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# Efficacy of perineural versus intravenous dexamethasone in prolonging the duration of analgesia when administered with peripheral nerve blocks: a systematic review and meta-analysis

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**Background:** Perineural dexamethasone has been regarded as a promising adjunct for prolonging the duration of nerve blocks. However, it is uncertain whether its effects are due to local effects on the nerves or from systemic absorption. This systematic review aimed to compare the duration of postoperative analgesia associated with perineural versus intravenous dexamethasone as an adjunct to peripheral nerve blocks.

**Methods:** A total of 2,216 relevant academic articles were identified after a comprehensive search of PubMed, Embase, Scopus, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov from 1967 until 2020. All randomized controlled trials that compared perineural and intravenous dexamethasone as adjuncts to peripheral nerve limb blocks were included.

**Results:** Fifteen randomized controlled trials (1,467 cases; 738 perineural dexamethasone, 729 intravenous dexamethasone) were eligible. The primary outcome (duration of analgesia) was significantly longer in the perineural than in the intravenous dexamethasone group (mean difference [MD]: 2.72 h, 95% CI [1.42, 4.01], P < 0.001). Perineural dexamethasone was also found to prolong the sensory block (MD: 3.45 h, 95% CI [1.36, 5.54], P = 0.001) and lower 24 h postoperative pain scores (MD: −0.74 h, 95% CI [−1.40, −0.07], P = 0.03).

**Conclusions:** This review confirms the greater efficacy of perineural compared to intravenous dexamethasone in prolonging the analgesic duration of peripheral nerve blocks. However, the extent of prolongation was small and may not represent a clinically meaningful difference.

**Keywords:** Acute pain; Conduction anesthesia; Enhanced recovery after surgery; Nerve block; Pharmaceutic adjuvants; Postoperative pain.

## Introduction

Moderate-to-severe pain is common after orthopedic surgery. Peripheral nerve blocks are thus frequently employed during these surgeries to improve perioperative pain control and reduce opioid consumption and opioid-related side effects [1].

One of the major problems with single-shot peripheral nerve blocks is the relatively short duration of action of the local anesthetics currently available. Consequently, pa-

tients may experience significant pain after the block has worn off [2]. Perineural catheters have thus been used to extend the duration of analgesia. However, these catheters can be challenging to perform, time- and labor-intensive to manage, and also carry the risk of block failure. They are also susceptible to a number of complications, such as catheter dislodgement, pump-related issues [3] and catheter site infections [4]. Furthermore, given the increasing pressure on hospitals to discharge patients early, the use of perineural catheters may become less relevant in the future.

Consequently, an adjuvant that can prolong the duration of a peripheral nerve block is highly desirable. Several systematic reviews and meta-analyses have established the superiority of perineural dexamethasone in extending the duration of the block effects [5–7]. In 2017, a meta-analysis conducted by Pehora et al. [6] estimated that perineural dexamethasone prolonged the duration of peripheral nerve blocks by 6.7 hours compared to placebo. However, the mechanism of action underlying this phenomenon is unclear. Some possible explanations include the systemic absorption of dexamethasone leading to anti-inflammatory effects [8] and local effects, such as the modulation of C-fibers and local vasoconstriction [9,10]. Previous meta-analyses, which have included studies conducted up to 2018, have shown that perineural dexamethasone results in a longer duration of action compared to similar doses of intravenous dexamethasone, ranging from 0.48 to 3.96 h [11–13].

More recent randomized controlled trials (RCTs) examining the effects of perineural versus intravenous dexamethasone have been conducted [14–17]. This review thus aims to provide an update with the current literature pertaining to the efficacy of perineural compared with intravenous dexamethasone in prolonging the analgesic duration of peripheral nerve blocks for upper and lower limb surgeries.

## Materials and Methods

This systematic review and meta-analysis followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO registration number CRD420 20210257).

### Search methods

An electronic search was conducted using the following databases from January 1967 until November 2020: PubMed, Embase, Scopus, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov. The following search terms were used: ("Perineural Dexamethasone" OR "Perineural Steroid" OR "Dexamethasone" OR "Steroid") AND ("Nerve block" OR "Peripheral nerve block" OR "Regional anaesthesia" OR "Regional anesthesia").

Two reviewers (E.T. and Y.T.) independently reviewed the titles and abstracts of all search entries to exclude irrelevant studies. The full texts of the remaining studies were further examined for inclusion according to the inclusion and exclusion criteria. Disagreements regarding study eligibility were arbitrated by a third reviewer (C.L.).

### Selection criteria

The inclusion criteria were as follows: RCTs (published or unpublished) involving adult patients undergoing upper or lower limb surgeries that compared the duration of analgesia (defined as time to first analgesia request or time to first pain sensation) following perineural versus intravenous dexamethasone. All RCTs that fulfilled the criteria were included in the analysis, without language restrictions.

