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The efficacy of dexamethasone on pain management for knee arthroscopy

A meta-analysis of randomized controlled trials

Chuangang Peng, MD, Chen Li, MD, Baoming Yuan, MD, Jianhang Jiao, MD*

Abstract

Introduction: The impact of dexamethasone on pain management for knee arthroscopy remains controversial. We conduct a systematic review and meta-analysis to explore the influence of dexamethasone for knee arthroscopy.

Methods: We search PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases through October 2018 for randomized controlled trials (RCTs) assessing the effect of dexamethasone on pain intensity for patients with dental implant. This meta-analysis is performed using the random-effect model.

Results: Four RCTs involving 228 patients are included in the meta-analysis. Overall, compared with control group for knee arthroscopy, dexamethasone supplementation has no notable effect on pain scores at 4 to 6 hours (Std. MD = 0.99; 95% CI = −2.97 to 4.95; $P = .62$), but exerts significantly favorable promotion to pain scores at 12 hours (Std. MD = −1.06; 95% CI = −1.43 to −0.69; $P < .00001$), duration of block (Std. MD = 1.87; 95% CI = 0.65 to 3.10; $P = .003$), time to first analgesic requirement (Std. MD = 0.90; 95% CI = 0.51 to 1.29; $P < .00001$), analgesic consumption (Std. MD = -1.62; 95% CI = −2.31 to −0.93; $P < .00001$), and patient satisfaction (Std. MD = 1.15; 95% CI = 0.73 to 1.58; $P < .00001$).

Conclusions: Dexamethasone supplementation has importantly positive influence on pain control for knee arthroscopy.

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

Keywords: dexamethasone, knee arthroscopy, meta-analysis, pain management, randomized controlled trials

1. Introduction

Knee arthroscopy is widely performed for knee diseases, but many patients encounter moderate to severe acute postoperative pain.[1–5] Femoral nerve blockade is used to promote postoperative analgesia and benefits to hospital discharge.[6–8] The duration of nerve blockade action with ropivacaine is approximately 10 to 12 hours.[9–11] However, postoperative intravenous opioids are required in about 61% of patients with knee surgery after nerve blockade, while 3% of patients receiving femoral nerve blockade need intravenous opioids after knee arthroscopy without anterior cruciate ligament.[12]

Many adjuvants have been developed to prolong nerve blockade for a few hours.[13] For instance, dexamethasone exhibits promising results in significantly prolonging the duration of peripheral nerve blockade in various orthopedic procedures of the upper and lower extremities.[14,15] Dexamethasone added to ropivacaine is reported to increase the duration of analgesia of an interscalene block from an average of 11.8 to 22.2 hours.[16] This analgesia promotion is also confirmed by other studies, and the prolonged analgesia of perineural dexamethasone may be caused by the direct action on the nerve or through systemic absorption.[15,17]

However, the efficacy of dexamethasone supplementation for knee arthroscopy has not been well established. Recently, several studies on the topic have been published, and the results have been conflicting.[18–20] With accumulating evidence, we therefore perform a systematic review and meta-analysis of RCTs to compare the efficacy of dexamethasone supplementation vs placebo for knee arthroscopy.

2. Materials and methods

Ethical approval and patient consent are not required because this is a systematic review and meta-analysis of previously published studies. The systematic review and meta-analysis are conducted and reported in adherence to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[21]

2.1. Search strategy and study selection

Two investigators have independently searched the following databases (inception to October 2018): PubMed, EMbase, Web

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Orthopedic Medical Center of the Second Hospital of Jilin University, PR China.

** Correspondence: Jianhang Jiao, Orthopedic Medical Center of the Second Hospital of Jilin University, NO.218 Ziqiang Street, Nanguan District, Jilin 130041, PR China (e-mail: jianhang@jlu.edu.cn).*

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of science, EBSCO, and Cochrane library databases. The electronic search strategy is conducted using the following keywords: dexamethasone and knee arthroscopy. We also check the reference lists of the screened full-text studies to identify other potentially eligible trials.

