Meta-analysis

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The effect of mud therapy on pain relief in patients with knee osteoarthritis: A meta-analysis of randomized controlled trials

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Abstract

Objectives: A meta-analysis was conducted to examine the effect of mud therapy on pain relief in patients with knee osteoarthritis (OA).

Methods: A detailed search of PubMed®/MEDLINE® was undertaken to identify randomized controlled trials and prospective comparative studies published before 9 March 2013 that compared mud therapy with control group treatments in patients with knee OA.

Results: A quantitative meta-analysis of seven studies (410 patients) was performed. There was a significant difference between the groups in the visual analogue scale pain score (standardized mean difference [SMD] −0.73) and Western Ontario and McMaster Universities Osteoarthritis Index pain score (SMD −0.30), with differences in favour of mud therapy.

Conclusions: Mud therapy is a favourable option for pain relief in patients with knee OA. Additional high-quality randomized controlled trials need to be conducted to explore this issue further and to confirm this conclusion.

Keywords

Pain, mud therapy, knee, osteoarthritis, meta-analysis

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Introduction

Knee osteoarthritis (OA), one of the most common forms of arthritis, causes pain for ≥10% of people aged over 60 years.[1] Balneotherapy, defined as a mineral bath, is a conservative treatment that has been recommended by the European League Against

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Rheumatism (EULAR) as an effective option for hip OA.[2] In Japan, the traditional form of balneotherapy is water bathing in hot water springs; in Europe, balneotherapy involves bathing in minerals. Mud has been defined by the International Society of Medical Hydrology as a natural substance, consisting of varying amounts of organic and inorganic materials that are applied topically as therapeutic agents.[3] The heating effect of mud can relieve muscle spasms and pain.[4] Several randomized controlled trials have been undertaken to assess the use of mud therapy (also known as pelotherapy) in patients with knee OA, but its effectiveness remains controversial.[5–11] The current study hypothesized that mud treatment was effective, with important public health and clinical implications; a meta-analysis was therefore performed to determine the effect of mud therapy on pain relief in knee OA.

Materials and methods

Search strategy

The meta-analysis was conducted in accordance with PRISMA guidelines (http://www.prisma-statement.org/statement.htm). Two authors (H.L. and C.Z.) independently completed a search of the electronic databases PubMed®/MEDLINE®, using the following search terms: (mud OR pelotherapy OR peloid) AND (osteoarthritis). Databases were searched from the earliest records up to and including 9 March 2013, without language restrictions.

Inclusion and exclusion criteria

Studies were considered eligible if they met the following criteria: (i) patients had a diagnosis of knee OA; (ii) comparison of mud therapy and usual care or placebo or blank was made; (iii) data regarding visual analogue scale (VAS) pain or Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain were collected; (iv) study reported mean value and standard deviation or data required to calculate them; (v) sample size in each group had to be ≥ 10. Exclusion criteria were: (i) with experimental group containing other therapy; (ii) reviews; (iii) nonprospective comparative studies; (iv) data unavailable for meta-analysis.

Data extraction and quality assessment

The following data were independently extracted and recorded by two investigators (H.L. and G-H.L.): study characteristics (first author, year of publication); experimental group and control group; mean age; sex ratio; methodological quality; therapeutic information; duration of follow-up. The main outcome measures of the meta-analysis were VAS pain score and WOMAC pain score. Methodological quality of the selected studies was independently assessed by two investigators (H.L. and C.Z.), using the methodology quality assessment scale for randomized clinical trials.[12] The scale ranges between 0 and 7, and evaluates four aspects of randomized controlled trials: descriptions of randomization; concealment allocation; blinding; reporting of participant withdrawals. A score of 0 represents the poorest methodological quality and a score of 7 represents the strongest methodological quality.

Statistical analyses

Data were collected and analysed using RevMan software, version 5.0 (The Cochrane Collaboration, Oxford, UK). Homogeneity across studies was tested by the Q statistic with significance set at $P < 0.05$. The I^2 statistic was used as a second measure of heterogeneity, with 0% indicating no evidence of heterogeneity and 25%, 50% and 75% indicating low, moderate and high heterogeneity, respectively. A random-effects model was used in the case of

significant heterogeneity ($P < 0.05$ or $I^2 > 50\%$). Publication bias was assessed using funnel plots. The funnel plot is based on the fact that precision in estimating the underlying treatment effect will increase as the sample size of component studies increases. In the absence of bias the plot will show a symmetrical inverted funnel. On the contrary, if there is publication bias, funnel plots will often be skewed and asymmetrical.[13] A P-value ≤ 0.05 was considered statistically significant, unless otherwise specified.

