



Efficacy of intravenous dexamethasone on postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid: a systematic review and meta-analysis

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Abstract

Purpose Intravenous dexamethasone is recommended in elective caesarean delivery to decrease postoperative pain. However, the efficacy of spinal anaesthesia with an intrathecal long-acting opioid such as morphine or diamorphine for caesarean delivery has not been systematically investigated.

Methods We searched all randomized controlled trials (RCTs) of pregnant women undergoing caesarean delivery under spinal anaesthesia with an intrathecal morphine or diamorphine via MEDLINE, CENTRAL, EMBASE, ICTRP, and ClinicalTrials.gov on May 18, 2022. Primary outcomes were time to first rescue analgesia, consumption of oral morphine equivalents, and incidence of drug-related adverse reactions. We evaluated the risk of bias for each outcome using the Risk of Bias 2. We conducted a meta-analysis using a random effects model. We evaluated the certainty of evidence with the GRADE approach.

Results Five RCTs (455 patients) were included. The results of intravenous dexamethasone were as follows: time to first rescue analgesia (mean difference [MD] 0.99 h, 95% confidence interval [CI] – 0.86 to 2.84; very low certainty) and consumption of oral morphine equivalents (MD – 6.55 mg, 95% CI – 17.13 to 4.02; moderate certainty). No incidence of drug-related adverse reactions was reported (very low certainty).

Conclusion The evidence was very uncertain about the efficacy of intravenous dexamethasone on time to first rescue analgesia and the incidence of drug-related adverse reactions. Intravenous dexamethasone probably reduces the consumption of oral morphine equivalents. Anaesthesiologists might want to consider intravenous dexamethasone for postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid.

Keywords Caesarean delivery · Intrathecal morphine · Intravenous dexamethasone · Postoperative pain · Systematic review

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Introduction

Caesarean delivery is associated with postoperative pain that may influence recovery, psychological maternal well-being, and breastfeeding [1]. A multimodal analgesic regimen including an intrathecal long-acting opioid, non-steroidal anti-inflammatory drugs, and acetaminophen has been suggested to effectively control postoperative pain after caesarean delivery [2, 3]. Oral opioids are administered for postoperative pain, but opioid use and abuse after caesarean delivery has become alarming worldwide [4–6].

Intravenous dexamethasone is recommended in elective caesarean delivery to decrease postoperative pain. Several systematic reviews and meta-analyses have examined the efficacy of dexamethasone after caesarean delivery and reported decreased postoperative pain and prolonged time

to first analgesia [7–9]. However, the efficacy of intravenous dexamethasone on postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid has not been evaluated. All previous studies have included patients who underwent caesarean delivery under spinal anaesthesia without an intrathecal long-acting opioid [7–9]. Moreover, those previous studies included patients who underwent other surgical procedures or anaesthesia [7–9]. Since spinal anaesthesia is the most used anaesthetic technique for cesarean delivery in the developed world and the use of intrathecal morphine has gradually increased, its administration has become the standard practice [10, 11]. It is therefore clinically relevant to evaluate the efficacy of intravenous dexamethasone on postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid.

Materials and methods

Compliance with reporting guidelines

We published this protocol in Open Science Framework (<https://osf.io/42rsu/>). We followed the Preferred reporting items for systematic review and meta-analysis 2020 (PRISMA-2020) [12] and the recommendations listed in the Cochrane Handbook [13].

Eligibility criteria

The research question of this study was the efficacy of intravenous dexamethasone on postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid. We defined participants as pregnant women undergoing caesarean delivery who received spinal anaesthesia with an intrathecal long-acting opioid. We defined long-acting opioid as morphine or diamorphine [3]. We defined intervention as administration of intravenous dexamethasone during the perioperative period. We defined control as administration of a placebo, no intervention, or usual care.

