Original Article

Intra-articular infiltration analgesia for arthroscopic shoulder surgery: a systematic review and meta-analysis

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Summary

Phrenic-sparing analgesic techniques for shoulder surgery are desirable. Intra-articular infiltration analgesia is one promising phrenic-sparing modality, but its role remains unclear because of conflicting evidence of analgesic efficacy and theoretical concerns regarding chondrotoxicity. This systematic review and meta-analysis evaluated the benefits and risks of intra-articular infiltration in arthroscopic shoulder surgery compared with systemic analgesia or interscalene brachial plexus block. We sought randomised controlled trials comparing intra-articular infiltration with interscalene brachial plexus block or systemic analgesia (control). Cumulative 24-h postoperative oral morphine equivalent consumption was designated as the primary outcome. Secondary outcomes included visual analogue scale pain scores during the first 24 h postoperatively; time-to-first analgesic request; patient satisfaction; opioid-related side-effects; block-related adverse events; and any indicators of chondrotoxicity. Fifteen trials (863 patients) were included. Compared with control, intra-articular infiltration reduced 24-h postoperative analgesic consumption by a weighted mean difference (95%CI) of −30.9 ([−38.9 to −22.9]; $p < 0.001$). Intra-articular infiltration also reduced the weighted mean difference (95%CI) pain scores up to 12 h postoperatively, with the greatest reduction at 4 h (−2.2 cm [(−4.4 to −0.04]); $p < 0.05$). Compared with interscalene brachial plexus block, there was no difference in opioid consumption, but patients receiving interscalene brachial plexus block had better pain scores at 2, 4 and 24 h postoperatively. There was no difference in opioid- or block-related adverse events, and none of the trials reported chondrotoxic effects. Compared with systemic analgesia, intra-articular infiltration provides superior pain control, reduces opioid consumption and enhances patient satisfaction, but it may be inferior to interscalene brachial plexus block patients having arthroscopic shoulder surgery.

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Accepted: 3 June 2020
Keywords: Intra-articular infiltration analgesia; interscalene block; Laparoscopic surgeryarthroscopic shoulder surgerypostoperative pain control
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Introduction

Identifying phrenic-sparing techniques that provide effective pain control for shoulder surgery is an ongoing challenge [1]. Intra-articular local anaesthetic infiltration targets free nerve endings, nerve fibres of various diameters and mechanoreceptors involved in nociception that are localised to the glenohumeral joint and its capsule [2–5], and has been proposed as a promising analgesic modality for arthroscopic shoulder surgical procedures [6, 7]. Unlike peri-articular infiltration or subacromial injection that target the tissues surrounding the glenohumeral joint or the subacromial bursae, respectively, intra-articular infiltration involves peri-operative deposition of local anaesthetic within the shoulder joint itself [8] and may offer a viable

phrenic-sparing alternative to interscalene brachial plexus block.

To date, clinical trials examining the analgesic effects of intra-articular infiltration have yielded conflicting evidence, with some studies supporting [9, 10] and others contesting [8, 11] its efficacy. Importantly, several case reports have described chondrolysis affecting the glenohumeral joint following the use of intra-articular infiltration for pain control following shoulder surgery [12, 13]. The shoulder joint may be particularly vulnerable to this complication because of its relatively thin and sparse cartilage [14]. Whereas primarily associated with continuous intra-articular local anaesthetic infusions [15, 16], concerns relating to this complication may have curtailed the interest to explore the potential benefits of intra-articular infiltration. Indeed, there has been no systematic evaluation of the evidence for or against using intra-articular infiltration for postoperative analgesia following arthroscopic shoulder surgery. This systematic review and meta-analysis examines the analgesic efficacy and safety of intra-articular infiltration analgesia in arthroscopic shoulder surgery by comparison with systemic analgesia alone or interscalene brachial plexus block. We hypothesised that intra-articular infiltration was more effective in reducing postoperative analgesic consumption following arthroscopic shoulder surgery.

Methods

This review was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement guidelines [17] and was registered with the international prospective register of systematic reviews [18]. All trials were evaluated based on a pre-defined protocol not previously published.

Randomised control led trials comparing the analgesic efficacy of intra-articular infiltration with a control or with interscalene brachial plexus block in adult patients undergoing arthroscopic shoulder surgery were eligible for inclusion. Arthroscopic surgical procedures of the shoulder were the focus of this review, but given the anticipated paucity of literature, studies that examined open or combined arthroscopic/open surgeries were also considered. Intra-articular infiltration was defined as any technique involving administration of a local anaesthetic agent, with or without additives (e.g. adrenaline; nonsteroidal anti-inflammatory drugs; or opioids), into the glenohumeral joint. Studies combining intra-articular infiltration with other regional anaesthetic techniques (e.g. interscalene brachial plexus block or suprascapular nerve block) were excluded. The control group was defined as one that uses systemic analgesia for postoperative pain management. We aimed to evaluate the safety of intra-articular infiltration, thus we included both single-injection and continuous intra-articular infiltration to capture any differences in the potential risk of chondrotoxicity between the two modalities. A sub-group analysis of was planned to identify any differences between these two modalities. Non-human trials; retracted studies; and abstract-only articles published more than 2 years ago were excluded.

