Efficacy of joint lavage in knee osteoarthritis: meta-analysis of randomized controlled studies

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Abstract

Objective. Regarding the efficacy of joint lavage in the treatment of knee OA, we evaluated reports of randomized controlled trials (RCTs) to assess the efficacy of joint lavage alone or joint lavage combined with IA steroid injection to alleviate pain and improve function in knee OA.

Methods. We searched MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials for all reports published since 1966 of RCTs, evaluating either the efficacy of joint lavage alone or of joint lavage combined with steroid injection for knee OA on pain intensity and physical function. The time point for evaluation was a priori fixed at 3 months. Effect size (ES) was calculated to compare results across studies.

Results. From the 49 articles identified, reports of six RCTs were analysed for a total of 855 OA patients (511 in the treatment group and 344 in the control group). The pooled ES of the joint lavage vs placebo was not significant for pain intensity [ES = 0.17 (−0.37, 0.71)] or physical function [ES = −0.15 (−0.34, 0.04)], nor was the pooled ES of joint lavage combined with steroid injection vs joint lavage alone significant for pain intensity [ES = −0.82 (−2.47, 0.82)] or physical function [ES = 0.09 (−0.28, 0.45)].

Conclusions. This meta-analysis of RCTs investigating joint lavage for knee OA suggests that at 3 months, (i) joint lavage alone does not provide significant improvement in pain or function and (ii) the combination of joint lavage and IA steroid injection is no more efficacious than lavage alone.

Key words: Meta-analysis, Knee, OA, Joint lavage, Irrigation.

Introduction

OA of the knee is a major cause of disability. Current treatments aim to alleviate both pain and functional disability by a combination of pharmacological and non-pharmacological approaches [1, 2]. IA injections for knee OA are an important part of the treatment. They are widely used and recommended by international consensus [1, 2]. IA injections can involve hyaluronan or corticosteroids. Recent meta-analyses assessing the efficacy of corticosteroid injections found IA corticosteroid injections efficacious for short-term treatment of knee OA symptoms; the onset of action is fast but the efficacy lasts only ~2–4 weeks [3, 4].

Another local therapy for knee OA is joint lavage [5, 6], which aims to remove debris such as microscopic or macroscopic fragments of cartilage matrix, bone macromolecules and calcium crystals that may induce synovitis, a likely source of pain [7], and are a putative cause of chondrolysis [8]. Unblinded studies of joint lavage in knee OA have generally yielded favourable results [6], but a recent review suggested that a substantial and durable placebo effect might have accounted for the efficacy [6].

Given the lingering questions about the efficacy of joint lavage in the treatment of knee OA, we performed a systematic review with a meta-analysis of the results in published reports of randomized controlled trials (RCTs) investigating the efficacy of joint lavage alone or that of joint lavage with IA steroid injection in the treatment of symptomatic knee OA.
Patients and methods

Literature search
We searched MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials to obtain all reports published in English of RCTs of joint lavage in knee OA, published between 1966 and May 2009. The search in MEDLINE involved the use of key words ‘(lavage OR irrigation OR washing) AND knee AND randomized controlled trial’; that in EMBASE ‘Knee arthritis AND (lavage OR irrigation) AND randomized controlled trial’; and that in Cochrane ‘Irrigation AND randomized controlled trial AND knee’. In addition, reference lists of the papers initially identified were manually searched for additional relevant reports.

Study inclusion
Study design. We selected all reports of all parallel-group RCTs of knee OA evaluating the efficacy of (i) joint lavage without steroid injection vs control group or (ii) joint lavage with steroid injection vs joint lavage alone.

Study population. The study population included patients with OA as defined by the authors. In all cases, the patients fulfilled ACR [9] criteria for OA and/or the diagnosis was by radiography.

Intervention. Joint lavage was performed by use of one or two large needles or by arthroscopy.