We included randomized controlled trials that assessed the efficacy of intravenous dexamethasone on postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid. We did not apply language or country restrictions. We excluded pregnant women undergoing caesarean delivery under spinal anaesthesia without an intrathecal long-acting opioid and pregnant women undergoing caesarean delivery under combined spinal and epidural

anaesthesia. We included all published and unpublished articles, abstracts of conference, and letters. We excluded crossover trials, quasi-experimental studies, and quasi-randomized trials. We did not exclude studies based on the observation period or publication year.

Outcomes of interest

The primary outcomes of interest were time to first rescue analgesia (during the first 24 h after caesarean delivery), consumption of oral morphine equivalents (during the first 24 h after caesarean delivery), and incidence of drug-related adverse reactions (during the follow-up period). We defined the time to first rescue analgesia as the authors' definition. We calculated the consumption of oral morphine equivalents and converted opioids other than oral morphine to oral morphine equivalent doses (intravenous morphine: oral morphine = 1:2) [14]. We defined the incidence of drug-related adverse reactions as the authors' definition. We calculated the incidence of all adverse reactions. The numerator was the number of participants experiencing adverse reactions and the denominator was the total number of participants.

The secondary outcomes were the pain score at rest from 0 to 12 h after caesarean delivery, pain score at rest from 12 to 24 h after caesarean delivery, highest pain score at rest (during the first 24 h after caesarean delivery), and highest pain score on movement (during the first 24 h after caesarean delivery). We rescaled pain scores reported as numeric, verbal, or visual rating scales to 0 to 10 scores for pooled quantitative evaluations. If more than one measurement was assessed within the period, the one at the latest time point was used.

Information sources and search strategy

We searched the following databases: MEDLINE (PubMed); the Cochrane Central Register of Controlled Trials (Cochrane Library), and EMBASE (Dialog). We also searched the following databases for ongoing or unpublished trials: the World Health Organization International Clinical Trials Platform Search Portal (ICTRP) and ClinicalTrials.gov. Appendix 1 shows the search strategies. We checked the reference lists of the studies, including international guidelines and the reference lists of eligible studies (including studies awaiting classification) and articles citing eligible studies (including studies awaiting classification).

Selection process

After removing duplicates, two of four independent reviewers (YK, TT, YA, and HI) screened the titles and abstracts, followed by assessment of eligibility based on the full texts. We contacted the original authors if relevant data were

missing. Disagreements between the two reviewers were resolved by discussion, and if this failed, a third reviewer acted as an arbiter (KK).

Data collection process

Two of four independent reviewers (YK, TT, YA, and HI) performed independent data extraction of the included studies using a standardized data collection form [15].

Data items

The form included information on the trial setting (first author, year of publication, and country), study population (number of patients and anaesthetics), interventions (dexamethasone dose), and outcomes (time to first rescue analgesia, consumption of oral morphine equivalents, incidence of drug-related adverse reactions, and pain scores). Any disagreements were resolved by discussion, and if this failed, a third reviewer acted as an arbiter (KK).

Risk of bias assessment

Two of four independent reviewers (YK, TT, YA, and HI) evaluated the risk of bias independently for each outcome using the Risk of Bias 2 [16]. Disagreements between the two reviewers were discussed, and if this failed, a third reviewer (KK) acted as an arbiter, if necessary.

Effect measures

We pooled the mean differences (MDs) and 95% confidence intervals (CIs) for the following continuous variables: time to first rescue analgesia, consumption of oral morphine equivalents, and pain score. We summarized drug-related adverse reactions based on the definition in the original article, but we did not perform a meta-analysis.

Synthesis methods

Handling of missing data

We performed intention-to-treat analysis for all data as much as possible. We asked for data from the original authors if not presented in their study. For continuous data, we did not impute missing data based on the recommendation by the Cochrane Handbook [13]. We performed a meta-analysis of the available data in the original study. When original studies only reported standard errors or p values, we calculated the standard deviations based on Altman's method [17]. If we could not obtain these values when we contacted the authors, standard deviations were calculated by CIs and t

values based on the method recommended by the Cochrane Handbook [13] or a validated method [18]. Validity of these methods was analyzed by sensitivity analyses.