Studies that involved any ongoing trials, children or animals, surgeries with truncal blocks, drug preparations with other additives combined with dexamethasone, and studies that included different doses for each route were excluded.

### Quality assessment

Two reviewers (E.T. and Y.T.) independently assessed the validity of each included study using the revised Cochrane Collaboration risk-of-bias tool [19]. This tool addresses seven domains of possible bias in each study, including appropriate randomization process, adequate allocation concealment, blinding of the participants and personnel involved, outcome assessment process, missing outcome data, selective reporting of results, and any other types of biases [19] . The quality of evidence for each outcome in our review was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach [20]. For this approach, the grade of a study is decreased based on the degree of risk of bias, indirectness of the evidence, inconsistency and imprecision of effect estimates across studies, and the presence of possible publication or reporting biases. All discrepancies were resolved through a consensus process involving a third author (C.L.).


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### Data extraction

Two reviewers (E.T. and Y.T.) independently extracted the data onto a standardized form using Microsoft Excel version 2016 (Microsoft Corp., Redmond, 2015). The following data were collected from each study: authors' names; publication year; sample size; type of surgery; type of peripheral nerve block performed; local anesthetic used (type of local anesthetic, concentration, and volume); dose of dexamethasone administered; time to first analgesia request; time to first pain sensation; duration of sensory block; duration of motor block; postoperative cumulative opioid requirement; postoperative pain scores at various time points; and incidence of adverse events including postoperative nausea and vomiting, hyperglycemia, and prolonged paresthesia or motor block. If additional data were required, attempts were made to contact the authors of the studies to obtain the missing information. Any disagreements were resolved through discussion with a third reviewer (C.L.).

### Data analysis and statistical methods

To standardize the data for analysis, the outcomes assessing the duration of effect were converted to hours. Opioid use was converted to oral morphine analgesic equivalent doses using the Faculty of Pain Medicine of the Australian and New Zealand College of Anesthetists Opioid Calculator [21]. Data that were measured as median and interquartile range (IQR) were converted to approximate mean and standard deviation values using Hozo's validated formula [22].

Statistical analyses were performed using the Review Manager (RevMan) software version 5.4. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014 and R Studio software Version 1.2.1335, Boston: R Studio Inc., 2018.

Random-effects modelling was used for all pooled data. Continuous data were compared using mean differences and 95% CIs. Dichotomous data were pooled and analyzed using the Mantel-Haenszel odds ratio with 95% CIs. The $I^2$ test was used to estimate the degree of statistical heterogeneity. Sensitivity analysis was performed to assess the robustness of the results. Subgroup analyses were performed to detect any significant heterogeneity. Funnel plots and Egger's test were performed to evaluate the risk of publication bias. A trial sequential analysis for the primary outcome was performed using Trial Sequential Analysis Viewer (TSA Viewer) software version 0.9.5.10 Beta, Copenhagen: Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet 2016.

## Results

### Study selection and characteristics

A total of 2,198 articles were identified during the initial search, after which the 232 duplicates were removed (Fig. 1). After screening the titles and abstracts, 58 studies were identified for full-text review, of which 43 were excluded because they did not fulfil the inclusion criteria. Of note, two studies [23,24] were excluded because different doses of dexamethasone were used for the perineural and intravenous routes, and one study [25] was excluded because no surgery was performed. Finally, fifteen RCTs were included in this systematic review and meta-analysis. These 15 studies [14–17,26–36] included a total of 1,467 participants, of which 738 were in the perineural dexamethasone group and 729 were in the intravenous dexamethasone group.

The study conducted by Holland et al. [15] was a two-by-two factorial design study comparing both 4 mg and 8 mg of perineural dexamethasone with equivalent doses of intravenous dexamethasone. We therefore analyzed the data separately and labeled them Holland 2018 (Dexa 4 mg) and Holland 2018 (Dexa 8 mg), respectively.