We systematically searched electronic databases from inception to 31 March 2019 using terms specific to the following subject headings combined with Boolean operators: intra-articular infiltration analgesia; arthroscopic shoulder surgery; and postoperative pain. The details of the databases search have been presented earlier [19]. The search strategy is outlined in Supporting Information, Appendix S1.

The details of abstract screening, trial inclusion, data extraction and data pooling have been published earlier [19]. The included trials were critically appraised using the Cochrane risk of bias tool [20]. When not available, standardised imputations and assumptions were used to estimate data assumed to be missing at random [21].

The primary outcome was postoperative opioid analgesic consumption during the first 24 postoperative hours. Opioid consumption was converted into equi-analgesic oral morphine equivalents using standardised opioid conversion tables [22]. Secondary outcomes included pain levels at rest on the visual analogue scale (VAS) at 0, 2, 4, 8, 12 and 24 h postoperatively; time to first analgesic request; patient-reported satisfaction on a 10-point scale; incidence of opioid-related adverse effects (postoperative nausea and vomiting; pruritus; and respiratory depression); block-related adverse events; and any evidence of chondrolysis occurring within the first 12 months following intra-articular infiltration administration. This time-point was selected because any potential chondrotoxicity is generally detectable and/or is clinically symptomatic within 12 months following intra-articular infiltration [14]. Discrete pain scores not reported on a VAS and patient satisfaction scales other than the 10-point scale were converted to continuous values via linear transformation [23].

We planned to conduct sub-group analysis according to the type of comparator examined by stratifying the results for all outcomes into intra-articular infiltration vs. interscalene brachial plexus block and intra-articular infiltration vs. control comparisons. In the event that a study examined both comparisons, the relevant study arm(s) were included in each respective sub-group.

We pooled data using RevMan Version 5.3 (The Cochrane Collaboration, Copenhagen, Denmark). A DerSimonian random effects model was chosen because of the anticipated variability between studies [24]. Outcomes were not pooled in the event that fewer than three studies examined a particular outcome. The weighted mean difference and 95%CI was calculated as a pooled summary statistic for continuous, normally distributed postoperative outcomes (analgesic consumption; pain scores; time to first analgesic; and patient satisfaction scores). The odds ratio and 95%CI was calculated as the pooled summary statistic for dichotomous data (incidence of adverse events). Statistical significance was defined as a two-tailed p value <0.05. Publication bias was assessed using visual inspection of the funnel plot diagram for each of the pooled outcomes [25]. Trial sequential analysis was performed using TSA Software Version 0.9.5.10 Beta (Copenhagen Trial Unit, Denmark) to examine the required information size and adjust statistical thresholds for multiple-comparison type 1 error in the primary outcome analysis. Analyses were conducted using an 80% power and 5% type-1 error margin.

Statistical heterogeneity was quantified using the I^2 statistic, with a value >50% considered indicative of significant heterogeneity. Potential sources of heterogeneity within the primary outcome were identified a priori and used as covariates in a planned meta-regression analysis. These covariates included: timing of administration (pre-, intra- or postoperative); local anaesthetic used (bupivacaine, ropivacaine or lidocaine); total intra-articular infiltration dose; use of additives (adrenaline, opioids, etc.); administering clinician (surgeon or anaesthetist); surgical approach (arthroscopic alone or arthroscopic and/or open); nature of intra-articular infiltration (single-injection or continuous infusion); postoperative analgesic regimen (multimodal or opioid-based); and type of control group (systemic analgesia, with or without a sham block). We also planned sensitivity analysis by excluding the trials that included patients undergoing open surgery to further identify the effect of this confounder.

The evidence supporting pooled estimates was assessed according to the grades of recommendation, assessment, development and evaluation (GRADE) guidelines as very low; low; moderate; or high quality [26]. Each study was independently assessed by two authors (TG, EY) and the decision was corroborated by the senior author (FA).

Results

Our literature search identified 1392 unique titles; of these, 23 records remained after initial title and abstract review. The full text review of the 23 records identified 15 that met the eligibility criteria [8–11, 27–37] (Fig. 1).

