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The analgesic efficacy of pregabalin for shoulder arthroscopy

A meta-analysis of randomized controlled trials

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Abstract

Introduction: The efficacy of pregabalin for pain management of shoulder arthroscopy remains controversial. We conduct this meta-analysis to explore the influence of pregabalin versus placebo on the postoperative pain intensity of shoulder arthroscopy.

Methods: We have searched PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases through November 2019 for randomized controlled trials assessing the effect of pregabalin versus placebo on pain control of shoulder arthroscopy. This meta-analysis was performed using the random-effect model.

Results: Three randomized controlled trials were included in the meta-analysis. Overall, compared with control group for shoulder arthroscopy, pregabalin remarkably decreased pain scores at 0 to 1 hour (Std. MD = −0.57; 95% CI = −1.04 to −0.09; $P = .02$) and 12 hours (Std. MD = −0.37; 95% CI = −0.72 to −0.02; $P = .04$), as well as analgesic consumption (Std. MD = −1.84; 95% CI = −2.24 to −1.44; $P < .00001$), but showed no notable influence on pain scores at 24 hours (Std. MD = −0.54; 95% CI = −1.47 to 0.38; $P = .25$), nausea or vomiting (RR = 0.84; 95% CI = 0.53–1.33; $P = .45$), dizziness (RR = 1.14; 95% CI = 0.89–1.47; $P = .30$).

Conclusions: Pregabalin may benefit to pain control after shoulder arthroscopy.

Abbreviations: CI = confidence interval, RCTs = randomized controlled trials, SMD = standard mean difference.

Keywords: meta-analysis, pain management, pregabalin, randomized controlled trials, shoulder arthroscopy

1. Introduction

Arthroscopy has become common for the treatment of shoulder, knee, and hip diseases.[1–4] Many patients still encounter moderate to severe pain after arthroscopic surgery, and the pain is mainly derived from insertion of arthroscopic instruments into the joint, soft tissue dissection, and distention.[5–9] Postoperative pain after arthroscopic can complicate postoperative course by hindering patient early mobilization and rehabilitation.[10–12]

Intravenous opioid-based patient-controlled analgesia has been widely accepted to control postoperative pain, but leads to high incidence of opioid-related adverse effects such as respiratory depression, pruritus, constipation, and nausea.[13,14] The use of multimodal analgesic regimens comprising nonopioids may be effective to reduce opioid consumption without compromising the analgesic efficacy.[15,16] Pregabalin is a ligand of the α2-δ subunit of presynaptic voltage-gated calcium channels, and is widely used for neuropathic pain. It shows some potential in the multimodal approach for the control of postoperative pain without any apparent side effects.[17–19]

Recently, several studies have explored the efficacy of pregabalin versus placebo for the multimodal pain management of shoulder arthroscopy, but the results are conflicting.[20–22] With accumulating evidence, we therefore performed this meta-analysis of randomized controlled trials (RCTs) to explore the efficacy of pregabalin in patients with shoulder arthroscopy.

2. Materials and methods

Ethical approval and patient consent were not required because this was a meta-analysis of previously published studies. This meta-analysis was conducted and reported in adherence to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[23,24]

2.1. Search strategy and study selection

Two investigators have independently searched the following databases (inception to November 2019): PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases. The electronic search strategy was conducted using the following

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LC and BD contributed equally to this work.

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keywords "pregabalin," AND "arthroscopy," AND "shoulder." We also checked the reference lists of the screened full-text studies to identify other potentially eligible trials. The inclusive selection criteria were as follows: patients underwent shoulder arthroscopy; intervention treatments were pregabalin versus placebo; study design was RCT.

2.2. Data extraction and outcome measures

We extracted the following information: author, number of patients, age, female, body weight, duration of surgery, and detail methods in each group etc. Data were extracted independently by 2 investigators, and discrepancies were resolved by consensus. The primary outcomes were pain scores at 0 to 1 hours and 12 hours. Secondary outcomes included pain scores at 24 hours, analgesic consumption, nausea, vomiting, and dizziness.