The inclusive selection criteria are as follows:

1. population: patients undergoing knee arthroscopy; (
2. intervention: dexamethasone supplementation;
3. comparison: placebo;
4. study design: RCT.

2.2. Data extraction and outcome measures

We have extracted the following information: author, number of patients, age, female, weight or body mass index, American Society of Anesthesiologists (ASA), and detail methods in each group etc. Data have been extracted independently by 2 investigators, and discrepancies are resolved by consensus. We also contact the corresponding author to obtain the data when necessary.

The primary outcomes are pain scores at 4–6 hours and 12 hours. Secondary outcomes duration of block, time to first analgesic requirement, analgesic consumption, and patient satisfaction.

2.3. Quality assessment in individual studies

Methodological quality of the included studies is independently evaluated using the modified Jadad scale.[22] There are 3 items for Jadad Scale: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points). The score of Jadad Scale varies from 0 to 5 points. An article with Jadad score ≤ 2 is considered to be of low quality. If the Jadad score ≥ 3, the study is thought to be of high quality.[23]

2.4. Statistical analysis

We estimate the standard mean difference (Std. MD) with 95% confidence interval (CI) for continuous outcomes (pain scores at 4–6 hours and 12 hours, duration of block, time to first analgesic requirement, analgesic consumption, and patient satisfaction). A random-effects model is used regardless of heterogeneity. Heterogeneity is reported using the I^2 statistic, and $I^2 > 50\%$ indicates significant heterogeneity.[24] Whenever significant heterogeneity is present, we search for potential sources of heterogeneity via omitting 1 study in turn for the meta-analysis or performing subgroup analysis. All statistical analyses are 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. Four hundred twenty three potentially relevant articles are identified initially. Finally, 4 RCTs that meet our inclusion criteria are included in the meta-analysis.[18–20,25]

The baseline characteristics of the 4 eligible RCTs in the meta-analysis are summarized in Table 1. The 4 studies were published between 2016 and 2018, and sample sizes ranged from 40 to 78 with a total of 228. Drug administration included nerve block with dexamethasone,[18,19] intra-articular,[20] and intravenous dexamethasone.[25]

Among the 4 studies included here, 2 studies reported pain scores at 4–6 hours and 12 hours,[19,25] 2 studies reported duration of block and time to first analgesic requirement,[18,19] 2 studies reported analgesic consumption,[19,25] 2 studies reported and patient satisfaction.[19,20] Jadad scores of the 4 included studies vary from 3 to 5, and all 4 studies were

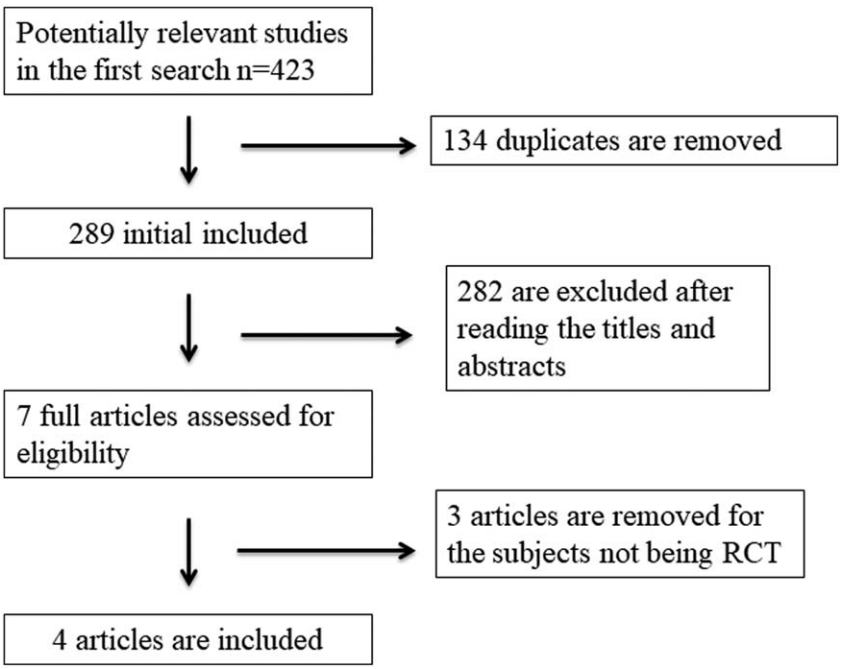

Figure 1. Flow diagram of study searching and selection process.