The 15 included trials represented a total of 863 patients, of which 408 received intra-articular infiltration, 162 received interscalene brachial plexus block and 293 belonged to eligible control groups. The characteristics of these studies, including sample size, intervention and control groups and reported outcomes are detailed in Table 1. All shoulder operations were completed under general anaesthesia. Eight trials compared intra-articular infiltration vs. control [8–10, 27–29, 34, 37]; four compared intra-articular infiltration vs. interscalene brachial plexus block [30, 31, 33, 35]; and three included both comparisons [11, 32, 36]. Intra-articular infiltration was administered by the orthopaedic surgeon in all but two trials [32, 36] where the anaesthetist performed intra-articular infiltration. When used, continuous intra-articular infiltration was compared with continuous interscalene brachial plexus block [10, 30] or continuous placebo injection [10, 27, 34, 37]. Analgesic outcomes were assessed by all trials, but chondrotoxicity was not distinctly defined as an outcome in any of the reviewed trials. The risk of bias summary table for the included studies is presented in Fig. 2.

Cumulative postoperative analgesic consumption was reported in 13 studies (732 patients), of which two designated it as a primary outcome [30, 32]. Two studies did not report standard deviation values and required imputation from pooled estimates [8, 9]. Compared with

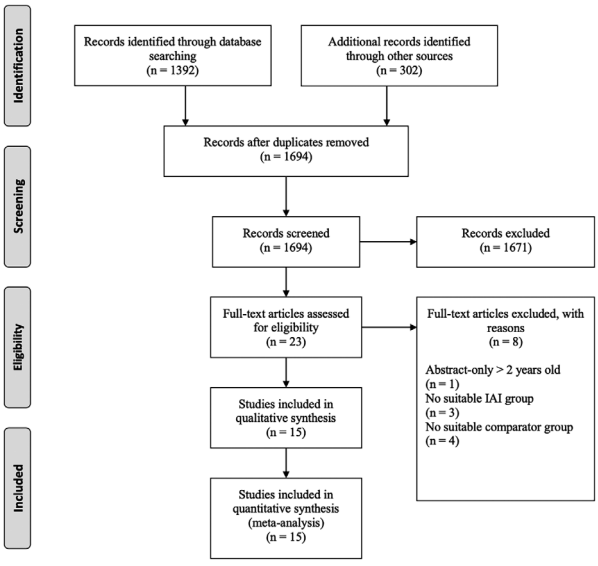

Figure 1 PRISMA study flow diagram depicting studies identified, included and excluded, with reasons. IAI, intra-articular infiltration analgesia.

Table 1 Included study characteristics, surgical and anaesthetic protocols and examined outcomes.