Results

The literature search initially identified 3196 citations, of which seven were considered eligible for inclusion in the meta-analysis (total $n = 410$).[5–11] A flow diagram, indicating the results of the literature search and the study selection procedure, is presented in Figure 1. Characteristics of the included studies are presented in Table 1.

Figure 2 details the results from the random-effects model combining all the standardized mean differences (SMD) for VAS pain score. Overall, the combined data

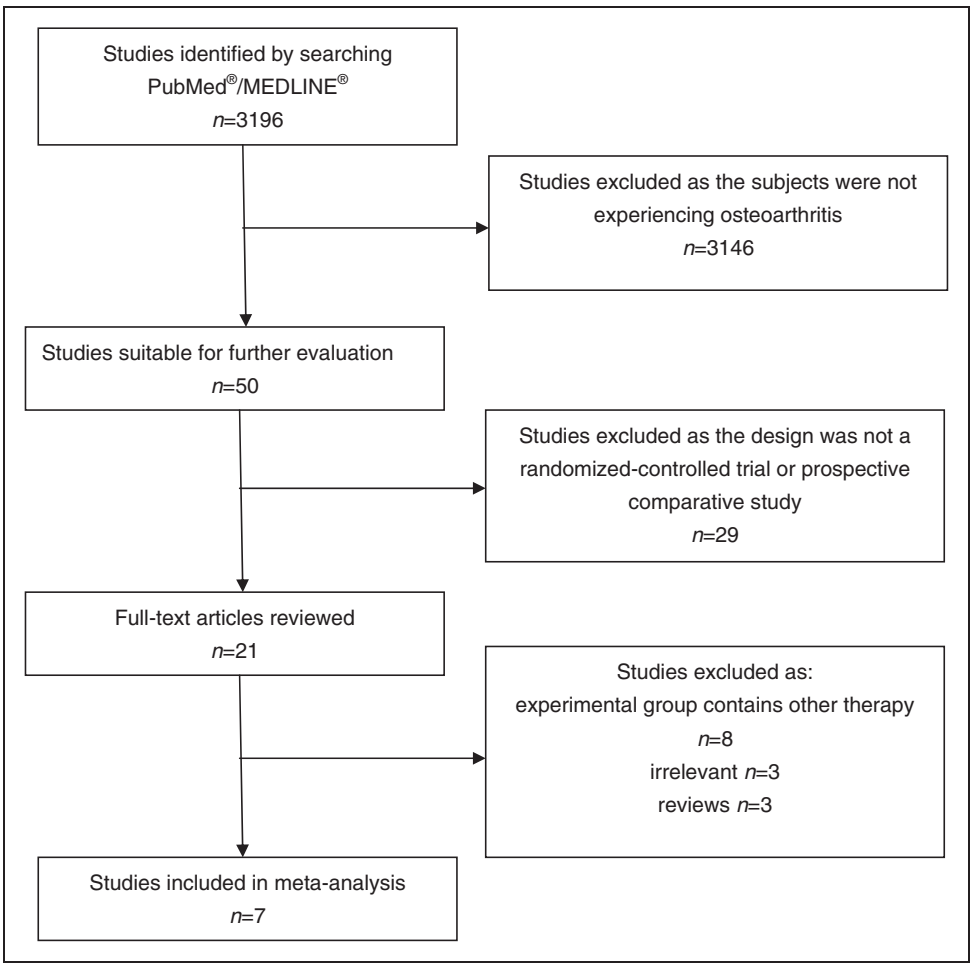

Figure 1. Flow diagram indicating results of the literature search and study selection procedure for a meta-analysis conducted to examine the effect of mud therapy on pain relief in patients with knee osteoarthritis.

Table 1. Principal characteristics of studies included in a meta-analysis conducted to examine the effects of mud therapy on pain relief in patients with knee osteoarthritis.