2.3. Quality assessment in individual studies

Methodological quality of the included studies was independently evaluated using the modified Jadad scale.[25] There were 3 items for Jadad scale: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points). The score of Jadad Scale varied from 0 to 5 points. An article with Jadad score$\leq$2 was considered to have low quality. If the Jadad score$\geq$3, the study is thought to have high quality.[26]

2.4. Statistical analysis

We estimate the standard mean difference (Std. MD) with 95% confidence interval (CI) for continuous outcomes (pain scores at 0–1 h, 12 h , and 24 h, analgesic consumption) and risk ratio (RR) with 95% CIs for dichotomous outcomes (nausea, vomiting, and dizziness). The random-effects model was used regardless of heterogeneity. Heterogeneity was reported using the I^2 statistic, and $I^2 > 50\%$ indicated significant heterogeneity.[24,27] Whenever significant heterogeneity was present, we searched for potential sources of heterogeneity via omitting one study in turn for the meta-analysis or performing subgroup analysis. All statistical analyses were performed using Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

3. Results

3.1. Literature search, study characteristics, and quality assessment

A detailed flowchart of the search and selection results is shown in Figure 1. Two hundred eight potentially relevant articles are initially identified and 3 RCTs are finally included in the meta-analysis.[20–22] The baseline characteristics of 3 eligible RCTs in the meta-analysis are summarized in Table 1. The 3 studies are published between 2010 and 2016, and the sample size is 187. The doses of pregabalin include 150 mg[20] and 300 mg twice[21] before the surgery, as well as 150 mg twice daily for 4 times.[22]

Among the 3 studies included here, 2 studies report pain scores at 0 to 1 hour,[20,21] 2 studies report pain scores at 12 hours,[21,22] 3 studies report pain scores at 24 hours,[20–22] 2 studies report analgesic consumption,[20,21] and 3 studies report nausea, vomiting, and dizziness.[20–22] Jadad scores of the 3 included studies vary from 3 to 5, and all three studies are considered to have high quality according to quality assessment.

3.2. Primary outcomes: pain scores at 0 to 1 and 12 hours

Compared with control group for shoulder arthroscopy, pregabalin results in significantly lower pain scores at 0 to 1 hour (Std. MD = −0.57; 95% CI = −1.04 to −0.09; $P = .02$) with low heterogeneity among the studies ($I^2 = 48\%$, heterogeneity $P = .16$) (Fig. 2) and 12 hours (Std. MD = −0.37; 95% CI = −0.72 to −0.02; $P = .04$) with no heterogeneity among the studies ($I^2 = 0\%$, heterogeneity $P = .76$) (Fig. 3).

3.3. Sensitivity analysis

Low or even no heterogeneity is observed among the included studies for the primary outcomes, so we do not perform sensitivity analysis via omitting one study in turn to detect the heterogeneity.

3.4. Secondary outcomes

In comparison with control group for shoulder arthroscopy, pregabalin exhibits no obvious impact on pain scores at 24 hours (Std. MD = −0.54; 95% CI = −1.47 to 0.38; $P = .25$; Fig. 4), but is associated with substantially reduced analgesic consumption (Std. MD = −1.84; 95% CI = −2.24 to −1.44; $P < .00001$; Fig. 5). There is no statistical difference of nausea or vomiting (RR = 0.84; 95% CI = 0.53–1.33; $P = .45$; Fig. 6), dizziness (RR = 1.14; 95% CI = 0.89–1.47; $P = .30$; Fig. 7) between 2 groups.