Assessment of heterogeneity

We evaluated the statistical heterogeneity by visual inspection of the forest plots and calculated the I^2 statistic. When there was substantial heterogeneity ($I^2 > 50\%$), we assessed the reason for the heterogeneity. The Cochrane χ^2 test was performed to generate the I^2 statistic, and a p value < 0.10 was defined as statistically significant.

Meta-analysis

Meta-analysis was performed using Review Manager software (Rev Man 5.4.2). We used a random-effects model.

Sensitivity analysis

We conducted the following sensitivity analyses for the primary outcomes to assess whether the results of the review were robust to the decisions made during the review process: (i) exclusion of studies using imputed statistics, (ii) inclusion of only the participants who completed the study with complete data, and (iii) missing participants. To verify the robustness of the results by seeking informative missingness odds ratio (IMOR), we set the informative missingness difference of means (IMDOM) as 0, standard deviation with the IMDOM as 1 in both groups, and IMDOM correlation between groups as 0. In the analysis, we set the values in mean, SD, and correlation of the IMDOM based on the assumption that there may be systematic differences between outcomes in missing and follow-up participants; however, there was uncertainty about the direction. We executed the command `metamiss2` on Stata/SE 16.1 to verify the robustness of the results by seeking the IMOR [19].

Reporting bias assessment

We searched clinical trial registry systems (ClinicalTrials.gov and ICTRP) and performed an extensive literature search for unpublished trials. To assess outcome reporting bias, we compared the outcomes defined in trial protocols with the outcomes reported in the publications. We did not assess the potential publication bias by visual inspection of the funnel plot because we found < 10 trials [13].

Certainty assessment

Two reviewers (YK and KK) evaluated the certainty of evidence based on the Grading of Recommendations,

Assessment, Development, and Evaluation (GRADE) approach [20]. Disagreements between the two reviewers were discussed, and if this failed, a third reviewer (MB) acted as an arbiter, if necessary. A summary of findings (SoF) table was made for the following outcomes based on the Cochrane Handbook [13]. We listed the time to first rescue analgesia, consumption of oral morphine equivalents, incidence of drug-related adverse reactions, pain score at rest from 0 to 12 h after caesarean delivery, pain score at rest from 12 to 24 h after caesarean delivery, highest pain score at rest, and highest pain score on movement in the SoF table.

Differences between the study protocol and the review

First, we checked the reference lists of the studies, including the international guidelines as well as the reference lists of eligible studies (including studies awaiting classification) and articles citing eligible studies (including studies awaiting classification). Second, we could not perform the subgroup analysis because of limited data.

Results

Search results and characteristics of the included trials

After removing duplicates, we identified 3398 records during the search conducted on May 18, 2022. Ninety records were identified, and 89 reports were assessed for their eligibility for this study by full-text screening. Finally, we excluded 79 reports and included five studies ($n = 455$) that fulfilled all the eligibility criteria, including citation searching (Fig. 1, Supplementary Table 1) [21–25].

As shown in Table 1, all studies [21–25] included patients with scheduled caesarean delivery and evaluated the effect of intravenous dexamethasone after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid. In all studies [21–25], participants in the steroid group received 8 mg of dexamethasone. Participants in three studies [22, 23, 25] received 200 µg of intrathecal morphine and participants in two studies [21, 24] received 150 µg of intrathecal morphine. Two studies [22, 24] described postoperative pain as their primary outcome, two other studies [23, 25] described postoperative nausea and vomiting as the primary outcome, and one study [21] described pruritus as the primary outcome.

