptoms, health-related quality of life or self-efficacy pain.

**Six to 12 months follow-up:** At six to 12 month follow-up, there was no evidence of effect for multicomponent therapy compared to control for pain, fatigue, sleep disturbances, depressed mood, health-related quality of life, or self-efficacy pain. There was strong evidence that positive effects on physical fitness (SMD 0.30, 95% CI 0.09 to 0.51; two RCTs) can be maintained in the long term (median follow-up seven months).

There was no evidence of publication bias. Results of sensitivity analysis were also reported.

**Authors’ conclusions**

There was strong evidence that multicomponent treatment had beneficial short-term effects on the key symptoms of fibromyalgia syndrome, including pain, fatigue and depressive mood, and of improved self-efficacy and physical fitness post-treatment. Strategies to maintain the benefits of multicomponent treatment in the long term need to be developed.

**CRD commentary**

The review question was specified and inclusion criteria were clearly defined for intervention, participants, outcomes and study design. Several relevant sources were searched. Efforts were made to reduce language but not publication bias. Formal assessment found no evidence of publication bias. Appropriate methods were used to select trials and extract data, but it was unclear whether similar methods were used for assessment of validity.
An appropriate validity assessment was conducted and the results appropriately informed the analysis. Trials were appropriately combined in a meta-analysis and heterogeneity was assessed. Results of heterogeneity tests were only reported for the main results. The authors reported that medication use was not controlled in most trials, so it was not possible to determine whether the effects reported are due solely to multicomponent therapy.

The authors’ conclusions appeared reasonable, but it should be borne in mind that results of some outcomes were based on a small number of trials.

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