

The efficiency and safety of dexamethasone for pain control in total joint arthroplasty

A meta-analysis of randomized controlled trials

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Abstract

Background: This meta-analysis aimed to evaluate the efficiency and safety of dexamethasone administration in total knee and hip arthroplasties.

Methods: Two researchers search the relevant studies independently including Embase (1980–017.04), PubMed (1966–017.04), ScienceDirect (1985–017.04), Web of Science (1950–2017.03), and Cochrane Library for potential relevant studies. After testing for heterogeneity between studies, data were aggregated for random-effects models when necessary. The results of dichotomous outcomes were expressed as risk difference (RD) with a 95% confidence intervals (CIs). For continuous various outcomes, mean difference (MD) or standard mean difference (SMD) with a 95% confidence intervals (CIs) was applied for assessment. Meta-analysis was performed using Stata 11.0 software.

Results: Four randomized controlled trials (RCTs) including 361 patients met the inclusion criteria. The present meta-analysis indicated that there were significant differences between groups in terms of visual analogue scale (VAS) score at 12 hours (SMD = -0.579, 95% CI: -0.780 to -0.357, $P = .000$), 24 hours (SMD = -0.820, 95% CI: -1.036 to -0.604, $P = .000$), and 48 hours (SMD = -0.661, 95% CI: -1.149 to -0.172, $P = .008$). Dexamethasone was associated with a lower opioid consumption at 12 hours (SMD = -0.245, 95% CI: -0.465 to -0.025, $P = .029$), 24 hours (SMD = -0.285, 95% CI: -0.505 to -0.064, $P = .011$), and 48 hours (SMD = -0.989, 95% CI: -1.710 to -0.267, $P = .007$).

Conclusion: Dexamethasone could significantly reduce postoperative pain scores and opioid consumption within the 1st 48 hours following total joint arthroplasty (TJA). The overall evidence quality was moderate to low, further high-quality RCTs are needed to identify the optimal dose of dexamethasone for reducing pain after TJA.

Abbreviations: LOS = length of stay, RCT = randomized controlled trial, TJA = total joint arthroplasty, VAS = visual analogue scale.

Keywords: dexamethasone, meta-analysis, pain control, total joint arthroplasty

1. Introduction

Total joint arthroplasty (TJA) is considered to be successful procedure for the treatment of degenerative arthritis. However, following the procedure, 30% to 77% of patients suffer moderate to severe postoperative pain.^[1] Moreover, nausea and vomiting are the most frequent adverse effects of the anesthesia, with a

reported incidence of 20% to 83%.^[2,3] Appropriate postoperative pain control is essential for early recovery and better functional outcomes. Besides, optimal pain management may decrease length of stay (LOS) and the risk of thromboembolism, such as deep vein thrombosis and pulmonary embolism. Several strategies have been proposed to minimize postoperative pain, nausea, and vomiting following TJA including peripheral nerve block, local infiltration anesthesia, and intrathecal morphine.^[4–6] However, additional opioid administration, which is frequently performed as a beneficial adjunct to multimodal regimes for pain relief, may result in adverse effects, for instance, nausea, vomiting, respiratory depression, and urinary retention. Postoperative pain management has been an interesting topic for a few decades, and optimal anesthesia remains controversial.

Dexamethasone is a high-potency, long-acting glucocorticoid that has been widely used in the field of orthopedics. Dexamethasone has been reported to inhibit peripheral phospholipase, which decreases the pain-aggravating agents from the cyclooxygenase and lipoxygenase pathways.^[7] Previous studies have shown the analgesic effect of dexamethasone in general and orthopedic surgery. In addition, preoperative administration of dexamethasone has been reported to reduce postoperative nausea and vomiting.^[8,9] However, some potential side effects associated with dexamethasone administration limit its regular use in surgical procedures, although Salerno and Hermann^[1] demonstrated that it was effective and safe for pain management.

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Currently, whether the administration of dexamethasone is effective and safe in reducing pain score and opioid consumption in TJAs remains unclear due to a lack of reliable evidence from high-quality randomized controlled trials (RCTs). Therefore, we performed the present systemic review and meta-analysis to evaluate the efficiency and safety of dexamethasone administration in total knee and hip arthroplasties.

2. Methods

This systematic review was reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. The study was approved by the ethics committee of the First People's Hospital of Jining.

2.1. Search strategy

Two researchers search the relevant studies independently including Embase (1980–017.04), PubMed (1966–017.04), ScienceDirect (1985–017.04), Web of Science (1950–2017.03), and Cochrane Library for potential relevant studies. Reference

lists of all the potential included studies and relevant reviews were hand-searched for any additional trials. No restrictions were imposed on language. The Mesh terms and their combinations used in the search were as follows: “analgesia” OR “pain management” OR “pain control” OR “total knee arthroplasty or replacement” OR “total hip arthroplasty or replacement” AND “dexamethasone”. A 3rd reviewer acted as a judge if there was any disagreement. The retrieval process is presented in Fig. 1.

2.2. Inclusion and exclusion criteria

Studies were considered eligible if they met the following criteria: 1) Published clinical RCTs; 2) Patients undergoing TJAs, experiment group received intravenous or topical injection of dexamethasone for pain management and control group received placebo or nothing; 3) Reported surgical outcomes, including visual analogue scale (VAS) scores, opioid consumption, LOS and postoperative adverse effects including the risk of nausea, vomiting. Studies would be excluded from present meta-analysis for incomplete data, case reports, conference abstract, or review articles.