Author	Included groups; timing of IAI (n)	Surgery (approach)	Analgesic regimen	Relevant reported outcomes
Aksu et al. [32]	**1** No intervention (20) **2** ISB (20) **3** IAI bupivacaine 0.5%; postoperative (20)	Rotator cuff repair; acromioplasty; Bankart repair; SLAP repair; articular cartilage repair (arthroscopic)	*Pre-operative*: Fentanyl 1 $\mu g.kg^{-1}$ i.v. *Postoperative*: Dexketoprofen 50 mg i.m.; morphine 0.1 $mg.kg^{-1}$ i.v.	Postoperative analgesic consumption Pain scores Patient satisfaction Adverse events
Axelson et al. [10]	**1** Continuous IAI saline; intra-operative (17) **2** Continuous IAI saline + i.v. ketorolac; intra-operative (17) **3** Continuous IAI ropivacaine 1% + morphine + ketorolac; intra-operative (16)	Bankart repair (open/arthroscopic)	*Pre-operative*: Paracetamol 1 g p.o. *Intra-operative*: Fentanyl 1–2 $\mu g.kg^{-1}$ i.v. *Postoperative*: Morphine 1–2 mg i.v.; dextropropoxyphene 50 mg p.o.; acetaminophen 1 g p.o.; ketorolac 30 mg i.v. (Group 2)	Postoperative analgesic consumption Pain scores Patient satisfaction Time to first analgesic request
Beaudet et al. [33]	**1** ISB (30) **2** IAI bupivacaine 0.25% + lidocaine 2%; pre-/postoperative (30)	Rotator cuff repair; shoulder prosthesis; proximal humerus repair; distal clavicle repair (open/arthroscopic)	*Pre-operative*: Remifentanil 0.5–4 $\mu g.kg\text{-}^{-1}$ i.v. *Intra-operative*: Remifentanil 0.5 $\mu g.kg^{-1}.min^{-1}$ i.v. *Postoperative*: Hydromorphone 0.5 mg i.v.; acetaminophen 1 g; hydromorphone 2–8 mg	Postoperative analgesic consumption Pain scores Patient satisfaction Adverse events
Cheong et al. [34]	**1** IAI saline; postoperative (20) **2** Continuous/PCA IAI ropivacaine 0.25%; postoperative (20) **3** Continuous/PCA IAI ropivacaine 0.25% + fentanyl; postoperative (20)	Rotator cuff repair; SLAP repair (arthroscopic)	*Pre-operative*: Alfentanil 15 $\mu g.kg^{-1}$ i.v.	Pain scores
Contreras-Dominguez et al. [35]	**1** Continuous ISB (24) **2** IAI ropivacaine 0.2%; intra-operative (23)	Acromioplasty (arthroscopic)	*Pre-operative*: Ketoprofen 100 mg i.v.; alfentanil 7 $\mu g.kg^{-1}$ i.v. *Intra-operative*: Alfentanil 0.3 $\mu g.kg^{-1}$ i.v. *Postoperative*: Ketoprofen 50 mg i.v.; morphine 1.5 mg bolus i.v. PCA	Postoperative analgesic consumption Pain scores Adverse events Patient satisfaction
Doss et al. [9]	**1** IAI morphine; NR (10) **2** IAI ropivacaine 0.2%; NR (10) **3** IAI ropivacaine 0.2% + morphine; NR (10)	Shoulder arthroscopy (arthroscopic)	*Postoperative*: Acetaminophen 500 mg p.o.; codeine 30 mg p.o.	Postoperative analgesic consumption Pain scores Time to first analgesic request Adverse events
Fontana et al. [36]	**1** No intervention (20) **2** ISB (20) **3** IAI levobupivacaine 0.5%; pre-operative (19)	Debridement; decompression; acromioplasty; rotator cuff repair (arthroscopic)	*Pre-operative*: Fentanyl 2 $\mu g.kg^{-1}$ i.v. *Intra-operative*: Ketorolac 30 mg i.v. *Postoperative*: Fentanyl 1 $mg.kg^{-1}$ bolus i.v. PCA	Postoperative analgesic consumption Pain scores Patient satisfaction
Im et al. [37]	**1** i.v. PCA (32) **2** Continuous IAI bupivacaine 0.25%; NR (39)	Debridement; capsular release; Bankart repair; rotator cuff repair; SLAP repair (arthroscopic)	*Postoperative*: Diclofenac 75 mg p.o.	Pain scores Adverse events
Niiyama et al. [27]	**1** No intervention (10) **2** No intervention (10) **3** Continuous IAI lidocaine 1%; postoperative (10)	Intra-articular; extra-articular surgery (arthroscopic)	*Postoperative*: Diclofenac 50 mg p.o.	Postoperative analgesic consumption Pain scores
Panigrahi et al. [28]	**1** IAI saline; postoperative (20) **2** IAI ropivacaine 0.2%; postoperative (20) **3** IAI ropivacaine 0.2% + dexamethasone; postoperative (20)	Diagnostic arthroscopy; rotator cuff repair; bicipital tenodesis; SLAP repair; stiff shoulder release; Bankart repair (arthroscopic)	*Postoperative*: Diclofenac 75 mg i.v.; tramadol 50 mg i.v.	Postoperative analgesic consumption Pain scores Time to first analgesic request Adverse events
Panigrahi et al. [29]	**1** IAI saline; postoperative (15) **2** IAI ropivacaine 0.2%; postoperative (15) **3** IAI ropivacaine 0.2% + dexamethasone; postoperative (15)	Bankart repair (arthroscopic)	*Postoperative*: Diclofenac 75 mg i.v.	Postoperative analgesic consumption Pain scores Time to first analgesic request
Park et al. [30]	**1** ISB (19) **2** Continuous IAI ropivacaine 0.25%; postoperative (19)	NR (arthroscopic)	*Postoperative*: Fentanyl 12 $\mu g.h^{-1}$ patch (Group 1); fentanyl 25 µg i.v.; pethidine 50 mg i.v.	Postoperative analgesic consumption Pain scores Adverse events

(continued)

Table 1 (*continued*)

Author	Included groups; timing of IAI (n)	Surgery (approach)	Analgesic regimen	Relevant reported outcomes
Scoggin et al. [8]	**1** Saline (20) **2** IAI morphine; postoperative (22) **3** IAI bupivacaine 0.25%; postoperative (22)	Acromioplasty; Bankart repair; labral tear; miscellaneous (arthroscopic)	*Intra-operative*: Fentanyl 1–8 $\mu g.kg^{-1}$ i.v. *Postoperative*: Oxycodone 5 mg p.o.; acetaminophen 500 mg p.o.; morphine 2 mg i.v.	Postoperative analgesic consumption Pain scores
Sicard et al. [31]	**1** Continuous ISB (49) **2** IAI ropivacaine 0.2% + ketoprofen; postoperative (50)	Total shoulder arthroplasty (open)	*Intra-operative*: Sufentanil 0.2–0.3 $mg.kg^{-1}$ i.v.; ketamine 0.15 $mg.kg^{-1}$ i.v. *Postoperative*: Acetaminophen 1 g p.o.; tramadol p.o. (dose NR); efopam p.o. (dose NR); morphine i.v. (dose NR)	Postoperative analgesic consumption Pain scores Adverse events
Singelyn et al. [11]	**1** No intervention (30) **2** ISB (30) **3** IAI bupivacaine 0.25%; postoperative (30)	Acromioplasty (arthroscopic)	*Pre-operative*: Sufentanil 0.3 $\mu g.kg^{-1}$ i.v. *Intra-operative*: Sufentanil 5 µg i.v. *Postoperative*: Propacetamol 2 g i.v.; morphine 5–10 mg i.v.	Postoperative analgesic consumption Pain scores Adverse events Patient satisfaction