Table 2 shows the risk of bias summary for each outcome of the included studies, ranging from low to high. For time

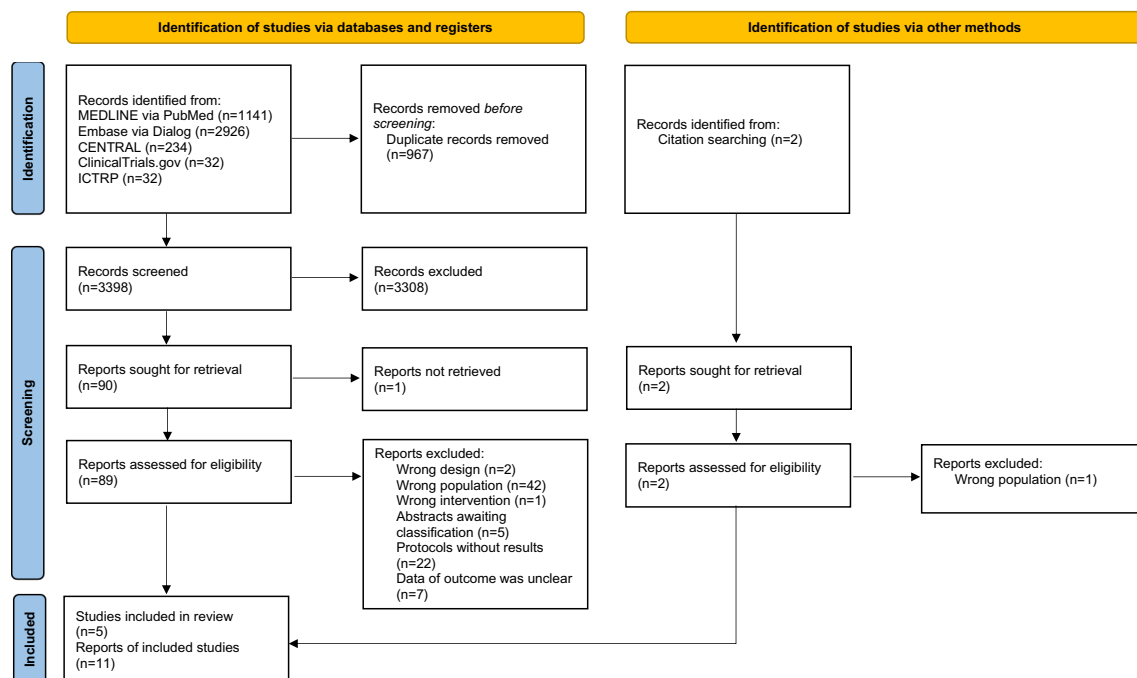


Fig. 1 PRISMA 2020 flow diagram. *CENTRAL* Cochrane Central Register of Controlled Trials, *ICTRP* International Clinical Trials Registry Platform

Table 1 Characteristics of the included studies

Author	Year	Country	Number of patients	Spinal anesthesia	Steroid group	Control group	Postoperative analgesia	Primary outcome
Ankouni	2021	Lebanon	98	L3/4 or L4/5, 0.5% hyperbaric bupivacaine 10 mg, Morphine 150 µg	Dexamethasone 8 mg	Ondasetron 4 mg	Paracetamol 1 g i.v. every 6 h and ketoprofen 100 mg i.v. once in 24 h for VAS score > 2	Pruritus
			26		Ondasetron 4 mg	Normal saline	Ketorolac 30 mg i.v. every 6 h, morphine i.v. or oxycodone 5 mg/acetaminophen 325 mg p.o. on patient request (Pain in the PACU was treated with morphine 2 mg i.v. every 10 min, up to a maximum dose of 10 mg, on patient request)	
Ituk	2018	USA	26	L2/L3 or L3/L4, 0.75% hyperbaric bupivacaine 12 mg, fentanyl 25 µg, morphine 200 µg	Dexamethasone 8 mg	Normal saline	Total opioid consumption at 24 h	
Jadon	2016	India	50	L3/4, 0.5% hyperbaric bupivacaine 12.5 mg, morphine 200 µg	Dexamethasone 8 mg	Normal saline	Diclofenac 75 mg i.m. if VAS score > 3 or on patient demand, combination of pentazocine 30 mg i.m. and promethazine 25 mg i.m., if the patient continued to complain of pain (VAS score > 3) even after 45 min of administration of diclofenac	PONV
Mehdirattia	2021	USA	25	Hyperbaric bupivacaine 12 mg, fentanyl 15 µg, morphine 150 µg	Dexamethasone 8 mg	Normal saline	Naproxen 500 mg i.v. every 12 h and acetaminophen 975 mg i.v. every 6 h, fentanyl i.v. as needed (25 mcg for NRS score 4–6 and 50 mcg for NRS score 7–10) at PACU, oxycodone 5 mg p.o. for NRS score 4–6 and 10 mg p.o. for NRS score 7–10 every 4 h as needed, morphine 2 mg i.v. experienced intolerable pain not initially relieved by oral analgesia	Total opioid consumption at 24 h
Wu	2007	China	30	L3/4 or L4/5, 0.5% hyperbaric bupivacaine 10 mg, morphine 200 µg	Dexamethasone 8 mg	Normal saline	Diclofenac 75 mg i.m. on patient request or if experiencing pain (VAS score > 3)	PONV