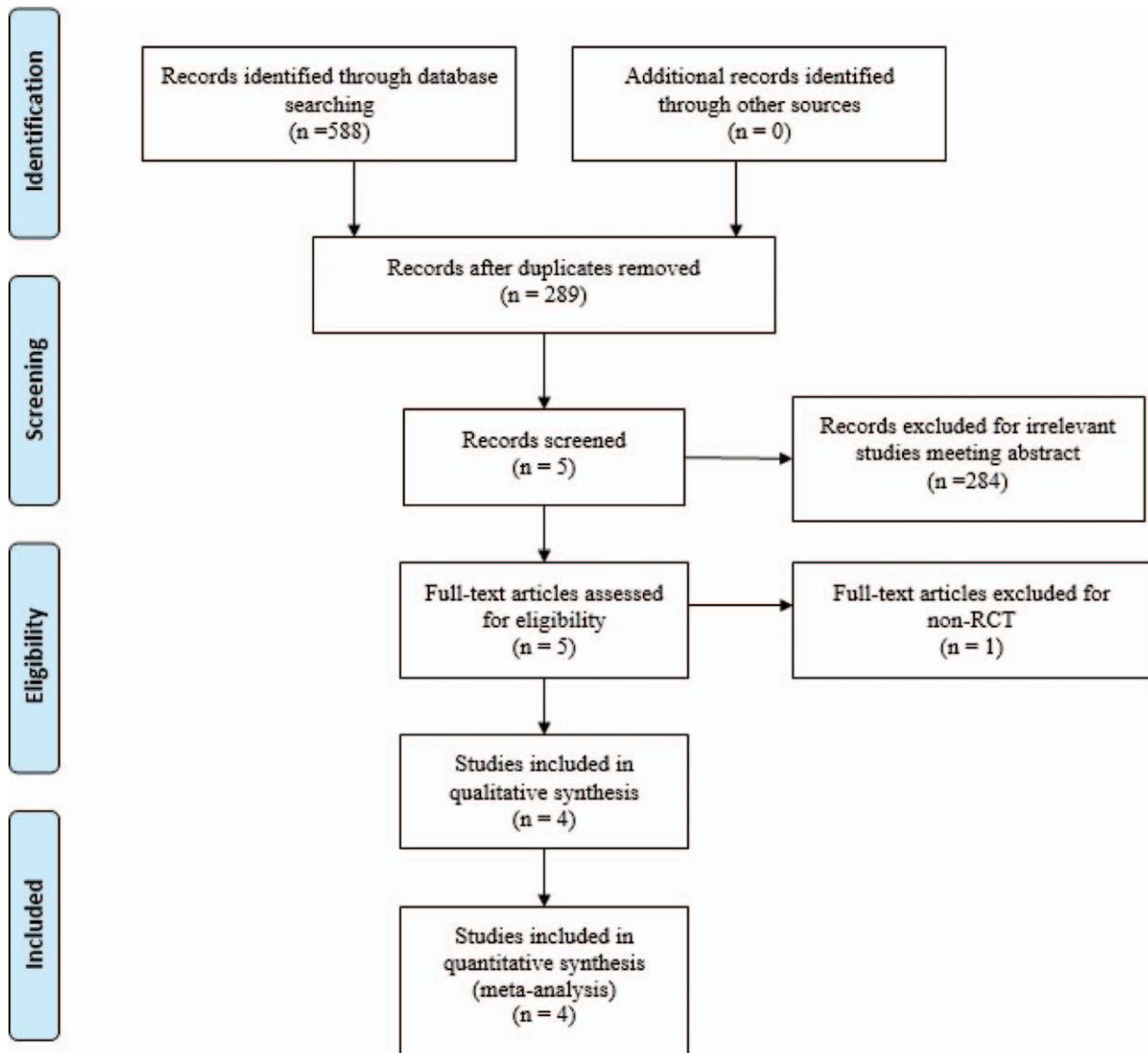


Figure 1. Search results and the selection procedure.

2.3. Selection criteria

Two authors independently reviewed all the abstracts of the potential studies identified by the above searches. After an initial decision, full text of the studies that potentially met the inclusion criteria were reviewed and final decision was made. A senior reviewer is consult in case of disagreement regarding which studies to include.

2.4. Data extraction

A standard form for data extraction is printed for data extraction. Two authors independently extracted the relevant data from the included articles. Details of incomplete data of included studies are obtained by consulting the corresponding author. Following data were extracted: First author names, published year, sample size, study design, comparable baseline, dosage of dexamethasone, and duration of follow-up. Other relevant data were also extracted from individual studies.

2.5. Quality assessment

Quality assessment of the included RCTs was assessed by 2 authors independently which used the Cochrane Collaboration tool. We conducted “risk of bias” table including the following key points: random sequence generation, allocation concealment, blinding, incomplete outcome data, free of selective reporting, and other bias, each item was recorded by “Yes,” “No,” or “Unclear.”

The qualities of evidence of main outcomes in present meta-analysis were evaluated using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) system including the following items: risk of bias, inconsistency, indirectness, imprecision, and publication bias which was assessed according to guideline panels of GRADEpro software. The recommendation level of evidence is classified into the following categories: high, which means that further research is unlikely to change confidence in the effect estimate; moderate, which means that further research is likely to significantly change confidence in the effect estimate and may change the estimate; low, which means that further research is likely to significantly change confidence in the effect estimate and to change the estimate; and very low, which means that any effect estimate is uncertain.