Outcome measures
We selected articles of RCTs with pain and/or functional status outcomes. We extracted data on efficacy (along with their measurements of dispersal) as measured by pain or functional assessment at 3 months after joint lavage. This time point was a priori decided to be clinically relevant for the assessment of the efficacy of joint lavage. The pre-specified primary outcome of our meta-analysis was pain level as currently recommended for OA trials [10]. If an article provided data for more than one pain variable, we extracted the pain outcome that was highest on a previously described hierarchy of pain-related outcomes. In this hierarchy, global pain takes precedence over pain on walking, the WOMAC pain subscore, the Lequesne index and pain during activities other than walking [10–12]. The secondary outcome was the measure of physical function, as assessed by the WOMAC function subscore, the Lequesne index or the AIMS2-WB. Efficacy was assessed by the change in overall pain intensity and/or physical functional status between baseline and the time point for evaluation.

Methodological quality
The articles that fulfilled the inclusion criteria underwent a quality check by using the Jadad scale [13]. The Jadad score is obtained from a possible 5-point scale, high scores indicating high quality, by Yes/No answers to two questions for randomization and masking and one question evaluating the reporting of withdrawals and dropouts.

One point is given for each of the following: if the study is described as randomized, if the study is described as double-blind and if there is a description of withdrawals or dropouts. Two additional points are given if the method of randomization and the method of double blinding are appropriately described. Two points can be deducted if the method of randomization or the method of blinding are inappropriate [4].

Data extraction
Two of us (J.A. and P.R.) independently extracted data from articles using a customized form. Disagreements were resolved by discussion. Information recorded included first author; publication year; mean age, height, weight and BMI of participants; sex proportion; radiographic localization and grade of OA, number of knee effusions; trial duration; type of lavage and corticosteroid injection; type of comparator; number of patients in active and control groups; and outcome measures used to assess efficacy a priori defined. If numerical data could not be extracted from the text, we interpreted means and measures of dispersion from figures in the report.

Statistical analysis
To measure the magnitude of the effect of treatment for pain intensity and physical function, we calculated the effect size (ES). The ES is a standard used to determine the degree of improvement (or otherwise) of a particular therapy after accounting for any placebo effect. The ES is calculated as the ratio of the treatment effect (mean differences in treatment group minus differences in placebo group) to the pooled s.d. of these differences. This calculation entails the use of means, for both baseline and final data (or baseline and change during study) with a measure of variability such as s.d. To compare results across studies, we aimed to calculate the ES in all studies and used RevMan (Review Manager 5, The Nordic Cochrane Centre, Copenhagen). If the s.d. was given for only one trial arm, it was used as the baseline s.d. for both arms. However, if no measurement of variability was given, the ES could not be extrapolated and the study could not be included. By convention, an ES < 0.2 is usually considered trivial; >0.2–0.5 small; >0.5–0.8 moderate; >0.8–1.2 important and >1.2 very important [14]. In our study, a negative ES favoured the placebo or control, and a positive ES the active treatment.

We pooled the ES of joint lavage vs placebo or joint lavage plus corticoid injection vs lavage alone for pain intensity and physical function at 3 months. Sensitivity analyses calculated within subgroups of studies decided a priori were performed to assess the robustness of the main conclusions and explain heterogeneity. Statistical heterogeneity was tested by Q-test ($C^2$) [15]. This test allows description of the percentage of total variation across trials that is attributable to statistical heterogeneity rather than chance. $I^2$-values of 25, 50 and 75% correspond to low, moderate and high between-trial heterogeneity of results, respectively [16]. A random-effects model...
based on Q-statistics for heterogeneity was used for heterogeneous trials.

Results

Included studies

The result of the article selection process is reported in Fig. 1. From the 49 articles identified, we included six [17–22] reports of parallel-group RCTs comparing efficacy of (i) joint lavage vs placebo or (ii) joint lavage combined with steroid injection vs joint lavage alone that presented analysed data. Three studies compared joint lavage vs placebo (sham lavage or minimal irrigation) [18–20], two studies compared joint lavage combined with steroid injection vs joint lavage alone [21,22] and one study evaluated the effects of joint lavage with or without corticosteroid injection vs placebo (1.5 ml of 0.9% normal saline) and joint lavage alone, respectively [17] (Table 1). Data for one study, with a limited number of patients (n = 10 per group) could not be analysed because of lack of extractable data in the report [23].