i.v., intravenously; p.o., per os; i.m., intramuscularly; PACU, post-anaesthetic care unit; VAS, visual analog scale; NRS, numeric rating scale; PONV, postoperative nausea and vomiting; USA, United States of America

Table 2 Risk of bias assessment

(A) Time to first rescue analgesia

Study ID	Experimental	Comparator	D1	D2	D3	D4	D5	Overall
Ituk2018	Dexamethasone	Saline	+	+	+	+	-	-
Jadon2016	Dexamethasone	Saline	+	+	+	+	!	!
Mehdiratta2021	Dexamethasone	Saline	+	+	+	+	+	+
		D1	Randomisation process			+	Low risk	
		D2	Deviations from the intended intervention			!	Some concerns	
		D3	Missing outcome data			-	High risk	
		D4	Measurement of the outcome					
		D5	Selection of the reported result					

(B) Consumption of oral morphine equivalents

Study ID	Experimental	Comparator	D1	D2	D3	D4	D5	Overall
Ituk2018	Dexamethasone	Saline	+	+	+	+	+	+
Mehdiratta2021	Dexamethasone	Saline	+	+	+	+	+	+
		D1	Randomisation process			+	Low risk	
		D2	Deviations from the intended intervention			!	Some concerns	
		D3	Missing outcome data			-	High risk	
		D4	Measurement of the outcome					
		D5	Selection of the reported result					

(c) Incidence of drug-related adverse reactions

Study ID	Experimental	Comparator	D1	D2	D3	D4	D5	Overall
Ituk2018	Dexamethasone	Saline	+	+	+	+	-	-
Mehdiratta2021	Dexamethasone	Saline	+	+	+	+	+	+
Wu2007	Dexamethasone	Saline	+	+	+	+	!	!
		D1	Randomisation process			+	Low risk	
		D2	Deviations from the intended intervention			!	Some concerns	
		D3	Missing outcome data			-	High risk	
		D4	Measurement of the outcome					
		D5	Selection of the reported result					

to first rescue analgesia, 33.3% of the overall risk of bias was low risk, 33.3% was some concerns, and 33.3% was high risk. Regarding consumption of oral morphine equivalents, all the overall risk of bias was low risk. Concerning the incidence of drug-related adverse reactions, 33.3% of the overall risk of bias was low risk, 33.3% was some concerns, and 33.3% was high risk. Especially in the selection of the reported result, there were many studies with some concerns

and high risk. For time to first rescue analgesia, 33.3% of the risk of bias in selection of the reported result was low risk, 33.3% was some concerns, and 33.3% was high risk. Regarding the consumption of oral morphine equivalents, all the risk of bias in the selection of the reported result was low risk. Concerning the incidence of drug-related adverse reactions, 33.3% of the risk of bias in the selection of the reported result was low risk, 33.3% was some concerns, and

33.3% was high risk. We could not obtain protocol data from some of the authors [23, 25].