2.6. Data analysis and statistical methods

All calculations were carried out with Stata 11.0 (The Cochrane Collaboration, Oxford, UK). Statistical heterogeneity was assessed based on the value of P and I^2 using the standard chi-square test. When $I^2 > 50\%$, $P < .1$ was considered to be significant heterogeneous. The random-effect model was performed for meta-analysis; otherwise, the fixed-effect model was used. When possible, subgroup analyses were conducted to explore the origins of the heterogeneity. The results of dichotomous outcomes (postoperative adverse effects, including the risk of nausea and vomiting) were expressed as risk difference (RD) with 95% confidence intervals (CIs). For continuous various outcomes (VAS scores, opioid consumption, and LOS), mean difference (MD) or standard mean difference (SMD) with a 95% confidence intervals (CIs) was applied for assessment. Subgroup analysis was conducted according to the dosage of dexamethasone.

3. Results

3.1. Search result

A total of 588 studies were preliminarily reviewed. By screening the titles and reading the abstracts and entire contents, 584 reports were excluded from present meta-analysis following inclusion criteria. No gray reference was included. Finally, 4 RCTs^[10-13] which had been published between 2008 and 2016 were enrolled in present meta-analysis and include 183 participates in the dexamethasone groups and 178 patients in the control groups.

3.2. Study characteristics

Demographic characteristics, the details about the included studies, are summarized in Table 1. The sample size of the included studies ranged from 40 to 193. All of them evaluated the efficiency and safety of dexamethasone for reducing postoperative pain in TJA. Experimental groups received intravenous or topical dexamethasone, while control groups received placebo or none. There is a variation in dosage of dexamethasone in experimental groups. Three studies^[10,11,13] performed general anesthesia and one^[12] performed spinal anesthesia. Patient control analgesia with opioid was applied in all participates for concomitant pain management. The follow-up period ranged from 1 to 12 months.

Table 1

Trials characteristics.

Studies	Reference type	Cases (D/C)	Mean age (D/C)	Female patient (D/C)	Surgical procedure (D/C)	Anesthesia	Dexamethasone intervention	Concomitant pain management	Follow-up
Kardash et al 2008 ^[12]	RCT	25/25	69/68.8	12/14	THA	Spinal anesthesia	E: intravenous 40 mg dexamethasone, C: equal volume normal saline	PCA with morphine	1 m
Backes et al 2013 ^[13]	RCT	41/37	65.1/66.3	NS	TJA	General anesthesia	E: intravenous 10 mg dexamethasone and ondansetron 4 mg, C: intravenous ondansetron 4 mg	PCA with hydromorphone	6 mo
Ikeuchi et al 2014 ^[10]	RCT	20/20	77/76	18/16	TKA	General anesthesia	E: periarticular 6.6 mg dexamethasone, C: none	PCA with fentanyl	12 mo
Sherif and Elersy 2016 ^[11]	RCT	97/96	62/63	57/58	TKA	General anesthesia along with FNB	E: perineural 8 mg dexamethasone, C: equal volume normal saline	PCA with morphine	2 mo

C = control group, D = dexamethasone groups, FNB = femoral nerve block, NS = not stated, PCA = patient controlled analgesia, RCT = randomized controlled trial, TJA = total joint arthroplasty, THA = total hip arthroplasty, TKA = total knee arthroplasty.

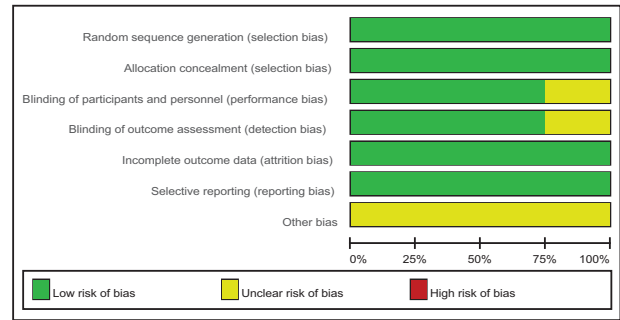
Table 2
Methodological quality of the randomized controlled trials.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Backes 2013	+	+	+	?	+	+	?
Ikeuchi 2014	+	+	?	+	+	+	?
Kardash 2008	+	+	+	+	+	+	?
Sherif 2016	+	+	+	+	+	+	?

3.3. Risk of bias assessment

Cochrane Collaboration tool was used to assess the RCTs (Table 2). All the RCTs^[10-14] provided clear inclusion and exclusion criteria, and suggested a methodology of randomization, demonstrating that the randomization algorithm was

Table 3
Risk of bias.



generated by a computer program. Furthermore, all RCTs stated allocation concealment was achieved by the sealed envelope approach. Double blinding was provided in 3 RCTs.^[11-13] Three studies^[10-12] attempted to blind the assessors. All of them suggest the outcomes for at least 95% of the patients. Each risk of bias item was presented as a percentage across all included studies. The percentage indicated the proportion of different levels of risk of bias for each item (Table 3).

3.4. Outcomes for meta-analysis

3.4.1. VAS scores at 12 hours. Four articles^[10-13] reported the outcomes of VAS scores at 12 hours following TJA. There was no significant heterogeneity among the studies ($\chi^2=4.09$, $df=3$, $I^2=26.7\%$, $P=.252$); therefore, a fixed-effects model was used. Pooled results demonstrated that VAS scores at 12 hours in control groups was significant higher than in dexamethasone groups (SMD = -0.579, 95% CI: -0.780 to -0.357, $P=.000$; Fig. 2).