Table 1

Characteristics of included studies.

NO.	Author	Dexamethasone group						Control group						Jada scores
		Number	Age (years)	Female (n)	Weight (kg) or body mass index (kg/m²)	ASA (I/II)	Methods	Number	Age (years)	Female (n)	Weight (kg) or body mass index (kg/m²)	ASA (I/II)	Methods	
1	Veneziano, 2018	23	15.1±2.0	12	24.6±3.7	12/11	femoral nerve block with ropivacaine 0.5% plus perineural dexamethasone 0.1 mg/kg (maximum 4 mg)	27	14.6±2.0	11	22.6±4.1	17/10	femoral nerve block with ropivacaine 0.5% and intramuscular saline	4
2	Ibrahim, 2018	30	29.17±8.78	1	83.1±12.34	–	adductor canal block with 20 mL bupivacaine 0.5% + 2 ml dexamethasone	30	27.7±7.13	0	80.3±10.29	–	adductor canal block with 20 mL bupivacaine 0.5% + 2 mL normal saline	5
3	Moeen 2017	20	31.8±9.40	5	71.15±5.81	13/7	18 ml intraarticular bupivacaine 0.25% with either dexamethasone 8 mg	20	29.85±7.94	5	69.8±5.17	12/8	18 mL intraarticular bupivacaine 0.25% with 2 mL of normal saline	4
4	Moyano, 2016	37	39.9	10	–	–	10 mg of intravenous dexamethasone	41	44.3	12	–	–	intravenous 0.9% normal saline	4

ASA = American Society of Anesthesiologists.

considered to be high-quality ones according to quality assessment.

3.2. Primary outcomes: pain scores at 4–6 hours and 12 hours

These outcome data are analyzed with the random-effects model, and compared to control group for knee arthroscopy, dexamethasone supplementation exerts no positive influence on pain scores at 4–6 hours (Std. MD = 0.99; 95% CI = −2.97 to 4.95; $P = .62$) with significant heterogeneity among the studies ($I^2 = 99\%$, heterogeneity $P < .00001$) (Fig. 2), but can significantly reduce pain scores at 12 hours (Std. MD = −1.06; 95% CI = −1.43 to −0.69; $P < .00001$) with no heterogeneity among the studies ($I^2 = 0\%$, heterogeneity $P < .00001$) (Fig. 3).

3.3. Sensitivity analysis

Significant heterogeneity is observed among the included studies for pain scores at 4–6 hours. Because there are just 2 RCTs included for the analysis of pain scores at 4–6 hours, 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 knee arthroscopy, dexamethasone supplementation is associated with remarkably increased duration of block (Std. MD = 1.87; 95% CI = 0.65 to 3.10; $P = .003$; Fig. 4) and time to first analgesic requirement (Std. MD = 0.90; 95% CI = 0.51 to 1.29; $P < .00001$; Fig. 5), reduced analgesic consumption (Std. MD = −1.62; 95% CI = −2.31 to −0.93; $P < .00001$; Fig. 6), and improved patient satisfaction (Std. MD = 1.15; 95% CI = 0.73 to 1.58; $P < .00001$; Fig. 7).