Primary outcomes

Table 3 shows the SoF table of the present study (For detailed information, see Supplementary Table 2.).

Time to first rescue analgesia

The evidence was very uncertain about the effect of intravenous dexamethasone on time to first rescue analgesia compared with a placebo (three studies, 199 participants: MD 0.99 h, 95% CI - 0.86 to 2.84, $I^2=77\%$; very low certainty evidence) (Fig. 2). First, we conducted sensitivity analysis by excluding studies using imputed statistics; however, the results were similar to those obtained in the original analysis (two studies, 99 participants: MD - 0.21 h, 95% CI - 0.72 to 0.30; $I^2=62\%$) (Supplementary Fig. 1). Second, we performed sensitivity analysis by including only the participants who completed the study with complete data; intravenous dexamethasone exhibited a significant effect in favor of the intervention (MD 2.00 h, 95% CI 0.55 to 3.45; $I^2=0\%$) (Supplementary Fig. 2). Finally, we performed sensitivity analysis by seeking the IMOR; however, the results were similar to those obtained in the original analysis (MD 0.99 h, 95% CI - 0.86 to 2.84; $I^2=76\%$) (Supplementary Fig. 3).

Consumption of oral morphine equivalents

Intravenous dexamethasone probably reduces consumption of oral morphine equivalents compared with a placebo (two studies, 99 participants: MD - 6.55 mg, 95% CI - 17.13 to 4.02; $I^2=0\%$; moderate certainty evidence) (Fig. 3). First, we conducted sensitivity analysis by excluding studies using imputed statistics; however, the results were similar to those obtained in the original analysis (one study, 52 participants: MD - 6.00 mg, 95% CI - 18.88 to 6.88) (Supplementary Fig. 4). Second, we performed sensitivity analysis by seeking the informative IMOR; however, the results were similar to those obtained in the original analysis (MD - 6.55 mg, 95% CI - 17.13 to 4.02; $I^2=0\%$) (Supplementary Fig. 5).

Incidence of drug-related adverse reactions

Three studies (159 participants) [21, 24, 25], assessed the incidence of wound complications. No complications were reported, but the evidence was very uncertain.

Secondary outcomes

The evidence was very uncertain about the effect of intravenous dexamethasone on the pain score at rest compared

with a placebo from 0 to 12 h after caesarean delivery (three studies, 346 participants: MD - 0.60, 95% CI - 1.36 to 0.15; $I^2=74\%$; very low certainty evidence) (Supplementary Fig. 6), and 12–24 h after caesarean delivery (two studies, 152 participants: MD 0, 95% CI - 0.47 to 0.47; $I^2=0\%$; low certainty evidence) (Supplementary Fig. 7).

Supplementary Table 3 shows the PRISMA 2020 Checklist of the present study.

Discussion

In this study, we examined the efficacy of intravenous dexamethasone on postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid. We showed that the evidence is very uncertain about the effect of intravenous dexamethasone on time to first rescue analgesia and incidence of drug-related adverse reactions, although intravenous dexamethasone probably reduces the consumption of oral morphine equivalents.

The evidence was very uncertain about the effect of intravenous dexamethasone on time to first rescue analgesia. A previous systematic review and meta-analysis illustrated that time to first rescue analgesia for post-caesarean pain was significantly longer with dexamethasone compared to controls with an MD of 2.64 h (95% CI 1.85 to 3.42; $I^2=17\%$; moderate certainty evidence) [8]. The previous study included patients who underwent caesarean delivery under spinal anaesthesia without an intrathecal long-acting opioid, and scheduled postoperative analgesics were not prophylactically administered [8]. Unlike a previous study [8], two of three of our included studies [22, 24] prescribed scheduled postoperative analgesics to the patients. Moreover, since all of our included studies used an intrathecal morphine, the additive effect of intravenous dexamethasone on time to first rescue analgesia might not be present.