4. Discussion

Shoulder arthroscopy has been widely used for shoulder diseases such as rotator cuff tear, and provides the improvement in shoulder function, the quality of sleep, and life.[28] The functional recovery of shoulder arthroscopy is affected by many factors such as pain control, anterior greater tubercle cysts, and operation technique.[29,30] Various methods have been developed to control postoperative pain after arthroscopic shoulder surgery, and they include subacromial/intra-articular infiltration of local anesthetic, suprascapular and/or axillary nerve block, and interscalene block.[31–33] However, these have some procedural difficulties and are limited by complications inherent in their invasive nature.[34] The use of nonsteroidal anti-inflammatory drugs and opioid drugs may result in some adverse events such as nausea, vomiting, and gastrointestinal bleeding. A multimodal approach is widely applied to reduce these opioid-related adverse effect.[35]

Gabapentinoids before surgical trauma were found to interact with other analgesics additively or synergistically to decrease inflammatory hyperalgesia.[36] Gabapentinoids as an adjunct to a multimodal approach can decrease opioid consumption for postoperative pain management.[37] Among the gabapentinoids, pregabalin demonstrated the analgesic efficacy for postoperative pain in various surgical settings.[38,39] Our meta-analysis has included 3 RCTs and 187 patients, and the results suggest that pregabalin leads to the substantial decrease in pain scores at 0–1 hours, 12 hours, and analgesic consumption for shoulder arthroscopy, but reveals no remarkable influence on pain scores at 24 hours. These indicate that pregabalin is effective for pain relief after shoulder arthroscopy, which is very crucial for the postoperative recovery.

Although there is no significant heterogeneity in this meta-analysis, several factors may lead to some bias. First, the doses of pregabalin are different, ranging from 150 mg to 600 mg daily for