3.4.2. VAS scores at 24 hours. Four studies^[10-15] reported VAS scores at 24 hours following TJA. There was no significant heterogeneity among the studies ($\chi^2=5.72$, $df=3$, $I^2=47.6\%$, $P=.126$); therefore, a fixed-effects model was applied. Pooled results demonstrated that the VAS scores at 24 hours in control

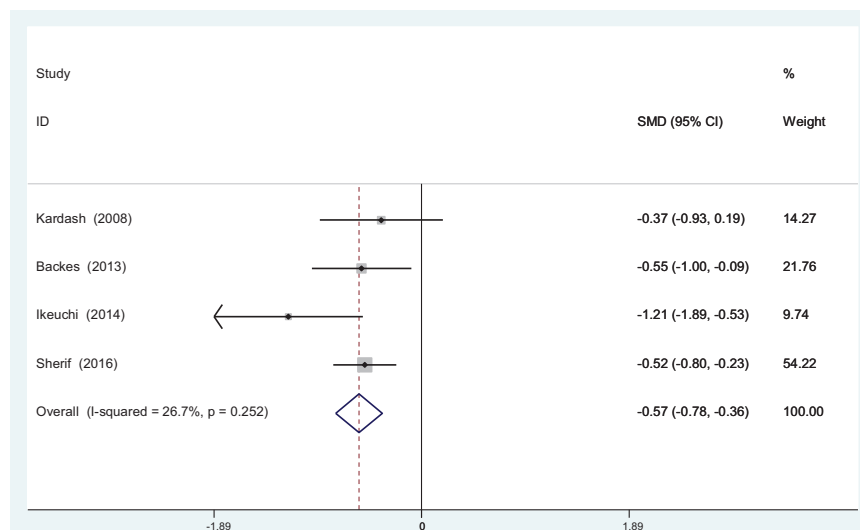


Figure 2. Forest plot diagram showing VAS scores at 12 hours following TJA. TJA=total joint arthroplasty, VAS=visual analogue scale.

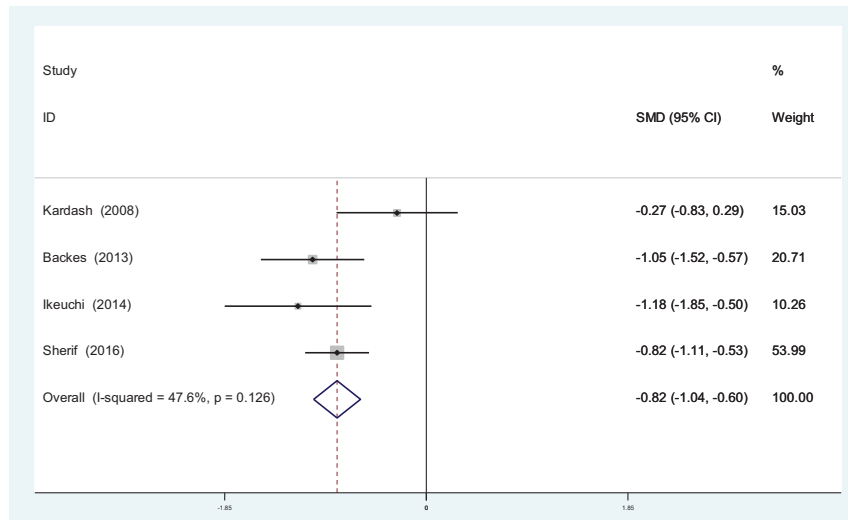


Figure 3. Forest plot diagram showing VAS scores at 24 hours following TJA. TJA=total joint arthroplasty, VAS=visual analogue scale.

groups were significantly higher than that in experimental groups (SMD = -0.820, 95% CI: -1.036 to -0.604, P = .000; Fig. 3).

3.4.3. VAS scores at 48 hours. Four reports^[10–15] provided the outcomes of VAS scores at 48 hours following TJA. There was significant heterogeneity among these studies; therefore, a random-effects model was used ($\chi^2 = 12.71$, $df = 3$, $I^2 = 76.4\%$, $P = .005$). Pooled results demonstrated that VAS scores at 48 hours in control groups were significantly higher than in experimental groups (SMD = -0.661, 95% CI: -1.149 to -0.172, $P = .008$; Fig. 4).

3.4.4. Opioid consumption at 12 hours. Opioid consumption at 12 hours after TJA was provided in 3 articles.^[11–13] No significant heterogeneity among these studies was found ($\chi^2 = 1.53$, $df = 2$, $I^2 = 0\%$, $P = .465$); therefore, a fixed-effects model was used. Opioid consumption at 12 hours in control groups was

significantly higher than in experimental groups (SMD = -0.245, 95% CI: -0.465 to -0.025, $P = .029$; Fig. 5).

3.4.5. Opioid consumption at 24 hours. Three studies^[11–13] provided data regarding opioid consumption at 24 hours after TJA. There was no significant heterogeneity among the pooled data ($\chi^2 = 1.42$, $df = 2$, $I^2 = 0\%$, $P = .491$), therefore a fixed-effects model was used. There was significance between the 2 groups in opioid consumption at 24 hours after TJA (SMD = -0.285, 95% CI: -0.505 to -0.064, $P = .011$; Fig. 6).