GA, general anaesthesia; IAI, intra-articular infiltration; i.m., intramuscular; ISB, interscalene block; i.v., intravenous; N/n, number; NR, not reported; PCA, patient-controlled analgesia; p.o., oral; POD, postoperative day; PRN, as needed; SLAP, superior labral tear from anterior to posterior.

control, intra-articular infiltration reduced 24-h postoperative analgesic consumption by a weighted mean difference (95%CI) of 30.9 mg (−38.9 to −22.9; $p < 0.001$; $I^2 = 95\%$). Compared with interscalene brachial plexus block, intra-articular infiltration was not different for postoperative opioid consumption, with a weighted mean difference of 21.7 mg (−5.1 to 48.6; $p = 0.11$; $I^2 = 100\%$). Figure 3 presents the forest plot diagram for these two sub-group comparisons.

Heterogeneity of the primary outcome in both sub-group comparisons was high. Meta-regression analysis for the intra-articular infiltration vs. control comparison identified covariates that were associated with increased opioid consumption. These were the timing of injection (pre- vs. intra- vs. postoperative; $p < 0.001$); type of local anaesthetic (bupivacaine vs. ropivacaine vs. lidocaine; $p = 0.007$); operator administering intra-articular infiltration (surgeon vs. anaesthetist; $p < 0.001$); and type of control group (patient-controlled analgesia vs. no patient-controlled analgesia; $p = 0.005$). Similarly, meta-regression analysis for intra-articular infiltration vs. interscalene brachial plexus block comparison revealed associations with type of local anaesthetic (bupivacaine vs. ropivacaine vs. lidocaine; $p = 0.001$); operator administering intra-articular infiltration (surgeon vs. anaesthetist; $p < 0.001$); and nature of intra-articular infiltration (single-injection vs. continuous infusion; $p = 0.008$). Notably, we did not detect an association between the intra-articular infiltration modality used (single-shot or continuous infusion) or the surgical approach and the postoperative opioid consumption.

Furthermore, sensitivity analysis by excluding studies that examined a combination of arthroscopic and/or open shoulder surgeries did not significantly alter the results [10, 31, 33]. A two-sided test for trial sequential analysis was conducted using a mean difference and variance of −30.9 and 53.2, respectively, for the intra-articular infiltration vs. control comparison, and −46.4 and 47.9, respectively, for the intra-articular infiltration vs. interscalene brachial plexus block comparison. Trial sequential analysis demonstrated that both the intra-articular infiltration vs. control (Fig. 4a) and intra-articular infiltration vs. interscalene brachial plexus block (Fig. 4b) sub-group comparisons met required information size thresholds, confirming the adequacy of sample size. This analysis confirmed that intra-articular infiltration was significantly different to control but not different from interscalene brachial plexus block with respect to postoperative opioid analgesic consumption, after adjusting for multiple comparisons. The GRADE strength of evidence was assessed as moderate for intra-articular infiltration vs. control, and very low for intra-articular infiltration vs. interscalene brachial plexus block.

All studies (863 patients) evaluated postoperative pain in the first 24 h following shoulder surgery. Compared with control, intra-articular infiltration consistently reduced pain scores at 0, 2, 4, 8 and 12 h postoperatively with no further benefit beyond 12 h. The magnitude of the reductions in pain scores varied between the least difference at 12 h of −1.1 (−1.7 to −0.5; $p < 0.001$; $I^2 = 89\%$) and the greatest difference at 4 hours of −2.2 cm (−4.4 to −0.04; $p < 0.05$;