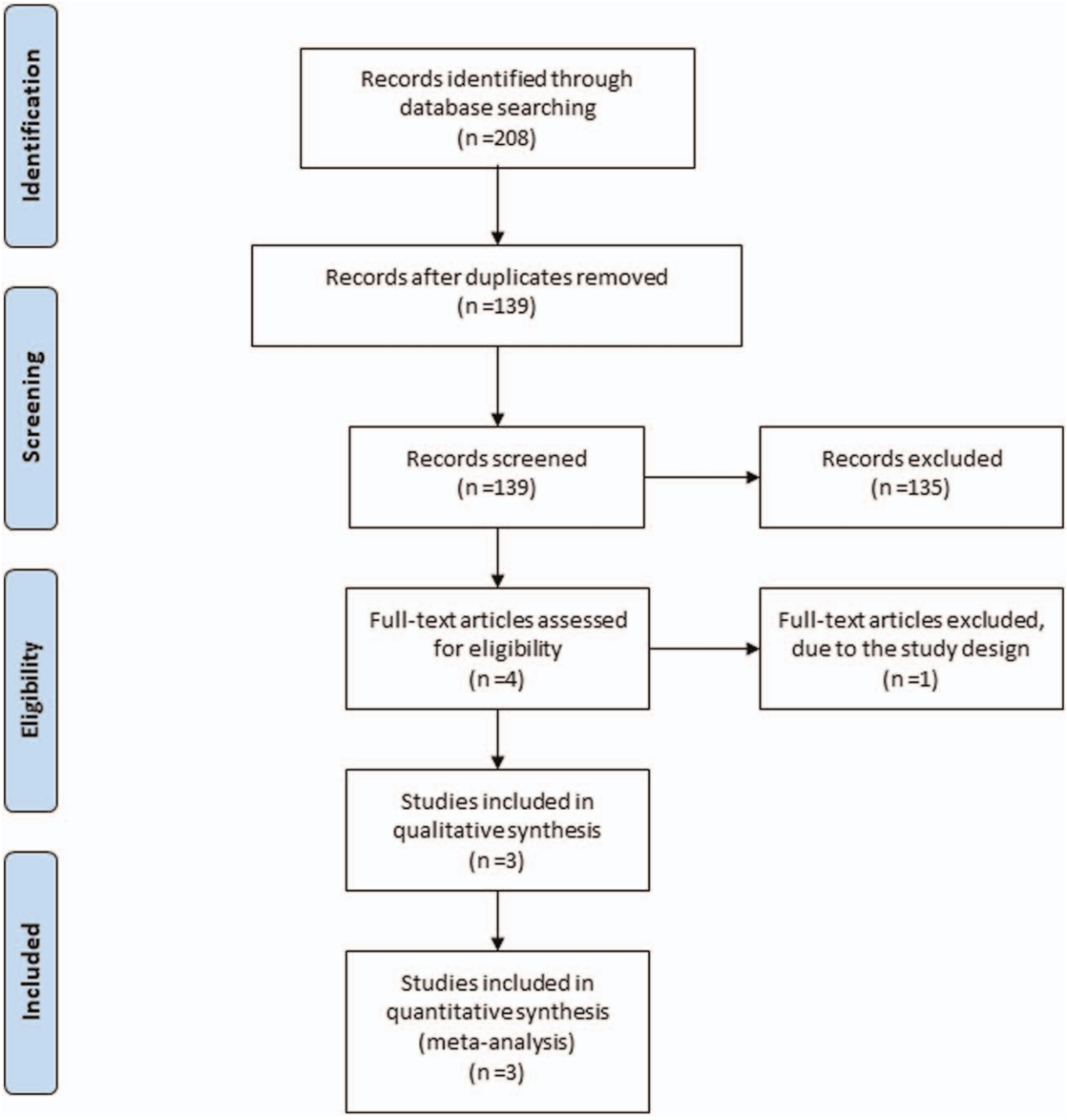

Figure 1. Flow diagram of study searching and selection process.

Table 1

Characteristics of included studies.

		Pregabalin group						Control group						
No.	Author	Number	Age (yrs)	Female (n)	Weight (kg)	Duration of surgery (min)	Methods	Number	Age (yrs)	Female (n)	Weight (kg)	Duration of surgery (min)	Methods	Jada scores
1	Ahn 2016	30	55 ± 9	17	64 ± 10	136 ± 31	Pregabalin 150 mg 1 h before anesthetic induction	30	51 ± 12	17	63 ± 13	138 ± 46	Placebo	4
2	Eskandar 2013	40	41.3 ± 14.7	18	75.2 ± 7.54	77 ± 19.89	Pregabalin 300 mg 12 and 1 h before surgery	40	42.15 ± 13.08	24	79.3 ± 7.88	82.5 ± 15.52	Placebo	5
3	Clendenen 2010	23	63 ± 11	6	—	—	150 mg, twice daily, administered orally for a total of four doses	24	60 ± 10	5	—	—	Placebo	3

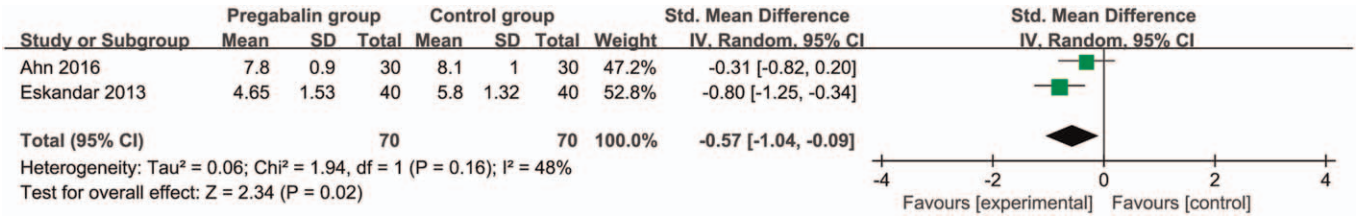

Figure 2. Forest plot for the meta-analysis of pain scores at 0 to 1 h.

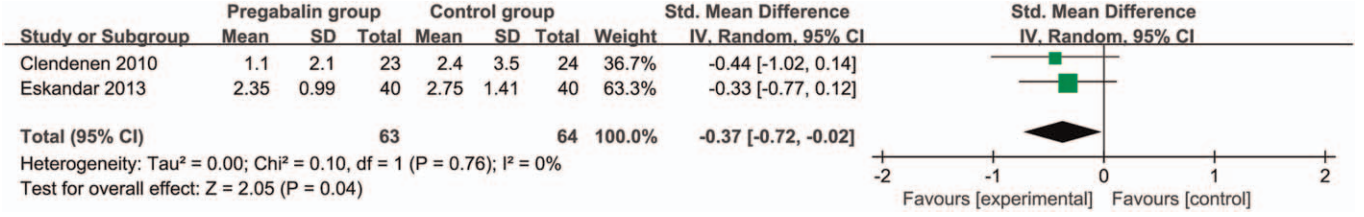

Figure 3. Forest plot for the meta-analysis of pain scores at 12 h.