3.4.6. Opioid consumption at 48 hours. Four studies^[11–13] reported the outcomes of opioid consumption at 48 hours following TJA. There was significant heterogeneity among these studies; therefore, a random-effects model was used ($\chi^2 = 15.14$, $df = 2$, $I^2 = 86.8\%$, $P = .001$). Pooled results demonstrated that opioid consumption at 48 hours in control groups was

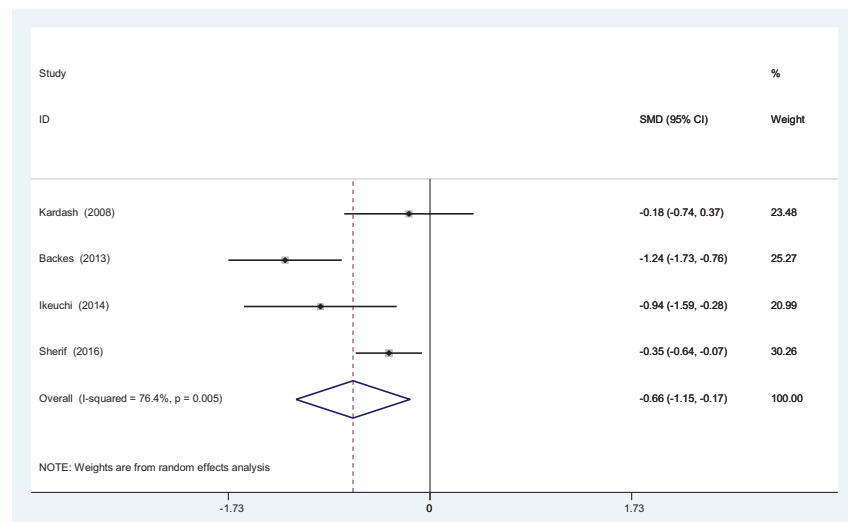


Figure 4. Forest plot diagram showing VAS scores at 48 hours following TJA. TJA=total joint arthroplasty, VAS=visual analogue scale.

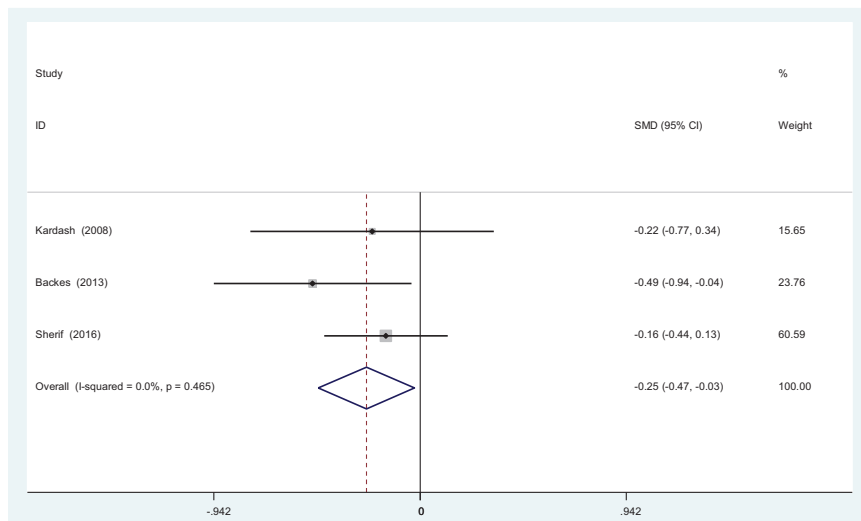


Figure 5. Forest plot diagram showing opioid consumption at 12 hours following total joint arthroplasty (TJA).

significantly higher than in experimental groups (SMD = -0.989, 95% CI: -1.710 to -0.267, P = .007; Fig. 7).

3.4.7. Length of hospital stay (LOS). Four studies^[10–13] reported the length of hospital stay between groups. Significant heterogeneity was identified in the pooled results; therefore, a random-effects model was used ($\chi^2 = 22.08$, $df = 3$, $I^2 = 86.4\%$, $P = .000$). There was no significant difference between the 2 groups (SMD = -0.373, 95% CI: -1.002 to 0.256, $P = .245$; Fig. 8).

3.4.8. The occurrence of nausea. The occurrence of nausea was provided in 4 studies.^[10–13] No significant heterogeneity among these studies was found; therefore, a fixed-effects model was used ($\chi^2 = 1.10$, $df = 3$, $I^2 = 0\%$, $P = .778$). There was a significant difference between the 2 groups (RD = -0.148, 95% CI: -0.218 to -0.078, $P = .000$; Fig. 9).

3.4.9. The occurrence of vomiting. Four studies reported the incidence of vomiting.^[10–13] We found no statistical heterogeneity, and a fixed-effects model was applied ($\chi^2 = 1.25$, $df = 3$, $I^2 = 0\%$, $P = .742$). The meta-analysis showed significant difference between groups. (RD = -0.166, 95% CI: -0.237 to -0.095, $P = .000$; Fig. 10).

3.4.10. Subgroup analysis and evidence level. The subgroup analysis was performed about the dose and for 2 types of arthroplasty in order to determine the outcome of VAS scores (Table 4). All subgroups were analyzed using the fixed model, which indicated that the 2 factors were the potential sources of heterogeneity. Only 3 studies reported opioid consumption, thus it was not suitable to conduct subgroup analysis. More RCTs were required for further analyses.

All main outcomes in this meta-analysis were evaluated using the GRADE system (Table 5).