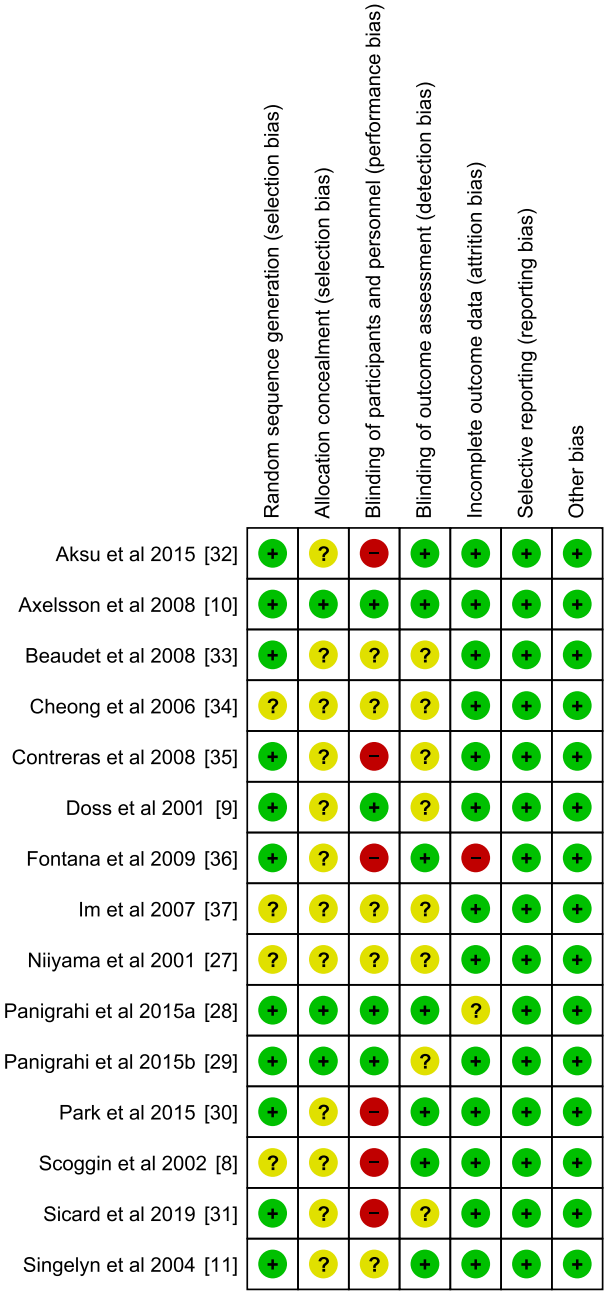

Figure 2 Summary table illustrating Cochrane risk of bias results for included studies.

I^2 = 99%). Supporting Information Table S1 presents the pooled results.

In contrast, interscalene brachial plexus block was superior to intra-articular infiltration at 2, 4 and 24 h; and it reduced pain scores by 2.4 (0.3 to 4.6; p = 0.03; I^2 = 100%); 2.4 (0.5 to 4.3; p = 0.02; I^2 = 99%); and 1.0 (0.1 to 1.9; p = 0.03; I^2 = 96%), respectively. The difference favoured interscalene brachial plexus block but did not reach the threshold of statistical significance at 0, 8 and 12 h postoperatively. The GRADE quality of evidence for postoperative pain ranged from very low to moderate.

Four studies [9, 10, 28, 29] reported data on time to first analgesic request, all of which were examining the intra-articular infiltration vs. control comparison. Compared with control, intra-articular infiltration prolonged the time to first analgesic request by 560 min (469 to 652; p < 0.001; I^2 = 18%). The GRADE quality of evidence was assessed as moderate.

Data on patient-reported satisfaction scales were reported by six studies [10, 11, 32, 33, 35, 36]. Of these, data could be extracted from four studies; two studies [11, 35] reported scores on a 100-point scale, whereas one study [32] used a 5-point scale and one study [10] used a 4-point scale. Compared with control, intra-articular infiltration improved patient satisfaction with postoperative pain management by 1.8 units (0.7 to 2.8; p < 0.001; I^2 = 82%). The GRADE quality of evidence was assessed as moderate.

In contrast, intra-articular infiltration was associated with reduced patient satisfaction with postoperative pain management when compared with interscalene brachial plexus block by 1.6 units (−2.6 to −0.6; p = 0.001; I^2 = 92%). The GRADE quality of evidence was assessed as low for this outcome.

Opioid-related side-effects (nausea/vomiting; pruritus; respiratory depression) were examined and reported in all but one study [8]. There was no difference in the pooled incidence of opioid-related side-effects between groups in any of the comparisons examined, and the GRADE quality of evidence for both comparisons was low (Supporting Information, Table S1).

Block-related complications were formally assessed and reported in six studies [11, 30–33, 35]. The adverse events encountered in these studies included paraesthesia (n = 2) [33] and local tenderness (n = 1) [11] in patients receiving intra-articular infiltration, and paraesthesia (n = 2) [33], ptosis (n = 2) [32] and injection site tenderness (n = 1) [11] in patients receiving interscalene brachial plexus block. There were no adverse events reported in patients receiving a control modality. The results of this outcome were not pooled because data were scant. Qualitatively, there were no differences between intra-articular infiltration and interscalene brachial plexus block in the risk of adverse events.