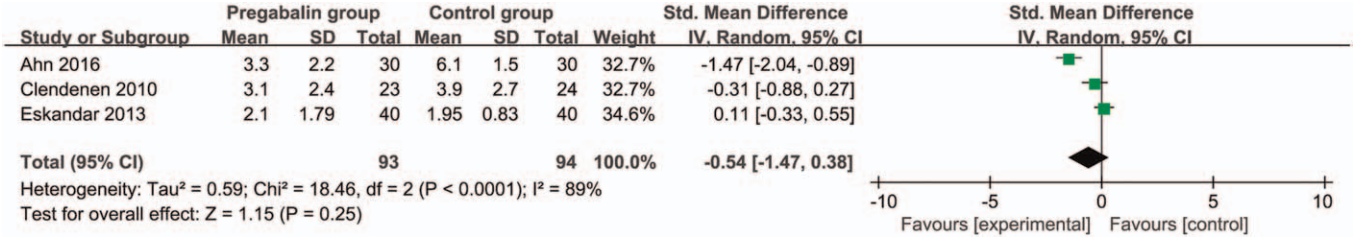

Figure 4. Forest plot for the meta-analysis of pain scores at 24 h.

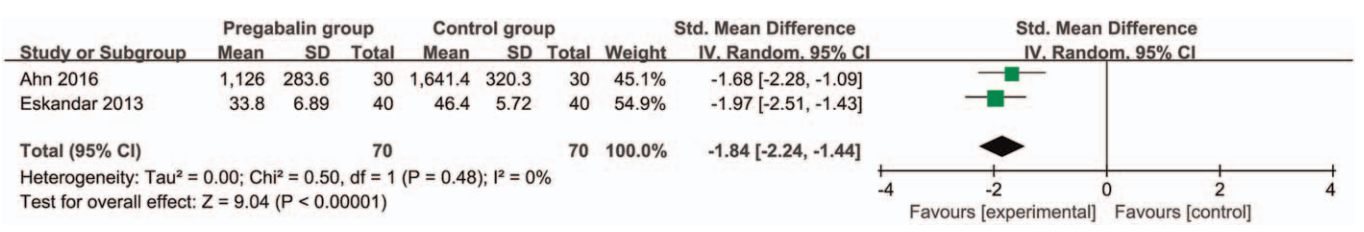

Figure 5. Forest plot for the meta-analysis of analgesic consumption.

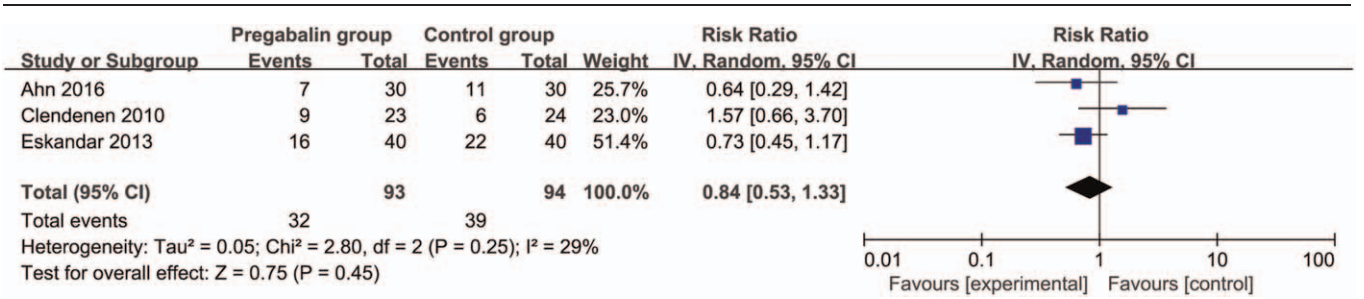

Figure 6. Forest plot for the meta-analysis of nausea and vomiting.