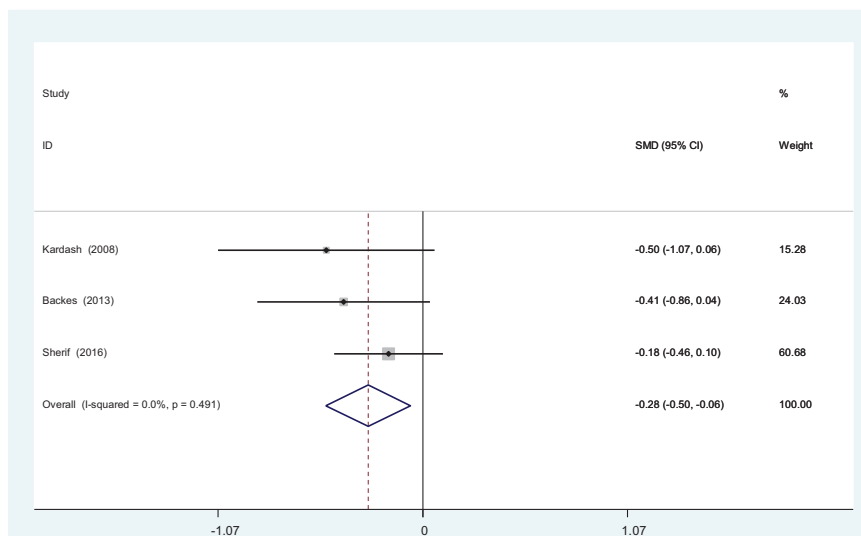


Figure 6. Forest plot diagram showing opioid consumption at 24 hours following total joint arthroplasty (TJA).

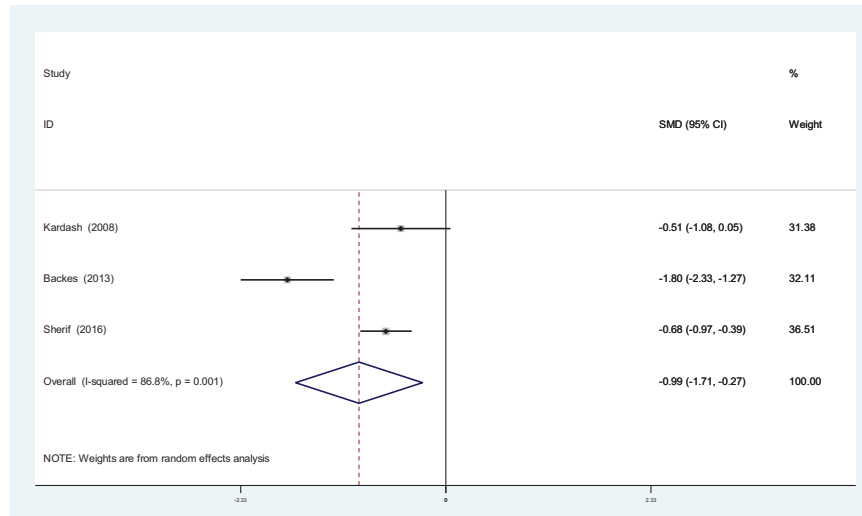


Figure 7. Forest plot diagram showing opioid consumption at 48 hours following total joint arthroplasty (TJA).

Inconsistency: when heterogeneity exists, but investigators fail to identify a plausible explanation, the quality of evidence should be downgraded by 1 or 2 levels. Limitations: low risk of bias would indicate “no serious limitations;” unclear risk of bias would indicate either “no serious limitations” or “serious limitations.” Indirectness: indirect population, intervention, comparator, or outcome may downgrade the quality rating by 1 or even 2 levels. Imprecise: results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of the effect. The quality of evidence should be downgraded by 1 or 2 levels. The overall evidence quality for each outcome was moderate to low which

means that further research is likely to significantly change confidence in the effect estimate and to change the estimate. This finding may lower the confidence in any recommendations.

4. Discussion

The occurrence of joint osteoarthritis has increased with an increase in the ageing population, and TJA is a successful treatment that can be widely performed to address joint osteoarthritis. However, pain control following TJA can be very challenging, yet, optimal analgesia may shorten hospital stays and result in decreased medical costs. Furthermore, early

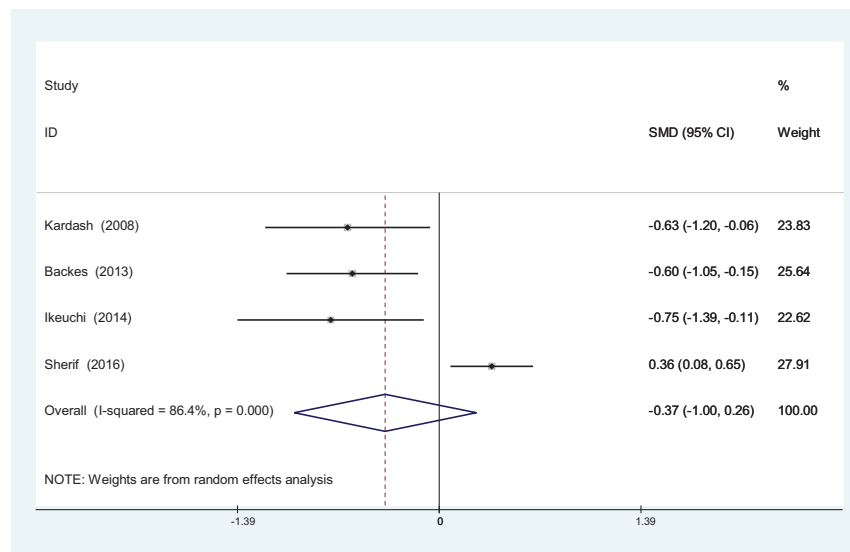


Figure 8. Forest plot diagram showing length of stay following total joint arthroplasty (TJA).