Three studies referred to arthroscopic joint lavage [18,19,21] and three to joint lavage involving needles [17,20,22]. The steroids administered at the end of the lavage were cortivazol (3.75 mg in 1.5 ml) [17], methylprednisolone acetate (120 mg) [21] or triamcinolone acetonide (40 mg) [22]. All trials were reported as randomized. The methodological quality scores ranged from 1 to 5 (Table 1).

Fig. 1 Flow diagram of articles evaluated for inclusion or exclusion.

Study population

The RCTs in our analysis involved 855 patients with OA (511 in the active group and 344 in the control group), all fulfilling the ACR criteria for knee OA. The mean age of patients in the treatment and control groups was 61.7 ± 6.2 and 61.5 ± 6.1 years, respectively; 51 and 53%, respectively, were female.

Efficacy of joint lavage vs placebo

Reports of four RCTs provided the required data on pain intensity for 212 participants who received the active treatment and 228 who received placebo. A comparison of efficacy of joint lavage vs placebo for pain intensity favoured joint lavage, but the pooled ES was minimal and not significant (ES = 0.17; 95% CI = 0.37, 0.71) and the CI overlapped 0 (Fig. 2A). The heterogeneity was significant (Q = 21.8 for df = 3; P < 0.0001, I² = 86%). On sensitivity analyses, with exclusion of one outlier (highest ES and largest CI) [17], the heterogeneity was no longer significant (Q = 2.56 for df = 2; P = 0.28), and the pooled ES was close to significance, but in favour of placebo (−0.15; 95% CI = −0.38, 0.08), which contradicted the results of our primary analysis. We could not perform sensitivity analyses among subgroups a priori defined because of the low number of included studies and the lack of data provided.

The same four placebo-controlled studies evaluated the effect of joint lavage on physical function for 212 participants receiving the active treatment and 228 receiving placebo. The efficacy of joint lavage vs placebo for physical function was in favour of placebo, although not significant (ES = −0.15; 95% CI = −0.34, 0.04) (Fig. 2B). These results were homogeneous (Q = 2.41 for df = 3; P = 0.49).

Efficacy of joint lavage with corticosteroid injection vs joint lavage alone

Reports of three RCTs provided the required data on pain intensity for 299 participants who received joint lavage plus corticoid injection and for 116 patients who received joint lavage alone. The efficacy for pain intensity was in favour of joint lavage alone, although not significant (ES = −0.82; 95% CI = −2.47, 0.82) (Fig. 3A). The heterogeneity of results was significant (Q = 78.42 for df = 2; P < 0.00001; I² = 97%). On sensitivity analyses, with exclusion of one outlier (highest ES and largest CI) [22], heterogeneity became non-significant (Q = 2.56 for df = 2; P = 0.28) but did not change the validity of our results.

Two of the three RCTs provided data to assess the efficacy of joint lavage with corticosteroid injection vs joint lavage alone for physical function, but data were non-significant, and no robust conclusion could be drawn (ES = 0.09; 95% CI = −0.28, 0.45) (Fig. 3B).

Discussion

Our systematic review and meta-analysis of reports published since 1966 of RCTs, comparing joint lavage vs placebo for patients with knee OA, found no robust
evidence for a clinically relevant effect of joint lavage over placebo at 3 months. Moreover, our results show that the combination of joint lavage and IA steroid injection is no more efficacious than joint lavage alone.