Intravenous dexamethasone probably reduces the 24-h consumption of oral morphine equivalents compared with a placebo. This result was consistent with that of a previous systematic review and meta-analysis that included patients who underwent various surgical procedures under spinal analgesia; it showed a statistically reduction in the consumption of intravenous morphine equivalents of 4.01 mg (95% CI - 5.01 to - 3.01; $I^2=0\%$; high certainty evidence) [7]. Herein, we examined spinal anaesthesia with an intrathecal long-acting opioid for caesarean delivery. Therefore, anaesthesiologists might want to consider intravenous dexamethasone for postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid.

No drug-related adverse reactions were reported after administering intravenous dexamethasone for caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid, but the evidence was very uncertain.

Table 3 Summary of findings: efficacy of intravenous dexamethasone on postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid: a systematic review and meta-analysis

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with a placebo	Risk with dexamethasone				
Time to first rescue analgesia	The mean time to first rescue analgesia was 10.18 h	MD 0.99 h higher (0.86 lower to 2.84 higher)	–	199 (3 RCTs)	⊕○○○ Very low ^a	–
Consumption of oral morphine equivalents	The mean consumption of oral morphine equivalents was 33.69 mg	MD 6.55 mg lower (17.13 lower to 4.02 higher)	–	99 (2 RCTs)	⊕⊕⊕○ Moderate ^b	–
Incidence of drug-related adverse reactions	In three studies, authors reported that they assessed for the incidence of wound complications. No complications were reported		–	159 (3 RCTs)	⊕○○○ Very low ^c	–
Pain score at rest from 0 to 12 h after caesarean delivery	The mean pain score at rest from 0 to 12 h after caesarean delivery was 2.84	MD 0.6 lower (1.36 lower to 0.15 higher)	–	346 (3 RCTs)	⊕○○○ Very low ^d	–
Pain score at rest from 12 to 24 h after caesarean delivery	The mean pain score at rest from 12 to 24 h after caesarean delivery was 2.31	MD 0 (0.47 lower to 0.47 higher)	–	152 (2 RCTs)	⊕⊕○○ Low ^e	–
Highest pain score at rest	–	–	–	–	–	No studies reported the outcome
Highest pain score on movement	–	–	–	–	–	No studies reported the outcome

Dexamethasone compared to a placebo, no intervention, or usual care for postoperative pain

Patient or population: pregnant women undergoing caesarean delivery

Setting: pregnant women undergoing caesarean delivery who received spinal anaesthesia with an intrathecal long-acting opioid

Intervention: intravenous dexamethasone

Comparison: control (placebo, no intervention, or usual care)

CI confidence interval, MD mean difference, GRADE, Grading of Recommendations, assessment, development, and evaluation, *no* number

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

^aDowngraded by two levels for risk of bias (two of three studies were at high risk of bias and had an unclear risk of bias), one level for inconsistency ($I^2=77\%$ and P value for heterogeneity=0.01) and one level for imprecision (small sample size [$n=199$] and 95% CI includes no clinical effect and a clinical effect)

^bDowngraded by one level for imprecision (small sample size [$n=99$] and 95% CI includes no clinical effect and a clinical effect)

^cDowngraded by two levels for risk of bias (two of three studies were at high risk of bias and had an unclear risk of bias) and one level for imprecision (small sample size [$n=159$])

^dDowngraded by one level for risk of bias (two of three studies had an unclear risk of bias), one level for inconsistency ($I^2=74\%$ and P -value for heterogeneity=0.02), and one level for imprecision (small sample size [$n=346$])

^eDowngraded by one level for risk of bias (one of two studies had an unclear risk of bias) and one level for imprecision (small sample size [$n=152$])