Despite its importance, chondrolysis was not designated as an outcome examined in any of the included studies; and authors of the included trials did not follow their study participants longitudinally to assess for any radiologic or clinical evidence of chondrolysis. Additionally,

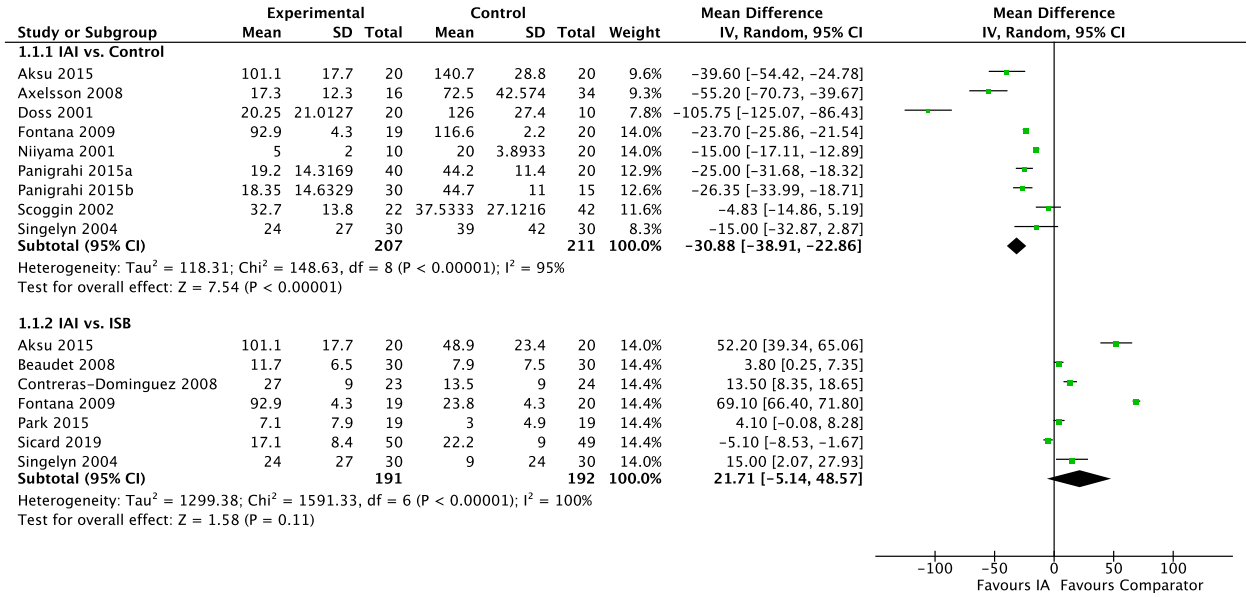

Figure 3 Forest plot illustrating effect sizes for pooled cumulative 24-h postoperative opioid analgesic consumption in each sub-group comparison. The individual trials' weighted mean differences, standard error and the pooled estimates of the ratio of means are shown. The 95%CIs are shown as lines for individual studies and as diamonds for pooled estimates. IAI, intra-articular infiltration analgesia; SD, standard deviation.

there was no anecdotal reporting of chondrolysis in any of the studies.

Discussion

This systematic review and meta-analysis identifies important analgesic benefits associated with using intra-articular infiltration for pain control following arthroscopic shoulder surgery. Specifically, when compared with control, intra-articular infiltration reduced postoperative opioid analgesic consumption, improved pain scores up to 12 h, prolonged time to first analgesic request and enhanced patient satisfaction. In contrast, intra-articular infiltration was not different from interscalene brachial plexus block for postoperative analgesic consumption; but it was associated with less favourable pain scores and decreased patient satisfaction compared with interscalene brachial plexus block. The GRADE assessment of the quality of evidence ranged from very low to moderate, reflecting the limited size and scope of available literature. These results support using intra-articular infiltration as an analgesic alternative when interscalene brachial plexus block is not feasible or contraindicated.

The interest in identifying alternative analgesic modalities for use in patients having shoulder surgery who are not candidates for interscalene brachial plexus block is increasing [1, 38, 39]. Techniques such as suprascapular nerve block [40]; peri-articular infiltration analgesia [41]; and subacromial bursal infiltration analgesia [42] have been proposed. The mechanism underlying intra-articular analgesia in orthopaedic joint surgery is thought to involve direct blockade of intra-articular nerve endings [43, 44] as well as exerting an effect on peripheral synovial opioid receptors [45, 46]. Indeed, the abundance of free nerve endings and mechanoreceptors in the capsular surface of the glenohumeral joint and the contribution of capsular distention to acute pain following arthroscopic shoulder surgery support the direct blockade theory [2–5], differentiating it from peri-articular infiltration that acts on tissues surrounding the shoulder joint. These effects are also corroborated by evidence from other populations where intra-articular infiltration has demonstrated important analgesic benefits, such as hip [47, 48] and knee [49–51] procedures, where infiltration techniques have been integrated into the standard of care.