4. Discussion

Dexamethasone has been reported to be an effective adjuvant for peripheral nerve blocks, but its detail mechanism is undefined.[19] Previous studies proved that dexamethasone action may be through altering the inflammatory response and exert the direct effect on nociceptive C-fibers.[26] Prolonged analgesia when added to local anesthetics is either by inducing vasoconstriction and reducing the absorption of local anesthetic or by increased activity of inhibitory potassium channels on nociceptive C-fibers, decreased activity and prolonged sensory and motor blockade.[27]

The addition of dexamethasone (1 and 4 mg) to subsartorial saphenous nerve blocks reveals significantly increased duration of postoperative analgesia by 8–13 hours following anterior cruciate ligament reconstruction,[28] which is longer than the time in another study.[19] These may be caused by that the majority of patients in the Chisholm study obtained intravenous dexamethasone 4 to 8 mg, while the other study involves dexamethasone supplementation for nerve block. Our meta-analysis suggests that compared to control group for knee arthroscopy, dexamethasone supplementation has no remarkable impact on pain scores at 4–6 hours, but reveals important favorable influence on pain scores at 12 hours, duration of block, time to first analgesic requirement, analgesic consumption, and patient satisfaction.

One meta-analysis concluded that perineural dexamethasone can prolong the duration of analgesia and reduce postoperative

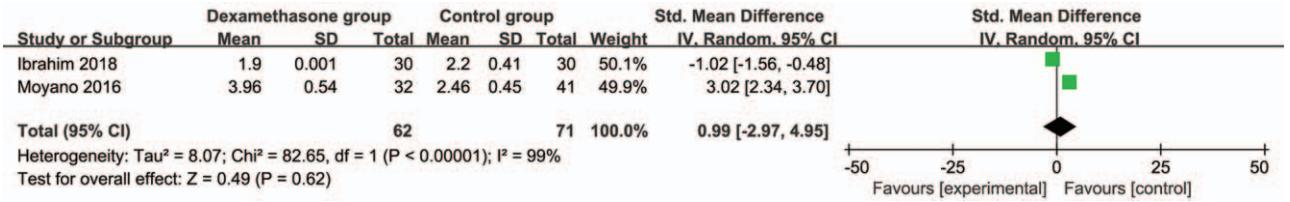

Figure 2. Forest plot for the meta-analysis of pain scores at 4–6 hours.

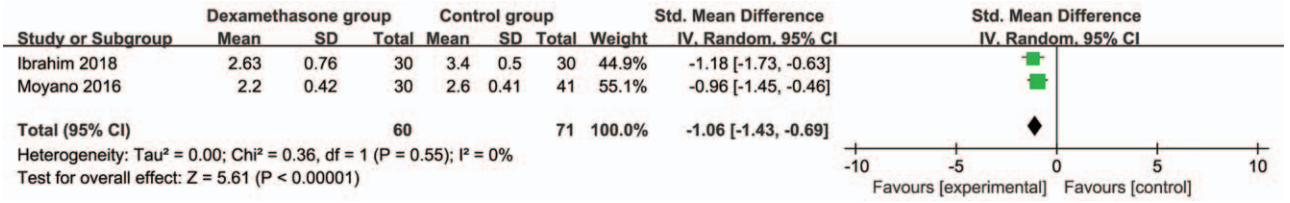

Figure 3. Forest plot for the meta-analysis of pain scores at 12 hours.

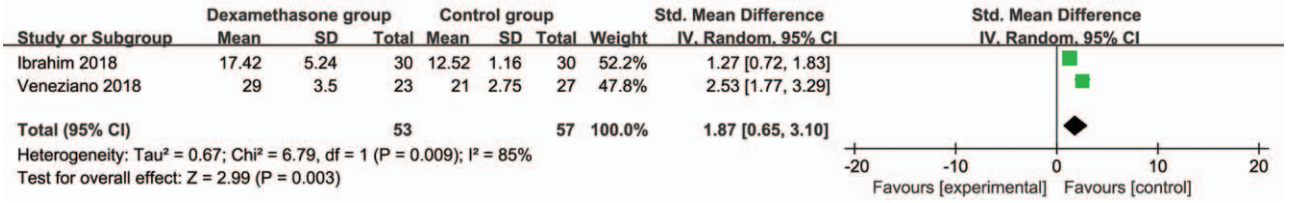

Figure 4. Forest plot for the meta-analysis of duration of block.