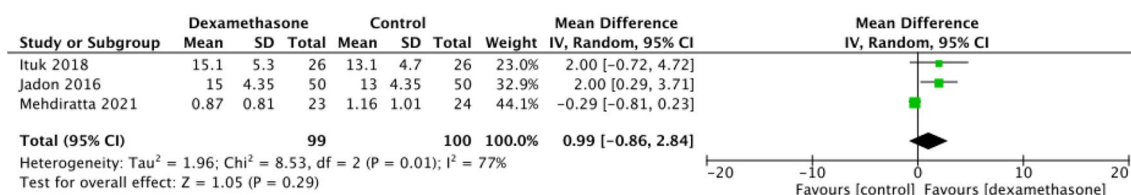


Fig. 2 Forest plot for time to first rescue analgesia. *SD* standard deviation, *CI* confidence interval

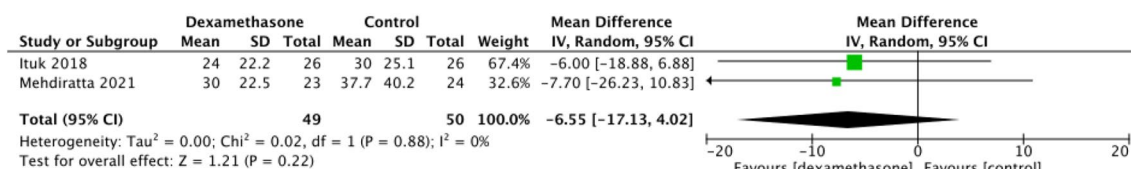


Fig. 3 Forest plot for consumption of oral morphine equivalents. *SD* standard deviation, *CI* confidence interval

A recent systematic review and meta-analysis found that a single intravenous dose of dexamethasone was not associated with a risk of infections, but delayed wound healing could not be definitively determined [26]. Another meta-analysis concluded that a single dose of dexamethasone (≤ 0.2 mg/kg) did not increase wound infection and did not delay wound healing [27]. We might be able to safely administer intravenous dexamethasone under the condition of a single dose of dexamethasone (≤ 0.2 mg/kg).

Our study has some limitations. First, we included only five studies; hence, further research is required to clearly indicate reduction of the consumption of opioids. Second, one included study [22] had potential bias in the selection of the reported result. Future studies with a similar scope and rigorous methods need to be performed. Finally, one included study [23] did not provide standard deviations. We calculated the standard deviations based on Altman's method [17] and a validated method [18]. Thus, we conducted sensitivity analysis by excluding studies using imputed statistic and made sure the results were the same.

The strengths of our study were that we examined the efficacy of intravenous dexamethasone on post-caesarean pain under spinal anaesthesia with an intrathecal long-acting opioid, which is recommended as the guideline for elective caesarean delivery [3]. To our knowledge, this is the first systematic review and meta-analysis to evaluate the analgesic effect of intravenous dexamethasone in pregnant women undergoing caesarean delivery who received spinal anaesthesia with an intrathecal long-acting opioid as the primary participants. The consumption of oral morphine, a social problem in terms of unnecessary opioid analgesic consumption [4–6], might be reduced. In addition, we performed a comprehensive search for evidence

according to the PRISMA statement [12] and used the GRADE approach [20] to assess the certainty of evidence.

The efficacy of intravenous dexamethasone on postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid is uncertain. However, intravenous dexamethasone probably reduces the consumption of oral morphine equivalents. Therefore, anaesthesiologists might want to consider intravenous dexamethasone for postoperative pain after caesarean delivery under spinal anaesthesia with an intrathecal long-acting opioid.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00540-023-03183-7>.

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Data availability The data generated and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflicts of interest Yuji Kamimura, Kyosuke Kamijo, Masahiro Banno, Tatsuya Tsuji, Yusuke Aoki, Hidekazu Ito, Motoshi Tanaka and Kazuya Sobue have no conflict of interest.

Registration Open Science Framework (<https://osf.io/42rsu/>).

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