Despite the analgesic benefits of intra-articular infiltration compared with systemic analgesia, the safety concerns relating to chondrotoxicity should not be fully dismissed. Whereas no clinically important complications were reported, the trials herein did not systematically evaluate patients for chondrotoxicity. However, a subsequent literature search that we conducted failed to capture any case reports describing incidents of chondrolysis published by any of the authors of the included trials. This finding was also corroborated through

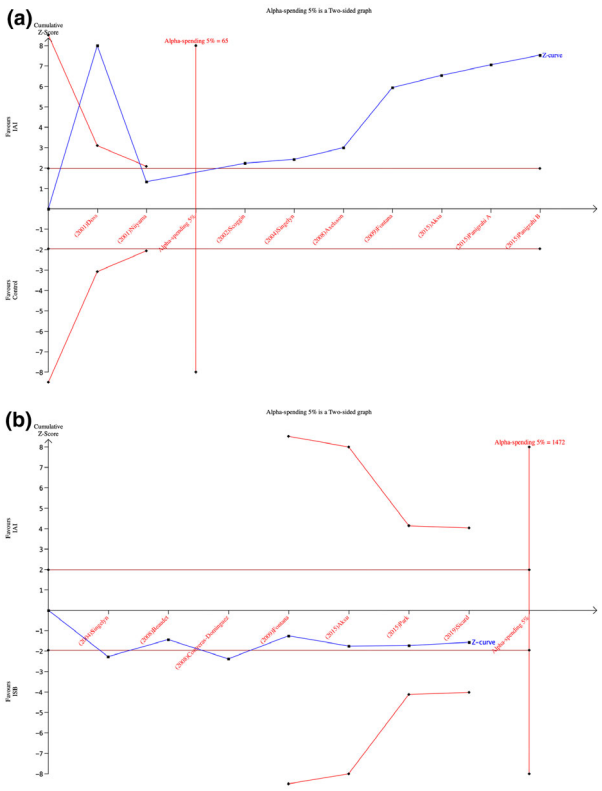

Figure 4 Trial sequential analysis for the comparison with (a) control and (b) interscalene brachial plexus block. The horizontal red lines represents the boundary at p = 0.05. The vertical red line depicts the required information size. The Z-curve crossing the boundary indicates adequate sample size.

our correspondence with those authors, making it unlikely that any cases were missed among the 408 patients who received single-injection intra-articular infiltration. Whereas this evidence of safety remains anecdotal, there is further evidence supporting safety of intra-articular infiltration from basic science research. Indeed, evidence from cellular studies has indicated that only prolonged administration (i.e. infusion exceeding 24 h, not single-injection) of local anaesthetic is a risk factor for chondrocyte necrosis [52, 53]. Besides duration of intra-articular infiltration exposure [54, 55], the clinical risk factors that have been associated with this complication include the use of high local anaesthetics concentrations (bupivacaine 0.5% and lidocaine 2%) [56] and the placement of suture anchors within the glenohumeral joint [14]. Interestingly, one study [52] found that ropivacaine, among other local anaesthetics, offers the lowest risk of chondrolysis. The thinner, non-weight bearing nature of glenohumeral cartilage seems to predispose the shoulder joint to this complication [54]. Previous systematic reviews [14, 57] examining this issue recommend abandoning the continuous infusion component of intra-articular infiltration and limiting the use of intra-articular infiltration to a single-injection. That said, the evidence of safety of single-shot intra-articular infiltration is still lacking, and the possibility of answering this question in the setting of a randomised controlled trial is remote, because chondrotoxicity with single-injection intra-articular infiltration seems to be a rare outcome. Therefore, decision-making should balance the theoretical risk of a rare complication against the potential benefits of intra-articular infiltration.

This review has several limitations. First, the number of included trials was small, limiting the quality of pooled evidence and ability to perform a meaningful sub-group analysis. Second, there was significant variability in the reporting outcomes of interest; and no trials examined chondrolysis as an outcome. Third, results were characterised by significant heterogeneity reflecting the diversity of clinical practice with regard to duration, dose and timing of intra-articular infiltration. However, heterogeneity was successfully explained by meta-regression analysis, which corroborates our findings. Of note, we did not detect an association between the benefits of intra-articular infiltration and the use of opioids as a local anaesthetic additive, although the analgesic effect of intra-articular infiltration may partially be mediated by synovial opioid receptors. Fourth, the majority of included studies did not include patients with pre-existing chronic pain or long-term opioid use, which represents an important population requiring optimised postoperative analgesia. Finally, whereas the benefits in improving pain scores were clinically meaningful, intra-articular infiltration did not reduce the risk of opioid-related side-effects. Conversely, the comprehensive and exhaustive literature search underscores the strength of this review.

This systematic review and meta-analysis demonstrated the analgesic efficacy of intra-articular infiltration following shoulder arthroscopy when a phrenic-sparing interscalene brachial plexus block alternative is needed. Single-injection intra-articular infiltration reduces opioid consumption, improves pain scores and enhances patient satisfaction, compared with control; however, interscalene brachial plexus block seems to provide superior pain control compared with intra-articular infiltration.

Acknowledgements

The review was registered in the PROSPERO database (CRD42019134979). The authors would like to thank M. Englesakis, University Health Network Librarian and Information Specialist, for her invaluable help with

constructing and conducting the literature search for this review. No external funding or competing interests declared.

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Supporting Information

Additional supporting information may be found online via the journal website.

Table S1. Pooled outcomes results.

Appendix S1. Literature search strategy.