Study (First author, year, citation)	Experimental group, *n*	Control group, *n*	Mean age, years, Experimental group/control group	Sex, F/M, Experimental group, control group	Methodological quality[a]	Duration of therapy	Last follow-up
Flusser D, 2002[5]	Mineral-rich mud, 40	Mineral-depleted mud, 18	64.7/64.8	33/7,16/2	4 (1/0/2/1)[a]	20 min 5 times/week 3 weeks	3 months after end of therapy
Güngen G, 2012[8]	Mud pack, 23	Hot pack, 21	65.0/61.9	13/10,12/9	4 (2/1/0/1)[a]	20 min 6 times/week 2 weeks	3 months after end of therapy
Mahboob N, 2009[7]	Mud therapy, 25	Placebo, 25	NR	NR	3 (2/0/0/1)[a]	20 min 30 days	After end of therapy
Odabasi E, 2008[6]	Mud pack, 30	Nylon-covered mud pack, 30	69.2/69.0	28/2,27/3	4 (2/1/0/1)[a]	30 min 5 times/week 3 weeks	6 months after end of therapy
Sarsan A, 2012[9]	Mud pack, 15	Hot pack, 12	52.4/53.6	NR	6 (2/1/2/1)[a]	20 min 5 times/week 2 weeks	6 months after end of therapy
Espejo Antúnez L, 2013[10]	Mud pack, 61	Routine drug treatment, 60	69.1/73.1	44/17,46/14	5 (2/2/0/1)[a]	30 min 11 times total	After end of therapy
Evcik D, 2007[11]	Mud pack, 25	Hot pack, 25	57.4/59.6	22/3,24/1	7(2/2/2/1)[a]	20 min 5 times/week 2 weeks	10 weeks after end of therapy

NR, not reported; F, female; M, male.

[a]Methodological quality scale[12] ranges between 0 and 7, and evaluated four aspects of randomized controlled trials: descriptions of randomization; concealment allocation; blinding; reporting of participant withdrawals. A score of 0 represented poorest methodological quality and 7 represented strongest methodological quality.

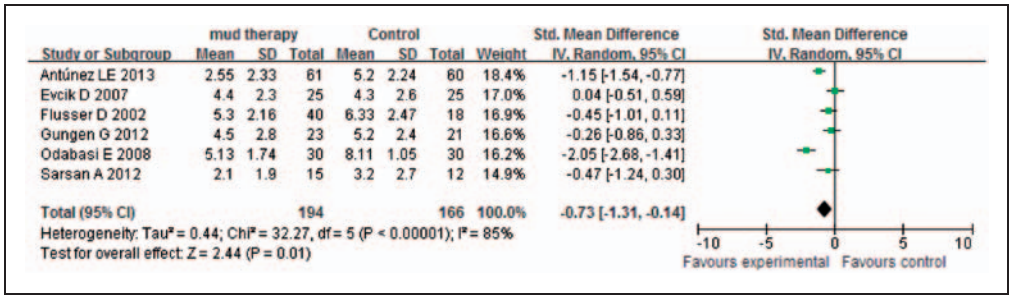

Figure 2. Forest plot of the mean differences in visual analogue pain scores with 95% confidence intervals (CI) in the mud therapy group versus control group, and the overall total, in six studies included in a meta-analysis conducted to examine the effect of mud therapy on pain relief in patients with knee osteoarthritis.

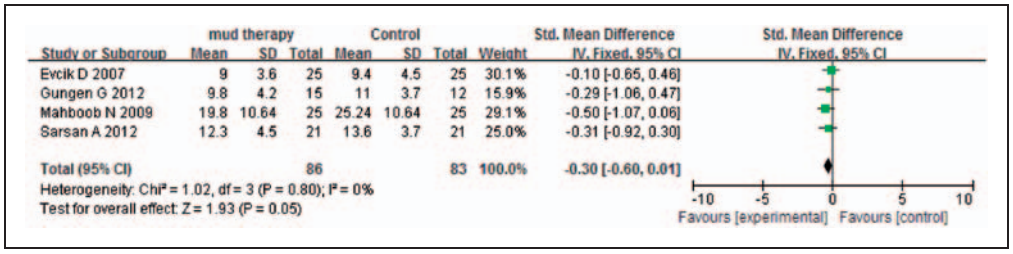

Figure 3. Forest plot of the mean differences in the Western Ontario and McMaster Universities Osteoarthritis Index pain scores with 95% confidence intervals (CI) in the mud therapy group versus control group, and the overall total, in four studies included in a meta-analysis conducted to examine the effect of mud therapy on pain relief in patients with knee osteoarthritis.
CI, confidence interval.

showed that patients with knee OA and who experienced mud therapy had significantly lower VAS scores (SMD −0.73; 95% confidence intervals [CI]: −1.31,−0.14; $P = 0.01$) compared with the control group. Substantial heterogeneity was observed ($P < 0.00001$; I^2 85%).