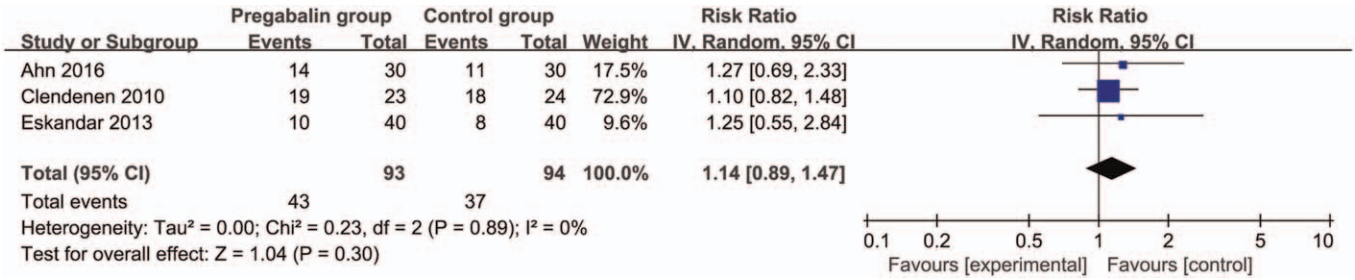

Figure 7. Forest plot for the meta-analysis of dizziness.

should arthroscopy. Second, 2 studies report pregabalin use before the surgery,[20,21] but the remaining study reports pregabalin after the surgery.[22] Preventive analgesia is a type of treatment before surgical stimuli and aims to prevent the central sensitization of the dorsal horn caused by incisional injury. Pregabalin has the ability to reduce central sensitization and hyperalgesia after tissue injury by inhibiting calcium influx in voltage-gated calcium channels.[40] Third, different procedures in shoulder arthroscopy produce various levels of pain intensity. Regarding the adverse events, the incidence of nausea, vomiting, and dizziness shows no statistical difference between 2 groups.

Our meta-analysis has included 3 RCTs and 187 patients at the follow-up of 1 to 24 hours, and allows the systematic assessment of pain intensity. Various procedures ranged from simple debridement to massive rotator cuff repair, which helps the general evaluation of pregabalin for shoulder arthroscopy. However, there are also several limitations. First, our analysis is based on 3 RCTs, and all of them have relatively small sample sizes ($n < 100$). Overestimation of the treatment effect is more likely in smaller trials compared with larger samples. Second, although there is no significant heterogeneity, different doses and methods of pregabalin, and various procedures may lead to some bias. Among the 3 included RCTs, 1 RCT involves the bankart repair and rotator cuff repair,[20] another RCT just provides the information of should arthroscopy. Thus, it is difficult to divide them into different procedures for meta-analysis, and the meta-analysis of different procedures may produce some bias. Third, it is not feasible to perform the meta-analysis of some important index such as discharge time based on current RCTs. Fourth, regarding the concomitant medications or regional anesthesia, 2 RCTs report induction with propofol and remifentanil [20] or thiopental and atracurium,[21] while the remaining RCT reports interscalene brachial plexus block with 30 mL of 0.5% ropivacaine,[22] which may have some influence on the pain assessment of pregabalin assessment.

5. Conclusions

Pregabalin may be effective and safe to relieve the pain after shoulder arthroscopy.

Author contributions

Funding acquisition: Bo Du, Chunhong Liu.
Investigation: Bo Du, Chunhong Liu.
Software: Shuang Cheng.
Validation: Yangming Jiang.
Visualization: Ling Cheng.
Writing – original draft: Ling Cheng, Xiaohong Tan, Ke Qian.
Writing – review & editing: Ling Cheng, Ke Qian.

Correction

The corresponding author originally appeared incorrectly as Ling Cheng. It has been corrected to Ke Qian.

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