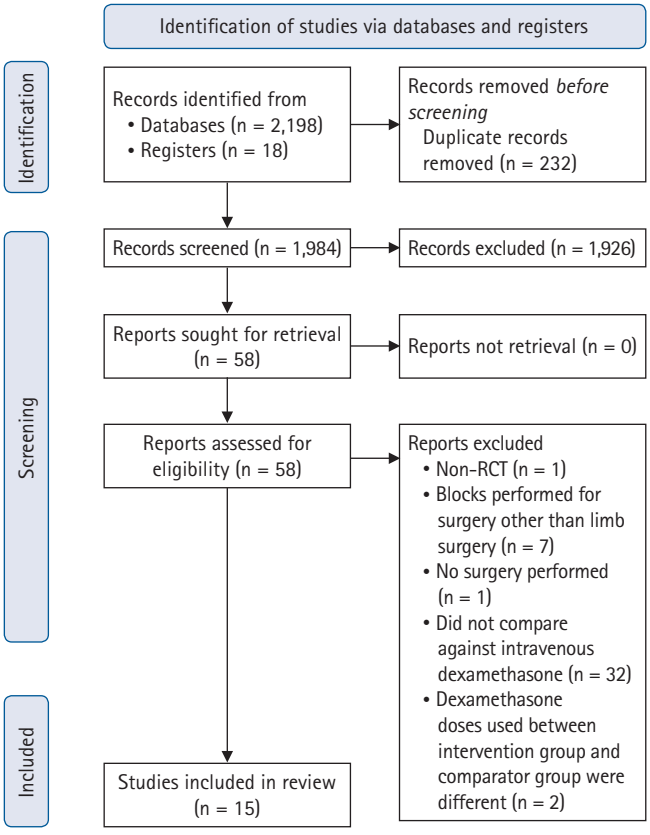


**Fig. 1.** PRISMA flow diagram.

For the upper limb surgery studies [14–17,29–36], the brachial plexus blocks were administered using different approaches. Nine of these studies used the interscalene approach [14–17,24,29,30,33,35,36], two used the supraclavicular approach [14,31], one the infraclavicular approach [34], and one used the axillary approach [32]. For the lower limb surgery studies [26–28], one performed femoral nerve blocks [26], and two performed sciatic nerve blocks [27,28]. Regarding the dose of dexamethasone, five studies used a range between 1 and 4 mg [15–17,30,36], ten used a range between 5 and 10 mg [15,26–29,31–35], and one study used a weight-calculated dose of 0.05 mg/kg [14]. For the anesthetic, five studies used ropivacaine 0.5% [16,29–31,33,35], three used ropivacaine 0.75% [27,30,36], four used bupivacaine 0.5% alone [15,17,31], one used bupivacaine 0.5% with lignocaine 2% and adrenaline [14], two used bupivacaine 0.25% with lignocaine 1% and adrenaline [32,34], and one used bupivacaine 0.5% with adrenaline [28]. The volume of the local anesthetic administered ranged from 5 to 30 ml. Specific details regarding the included studies and their block characteristics are summarized in Table 1.

## Risk of bias assessment

The risk of bias assessment results are shown in Fig. 2. No significant publication bias was detected according to the funnel plots or Egger's test (P = 0.386). As per the inclusion criteria, all studies included in the meta-analysis were RCTs.

## Primary outcome

*Duration of analgesia*

The primary outcome (the duration of analgesia) was reported in thirteen studies [14–17,26,27,29–32,34,35], with a total of 641 patients in the perineural dexamethasone group and 634 patients in the intravenous dexamethasone group. The duration of action was assessed either as the time to first pain sensation [15–17,27,31,32,34] or the time to first analgesia request [14,16,26,29,30,35]. Significant heterogeneity was observed among the studies. Overall, patients in the perineural dexamethasone group had a significantly longer duration of analgesia compared to the intravenous dexamethasone group (mean difference [MD]: 2.72 h, 95% CI [1.42, 4.01], moderate quality evidence, $I^2$ = 86%, P < 0.001) (Fig. 3). When analyzed separately, subgroup analyses still demonstrated a statistically significant prolongation of both time to first pain sensation (MD: 2.58 h, 95% CI [1.13, 4.03], $I^2$ = 74%, P < 0.001) and time to first analgesic request (MD: 2.69 h, 95% CI [0.26, 5.11], $I^2$ = 92%, P = 0.03) in the perineural dexamethasone group (Figs. 4 and 5). The trial sequential analysis indicated strong evi-