Figure 3 details the results from the random-effects model combining all the SMD for WOMAC pain score. Similarly, there was a significant difference between the two groups (SMD −0.30; 95% CI: −0.60, 0.01; $P = 0.05$). Substantial heterogeneity was not observed ($P = 0.80$; I^2 0%).

There was no evidence of publication bias (Figures 4 and 5).

Discussion

There is rapidly growing interest in nondrug and nonoperative treatments for the management of knee OA pain. This meta-analysis of six randomized controlled trials and one prospective comparative study provided evidence that mud therapy had a beneficial and significant effect on pain relief in patients with knee OA.

The effect of mud therapy in patients with knee OA has been examined in a systematic review and meta-analysis,[11] but evidence in that publication was limited because some of the included studies did not have either a 'usual care' group, a placebo group, or a

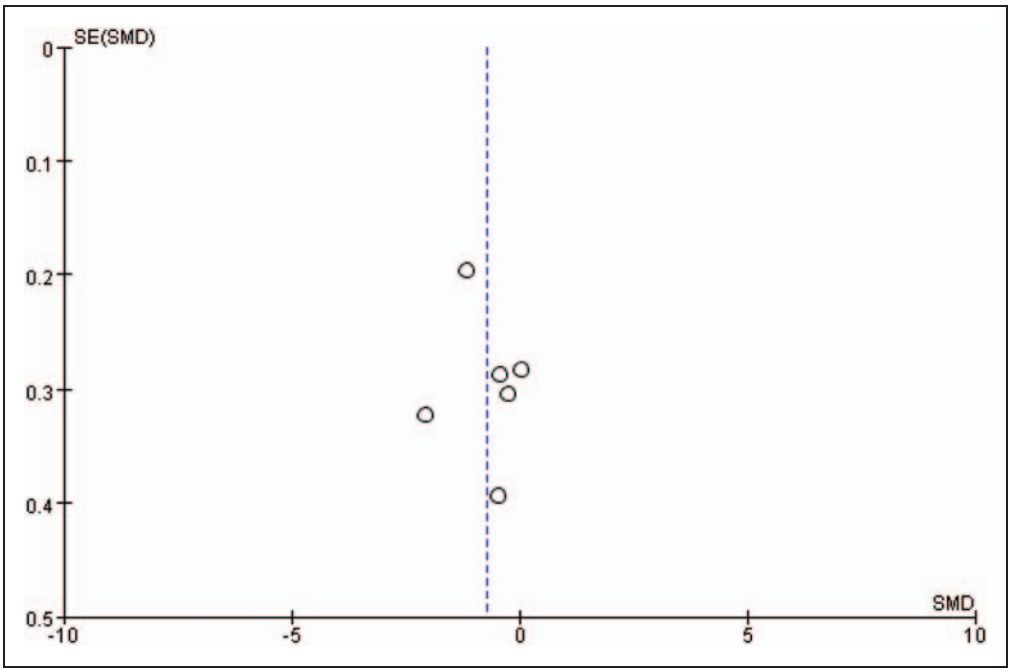

Figure 4. Funnel plot of the visual analogue pain scores provided no evidence of publication bias in studies included in a meta-analysis conducted to examine the effect of mud therapy on pain relief in patients with knee osteoarthritis.