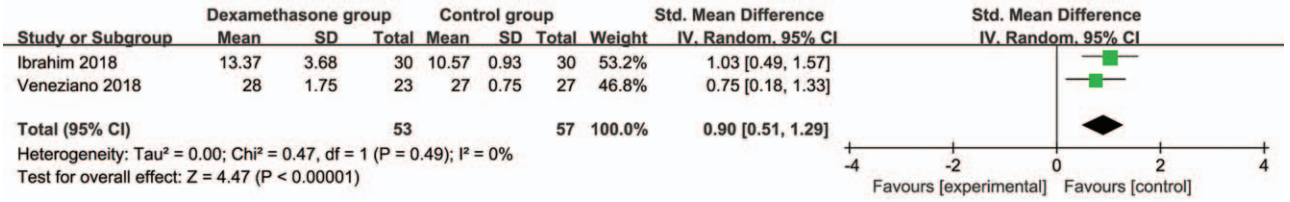

Figure 5. Forest plot for the meta-analysis of time to first analgesic requirement.

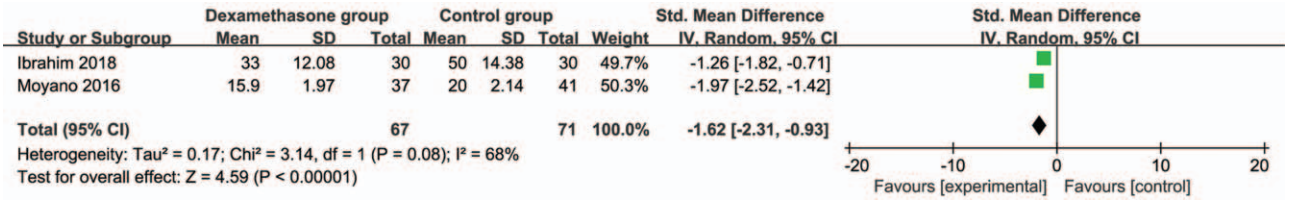

Figure 6. Forest plot for the meta-analysis of analgesic consumption.

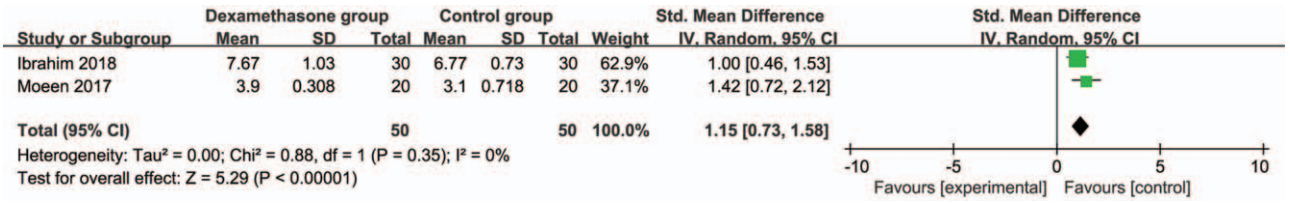

Figure 7. Forest plot for the meta-analysis of patient satisfaction.

morphine consumption and pain scores.[29] In addition, perineural dexamethasone enables the increase in the duration of interscalene block despite the dose and the administration route.[30] In contrast, other studies reveal that perineural dexamethasone has a minor effect on the quality and duration of bupivacaine sciatic and ankle blocks compared with systemic administration.[31] This confounding effect and the significant heterogeneity in this meta-analysis may result from the type of anesthesia methods, the routine and doses of dexamethasone administration.

This meta-analysis has several potential limitations. Firstly, our analysis is based on 4 RCTs, and all of them have a relatively small sample size ($n < 100$). These may lead to overestimation of the treatment effect in smaller trials. More RCTs with large sample size should be conducted to explore this issue. Next, various types of anesthesia methods, routine and doses of dexamethasone administration are included in this meta-analysis, which may have some impact on the pooling results. Finally, different operation procedures are involved for knee arthroscopy, and may also after the pooled results.

5. Conclusions

Dexamethasone supplementation can provide additional benefits for pain control in patients with knee arthroscopy.

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