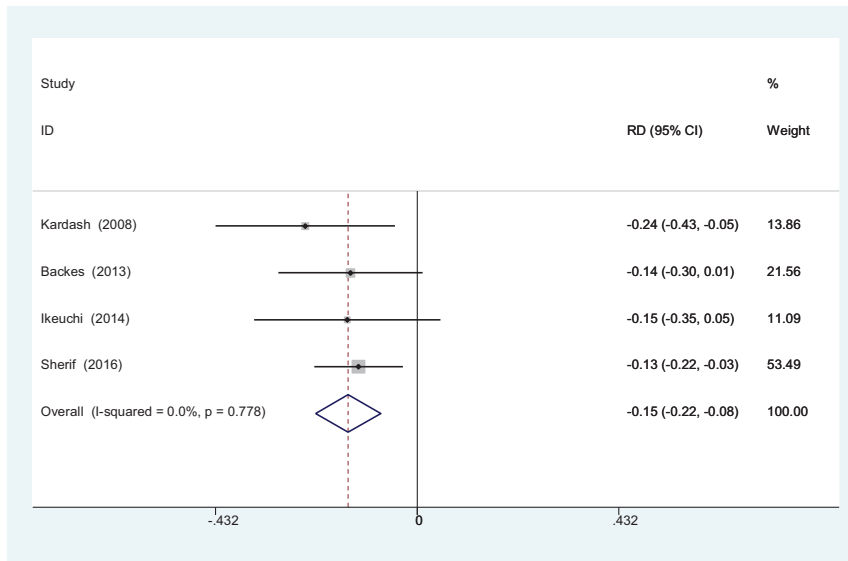


Figure 9. Forest plot diagram showing incidence of nausea following total joint arthroplasty (TJA).

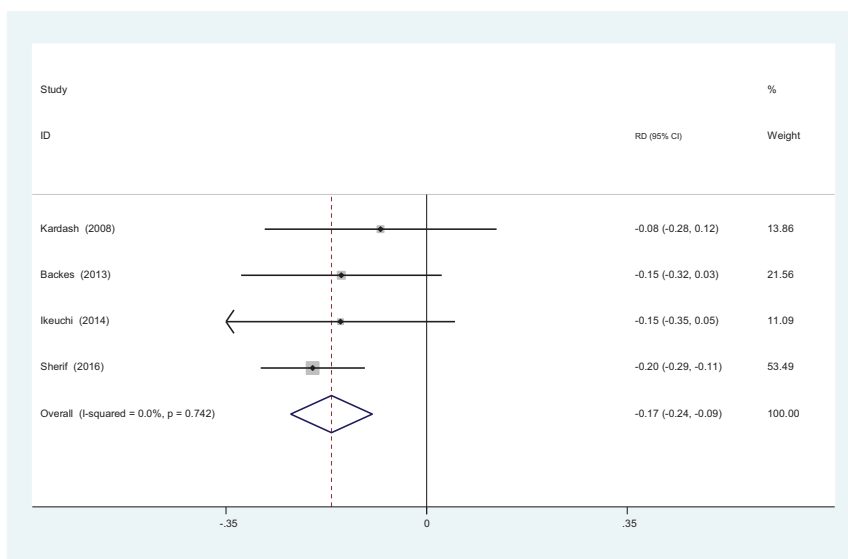


Figure 10. Forest plot diagram showing incidence of vomiting following total joint arthroplasty (TJA).

Table 4

The outcomes of subgroup analysis for VAS scores.

Variables	Studies (n)	Patients (n)	P	SMD (95% CI)	Heterogeneity P (I ²)	Model
VAS scores at 12 h						
TKA	2	233	.000	-0.526[-0.787, -0.264]	.872 (0%)	Fixed
THA and TJA	2	128	.000	-0.785[-1.148, -0.422]	.054 (73.2%)	Fixed
Dose of dexamethasone ≥ 10 mg	2	128	.000	-0.785[-1.148, -0.422]	.054 (73.2%)	Fixed
Dose of dexamethasone < 10 mg	2	233	.000	-0.526[-0.787, -0.264]	.872 (0%)	Fixed
VAS scores at 24 h						
TKA	2	233	.000	-0.877[-1.146, -0.608]	.339 (0%)	Fixed
THA and TJA	2	128	.000	-0.625[-0.826, -0.424]	.081 (39.7%)	Fixed
Dose of dexamethasone ≥ 10 mg	2	128	.000	-0.625[-0.826, -0.424]	.081 (39.7%)	Fixed
Dose of dexamethasone < 10 mg	2	233	.000	-0.877[-1.146, -0.608]	.339 (0%)	Fixed
VAS scores at 48 hours						
TKA	2	233	.001	-0.446[-0.706, -0.185]	.107 (61.5%)	Fixed
THA and TJA	2	128	.243	-0.207[-0.555, 0.140]	.905 (0%)	Fixed
Dose of dexamethasone ≥ 10 mg	2	128	.243	-0.207[-0.555, 0.140]	.905 (0%)	Fixed
Dose of dexamethasone < 10 mg	2	233	.001	-0.446[-0.706, -0.185]	.107 (61.5%)	Fixed

CI=confidence interval, SMD=standard mean difference, TJA=total joint arthroplasty, THA=total hip arthroplasty, TKA=total knee arthroplasty, VAS=visual analogue scale.

Table 5

The GRADE evidence quality for main outcome.