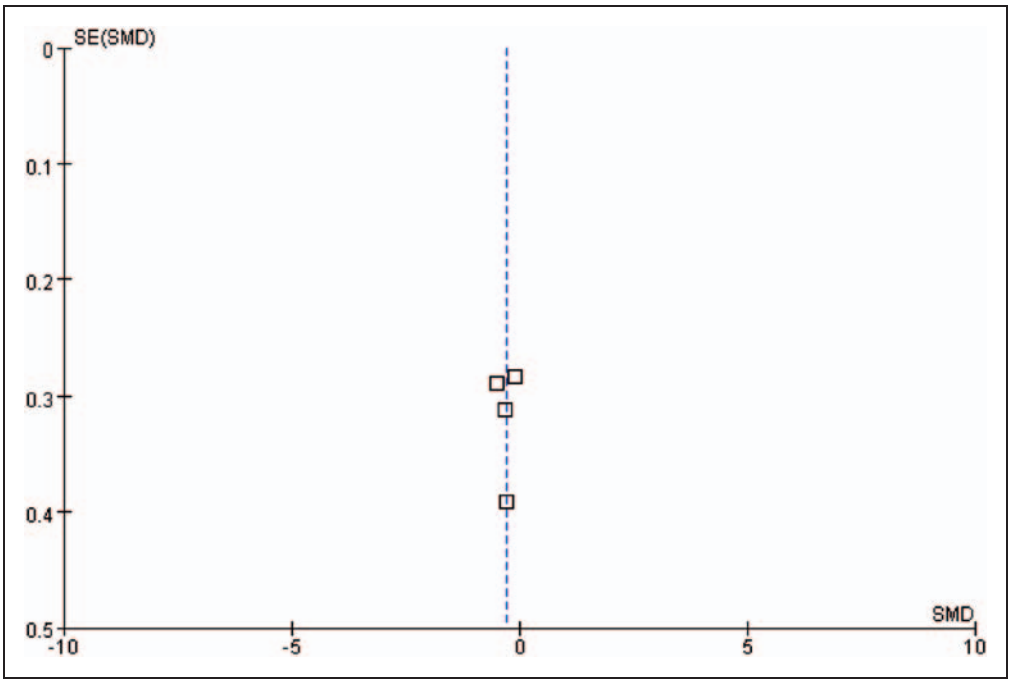

Figure 5. Funnel plot of the Western Ontario and McMaster Universities Osteoarthritis Index pain scores provided no evidence of publication bias in studies included in a meta-analysis conducted to examine the effect of mud therapy on pain relief in patients with knee osteoarthritis.

blank control group.[14,15] Of note, one of the included studies discussed the efficacy of mud pack treatment in relation to gonarthrosis, not just OA.[16] In addition, mud therapy was undertaken in combination with other treatments, such as mineral baths and manual massage.[17–19] Furthermore, the systematic review indicated that mud therapy was an effective therapy in the clinical management of knee OA, including relief of pain, without giving powerful and specific evidence. An improved understanding of this issue may have important public health and clinical implications.

Studies have investigated the effects of mud therapy in patients with knee OA,[20,21] and the beneficial effects of mud on reducing knee pain in these patients have been reported.[22,23] Such consequences are usually the result of its thermal effect, and findings of the present meta-analysis demonstrated that mud may have an impact on pain relief. However, the existing evidence is not enough to conclude definitively that mud therapy should be considered an alternative and effective treatment for pain relief in patients with knee OA.

Figure 2 shows that the overall effect of mud therapy was significant. Two individual trials demonstrated significant effects.[6,10] Six of the studies only included patients with moderate pain at baseline; one included those with severe pain.[6] In addition, only two of these studies used the 30-min single therapy time (the remaining studies used 20-min therapy times), raising the question of whether mud therapy has a dose-dependent effect. Future studies should address this question.

A major strength of the present meta-analysis is that all the included studies used a randomized controlled design, thus eliminating the possibility of inconsistency between different groups, and minimizing selection bias. Moreover, we excluded some studies where the experimental or control group combined mud therapy with other interventions. One potential limitation of the present meta-analysis was the relatively small number of included studies, which makes it difficult to draw firm conclusions. A second limitation was the substantial heterogeneity among studies for VAS pain score. A third limitation was whether the positive effects of mud therapy on pain relief might only be temporary: as the longest follow-up was 6 months, we are unable to clarify this issue.

In conclusion, mud therapy appears to be a favourable option for pain relief in patients with knee OA. However, the relatively small number of randomized controlled trials that have been undertaken to investigate mud therapy in OA calls into question the robustness of the analyses, so it is difficult to make definitive conclusions. Additional high-quality, randomized, controlled trials need to be conducted to explore the issues further.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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