Four RCTs assessed the efficacy of joint lavage for patients with knee OA vs a control group for pain and physical function. Although the overall effect for pain intensity was in favour of joint lavage, the benefits were small, with a minimal and non-significant ES and substantial heterogeneity of results, which limits the validity of this result. A sensitivity analysis to control heterogeneity produced a non-significant ES but favoured the placebo. The overall effects for physical function favoured the placebo and results were homogeneous. These data are unexpected because joint lavage is often proposed when conservative therapy fails to alleviate pain in knee OA [6, 24], especially with SF effusion [5]. However, these conclusions have been drawn mainly

**TABLE 1** Characteristics of RCTs assessing joint lavage alone or joint lavage combined with corticosteroid injection for knee OA

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of randomized patients</th>
<th>Design</th>
<th>Overall follow-up duration (weeks)</th>
<th>Treatments</th>
<th>Outcome extracted pain function</th>
<th>Jadad score (0-5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ravaud et al. [17]</td>
<td>98</td>
<td>Parallel, four arms</td>
<td>24</td>
<td>JL (1000 ml) + placebo vs JL + corticoid vs corticoid vs placebo</td>
<td>Lequesne index</td>
<td>3/5 (R = 2, B = 0, W = 1)</td>
</tr>
<tr>
<td>Kalunian et al. [19]</td>
<td>90</td>
<td>Parallel, two arms</td>
<td>52</td>
<td>JL (3000 ml) vs minimal irrigation (250 ml)</td>
<td>WOMAC pain</td>
<td>3/5 (R = 1, B = 2, W = 0)</td>
</tr>
<tr>
<td>Moseley et al. [18]</td>
<td>121</td>
<td>Parallel, three arms</td>
<td>104</td>
<td>JL (10 l) vs placebo vs debridement</td>
<td>WOMAC function</td>
<td>5/5 (R = 2, B = 2, W = 1)</td>
</tr>
<tr>
<td>Bradley et al. [20]</td>
<td>180</td>
<td>Parallel, two arms</td>
<td>52</td>
<td>JL (1000 ml) vs placebo</td>
<td>WOMAC function</td>
<td>5/5 (R = 2, B = 2, W = 1)</td>
</tr>
<tr>
<td>Smith et al. [21]</td>
<td>77</td>
<td>Parallel, two arms</td>
<td>24</td>
<td>JL + corticoid vs JL + placebo</td>
<td>Lequesne index</td>
<td>5/5 (R = 2, B = 2, W = 1)</td>
</tr>
<tr>
<td>Frias et al. [22]</td>
<td>205</td>
<td>Parallel, two arms</td>
<td>12</td>
<td>JL (3000 ml) + corticoid vs JL + placebo</td>
<td>Pain (VAS), Function: NA</td>
<td>1/5 (R = 1, B = 0, W = 0)</td>
</tr>
</tbody>
</table>

JL: joint lavage, performed in all cases using normal saline. Details of Jadad scores: randomization (R), blinding (B) methods and description of withdrawals/dropouts (W). KSPS: knee-specific pain scale; VAS: visual analogue scale; NA: not available.

**FIG. 2** Forest plot of trials comparing joint lavage with placebo on pain: (A)—heterogeneity: $\chi^2 = 21.85$, df = 3, $P < 0.0001$, $I^2 = 86\%$; test for overall effect: $Z = 0.62$, $P = 0.53$; or physical function; (B)—heterogeneity: $\chi^2 = 2.41$, df = 3, $P = 0.49$, $I^2 = 0\%$; test for overall effect: $Z = 1.59$, $P = 0.11$. 

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from observational studies, which do not provide strong evidence for efficacy, and thus must be interpreted with caution [6]. The first RCT that evaluated the effect of saline washout (2 l) vs saline injection (10 ml saline) for patients with knee OA found no benefit of saline washout for pain at 3 months. The negative results of this study, not included in our meta-analysis (data not extractable) [23], is in accordance with the results of two of the four RCTs analysed [18, 20]. Moreover, a recent RCT assessed the efficacy of an arthroscopic procedure, which combined joint lavage and arthroscopic debridement, together with optimized physical and medical therapy alone. The results of this study showed that arthroscopic surgery for knee OA provided no additional benefit to medical therapy [25].