Quality assessment		Other considerations			No of patients		Effect				
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Experimental groups	Control groups	Relative (95% CI)	Absolute	Quality	Importance
4	VAS scores at 12 h (follow-up 1 to 12 mo; better indicated by lower values) Randomised trials	No serious limitation	Serious	No serious indirectness	No serious imprecision	183	178	–	SMD 0.579 lower (0.780 to 0.375 lower)	⊕⊕⊕○ Moderate	Critical
4	VAS scores at 24 h (follow-up 1 to 12 mo; better indicated by lower values) Randomised trials	No serious limitation	Serious	No serious indirectness	No serious imprecision	183	178	–	SMD 0.820 lower (1.036 to 0.604 lower)	⊕⊕⊕○ Moderate	Critical
4	VAS scores at 48 h (follow-up 1 to 12 mo; better indicated by lower values) Randomised trials	No serious limitation	Serious	No serious indirectness	No serious imprecision	183	178	–	SMD 0.661 lower (1.149 to 0.172 lower)	⊕⊕⊕○ Moderate	Critical
3	Opioid consumption at 12 h (follow-up 1 to 6 mo; better indicated by lower values) Randomised trials	No serious limitations	Serious	No serious indirectness	Serious	163	158	–	SMD 0.245 lower (0.465 to 0.025 lower)	⊕⊕○○ Low	Critical
3	Opioid consumption at 24 h (follow-up 1 to 6 mo; better indicated by lower values) Randomised trials	No serious limitations	Serious	No serious indirectness	Serious	163	158	–	SMD 0.285 lower (0.505 to 0.064 lower)	⊕⊕○○ Low	Critical
3	Opioid consumption at 48 h (follow-up 1 to 6 mo; better indicated by lower values) Randomised trials	No serious limitations	Serious	No serious indirectness	Serious	163	158	–	SMD 0.989 lower (1.710 to 0.267 lower)	⊕⊕○○ Low	Critical

CI = confidence interval, SMD = standard mean difference, VAS = visual analogue scale.

rehabilitation exercise contributes to an early recovery and satisfactory functional outcome. Multiple perioperative pain management strategies have been implemented following TJA, including femoral nerve block (FNB), spinal analgesia, and periarticular or intraarticular injection of anesthetics.^[14–16]

Dexamethasone is a long-acting glucocorticoid that has been widely used as an analgesic, as well as an effective preventive treatment of postoperative nausea and vomiting. Henzi et al^[17] reported that a dose of 8 to 10 mg intravenous dexamethasone could further decrease the risk of postoperative nausea. Recently, studies have demonstrated that glucocorticoids show similar analgesic effects with supraclavicular blocks and interscalene blocks, an observation that has been attributed to their antiinflammatory effect. Sean et al^[18] demonstrated that triamcinolone acetonide combined with bupivacaine improved the analgesic effect and early recovery. For patients undergoing TJA, dexamethasone is injected as an adjunct to FNB and local infiltration analgesia for pain control. Kim et al^[19] demonstrated that dexamethasone injected in the interscalene brachial plexus could significantly reduce early postoperative pain for shoulder surgery. However, Christensen et al^[20] showed that dexamethasone had no beneficial effect on pain relief for patients undergoing total knee arthroplasty (TKA). It is plausible that different types and doses of glucocorticoid may alter the clinical efficiency of a specific glucocorticoid. The present meta-analysis indicated that the administration of dexamethasone could significantly reduce postoperative pain scores within the 1st 48 hours following TJA.

TJA is usually associated with severe pain in 60% and moderate pain in 30% of patients, especially in the 1st 48 hours.^[21] Although various analgesic methods have been implemented, they are insufficient in most cases and additional opioid, including oral or patient-controlled analgesia administration, have been applied as concomitant pain management. Opioid consumption is identified as an objective method to measure pain. Opioid-related adverse effects, such as dizziness, nausea, vomiting, orthostatic hypotension, and respiratory depression have been frequently reported in the literature.^[22,23] Besides the side effects described above, drug dependence is also an important issue that should be considered. Reducing opioid consumption could improve patients' satisfaction and expedite mobilization and rehabilitation. The present meta-analysis indicated that there was a significant reduction in opioid consumption in dexamethasone groups compared with controls. Further investigations are required due to the small sample size of the included studies.

Nausea and vomiting are common side effects that are frequently associated with oral or intravenous opioid. The overall incidence of nausea in the dexamethasone group (12/183) was low compared with that in the controls (38/178). We also identified a decreased risk of postoperative complications, which was partly attributable to less opioid consumption and the use of dexamethasone. Despite the benefits mentioned, dexamethasone's routine use in surgical procedures is still limited because of concerns over the numerous side effects associated with glucocorticoids. After reviewing the previous studies, we found no reliable evidence regarding the side effects of glucocorticoids after single-dose administration of dexamethasone^[17,24]; however, we would like to emphasize that only 4 studies were included in our meta-analysis. Furthermore, due to the small sample size, we did not perform investigations on dose-dependence.

The present meta-analysis exists some limitations that should be noted.

- (1) Only 4 RCTs were included in present meta-analysis, the sample size is relatively small.
- (2) Functional outcome is an important parameter, due to the insufficiency of relevant data, we fail to perform a meta-analysis.
- (3) Dose of dexamethasone is varied from each other, which may influence the results of the meta-analysis.
- (4) The duration of follow-up is relatively short which leads to underestimating complications.
- (5) Publication bias in present meta-analysis may influence the results.

Despite the limitations above, this is the 1st meta-analysis of recent RCTs to evaluate the efficiency and safety of dexamethasone administration in total knee and hip arthroplasties. Further large well-designed RCTs are still needed to validate this research.

5. Conclusion

Dexamethasone could significantly reduce postoperative pain scores and opioid consumption within the 1st 48 hours following TJA. The overall evidence quality was moderate to low, further high-quality RCTs are needed to identify the optimal dose of dexamethasone for reducing pain after TJA.

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