The combination of joint lavage and IA steroid injection was no more efficacious than joint lavage alone for knee OA. The combination procedure may have lacked efficacy because only small benefits of the steroids might persist at 3 months, our time point of assessment. Also, the magnitude and carry-over effects of lavage may outweigh the benefit of steroids, if any. However, preliminary data from a recent RCT of 60 patients with knee OA demonstrated that the combination of joint lavage and triamcinolone hexacetonide injection was less effective than triamcinolone hexacetonide injection alone at 3 months. Although intra-group analysis revealed both groups with statistically significant improvement throughout the 12-week period, inter-group analysis revealed no difference in pain or function [26].

In addition to lacking clinical relevance for pain relief, joint lavage may present several causes of discomfort for patients as compared with hyaluronan or corticosteroid injection: the total duration of a joint lavage (30–60 min) is longer than that required for one IA injection; bed rest might be recommended following the lavage, and low-molecular-weight heparin prescription is sometimes required. Moreover, the cost of joint lavage is much higher than that of one corticosteroid injection: €560 (not including the cost for 1 day in hospital), as compared with €30 for one steroid injection in our tertiary care hospital.

Our analysis has some limitations that deserve attention. Due to the low number of available reports of RCTs, we could not compare results of RCTs for (i) joint lavage combined with corticosteroid injection vs placebo (n = 1 report) [17] and (ii) joint lavage alone vs corticosteroid injection (n = 2 reports) [17, 27]. Also, because of the low number of patients enrolled in the studies analysed, perhaps our main limitation is lack of sufficient overall power to detect any benefit of joint lavage. Moreover, there is clinical heterogeneity among the interventions examined within both groups of studies analysed. Unfortunately, the RCTs we reviewed did not have subgroups, so we could not perform subgroup analysis with meta-regressions to explore potential effect modification by type of patient (sex, age and BMI), stage of OA, nature of the corticosteroid injected, disease duration or presence/absence of knee effusion. For example, the studies included did not examine specific indications or levels of disease at which joint lavage could be more effective. Because knee OA patients are different and need different individual treatment strategies at different times, future studies on joint lavage should include homogeneous groups of patients with knee OA and should perform subgroup analysis according to, for example, the presence of SF effusion, IA crystals and
meniscal tears. In addition, the investigated studies included patients recruited in tertiary care centres, so our findings are limited in their generalization to common clinical practice. Also, patients who participated in the trials were more likely to trust and expect benefits from the joint lavage, which may have positively influenced the results in the sham-procedure groups [18, 20]. Indeed, results for placebo have recently been demonstrated to be effective for OA, especially for subjective outcomes such as pain, stiffness, self-reported function and physician global assessment [28]. IA injection is commonly associated with a large placebo response that might limit the ability to detect benefits of the treatment [4, 29, 30]. Another limitation is the time chosen for the evaluation of effect. We chose 3 months because we considered that joint lavage should provide pain relief for a longer period than one IA injection, because of the increased time and resources required for lavage. Moreover, all reports of trials analysed provided data for that time. However, we could not assess the clinical relevance of joint lavage at other times (notably at 6 and 12 months) as these differed between studies. Finally, we cannot exclude the limitation of potential publication bias introduced in selecting studies for inclusion, because studies with significant results are more likely to be published than studies without significant results [31].

In conclusion, our findings from this meta-analysis of reports of RCTs investigating joint lavage alone or combined with IA steroid injection in knee OA suggest that the effects of joint lavage at 3 months are not clinically relevant to the alleviation of pain intensity and improvement of physical function as compared with placebo. The combination of joint lavage and steroid injection does not appear to provide any additional benefit. However, these data do not preclude that joint lavage may be helpful for some selected patients with knee OA, for example, those with chronic knee effusion or IA crystals.

**Rheumatology key messages**

- Joint lavage is no more efficacious than placebo at 3 months on pain and function.
- Combination of joint lavage and corticosteroid injection does provide additional benefit.

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