**Table 1.** Main Characteristics of Included Studies

| Study & Year | No. of participants (Perineural) | No. of participants (Intravenous) | Type of peripheral nerve block | Type of surgery | Type, dose of local anesthetic | Dose of dexamethasone (mg) |
|---|---|---|---|---|---|---|
| McHardy, 2020 [16] | 92 | 90 | Interscalene | Shoulder arthroscopy | Ropivacaine 0.5%, 5 ml | 4 |
| Godbole, 2019 [14] | 28 | 29 | Supraclavicular | Upper limb surgery | Lignocaine 2% with adrenaline 10 ml + bupivacaine 0.5%, 20 ml | 0.05 mg/kg |
| Holland, 2018 [15] - Dexa 4 mg | 68 | 68 | Interscalene | Shoulder arthroscopy | Bupivacaine 0.5%, 30 ml | 4 |
| Holland, 2018 [15] - Dexa 8 mg | 69 | 70 | Interscalene | Shoulder arthroscopy | Bupivacaine 0.5%, 30 ml | 8 |
| Kahn, 2018 [17] | 63 | 62 | Interscalene | Shoulder arthroscopy | Bupivacaine 0.5%, 15 ml | 1 |
| Sakae, 2017 [36] | 20 | 20 | Interscalene | Shoulder arthroscopy | Ropivacaine 0.75%, 20 ml | 4 |
| Leurcharusmee, 2016 [34] | 61 | 62 | Infraclavicular | Upper limb surgery | Bupivacaine 0.25% + lidocaine 1% + epinephrine 5 mcg/ml, 24 ml | 5 |
| Aliste, 2016 [32] | 75 | 75 | Axillary | Forearm surgery | Bupivacaine 0.25% + lidocaine 1% + epinephrine 5 mcg/ml, 24 ml | 8 |
| Rosenfeld, 2016 [35] | 42 | 37 | Interscalene | Shoulder surgery | Ropivacaine 0.5%, 28 ml | 8 |
| Chun, 2016 [33] | 50 | 49 | Interscalene | Shoulder arthroscopy | Ropivacaine 0.5%, 12 ml | 5 |
| Abdallah, 2015 [31] | 25 | 25 | Supraclavicular | Upper limb surgery | Bupivacaine 0.5%, 30 ml | 8 |
| Kawanishi, 2014 [30] | 12 | 10 | Interscalene | Shoulder arthroscopy | Ropivacaine 0.75%, 20 ml | 4 |
| Desmet, 2013 [29] | 49 | 49 | Interscalene | Shoulder arthroscopy | Ropivacaine 0.5%, 30 ml | 10 |
| Morales, 2016 [26] | 27 | 27 | Femoral | Knee replacement surgery | Ropivacaine 0.5%, 20 ml | 8 |
| Dawson, 2015 [27] | 30 | 30 | Sciatic | Foot surgery | Ropivacaine 0.75%, 20 ml | 8 |
| Rahangdale, 2014 [28] | 27 | 26 | Sciatic | Foot and ankle surgery | Bupivacaine 0.5%, + epinephrine 0.45 ml/kg to a max of 40 ml | 8 |


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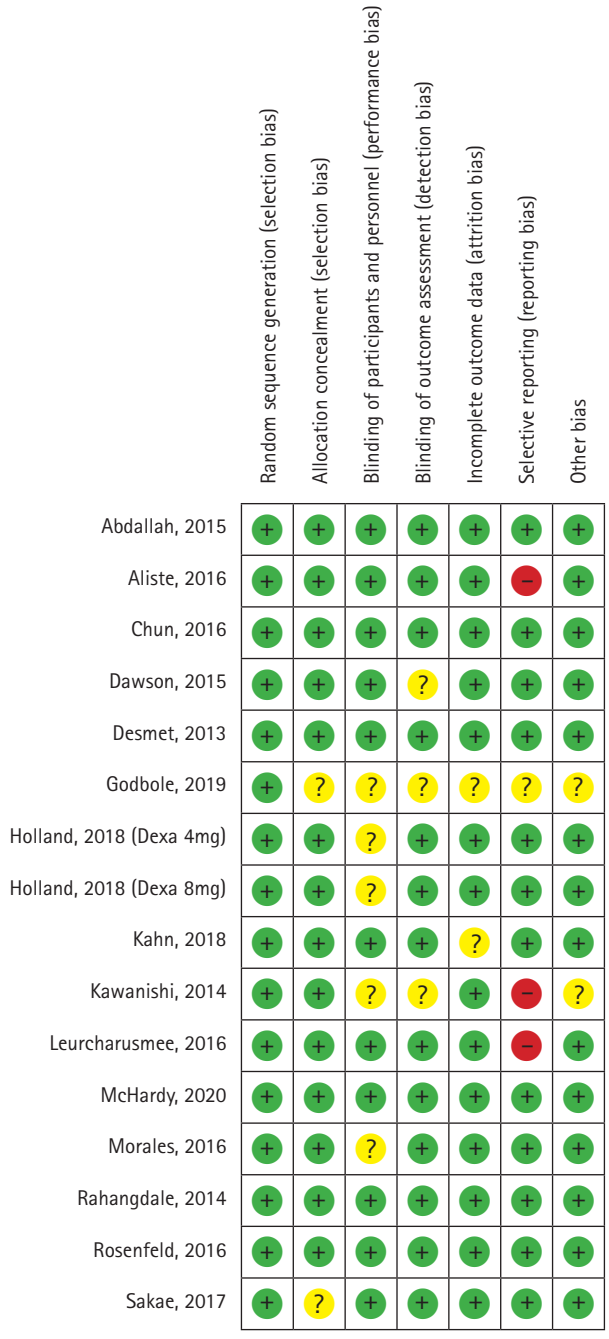


**Fig. 2.** Risk of bias table of included studies.

dence, and perineural dexamethasone was found to be superior to intravenous dexamethasone.

As shown in Fig. 3, the trial conducted by Morales-Muñoz et al. [26] yielded an effect size that was quite different from that of the other studies. This study investigated the addition of dexamethasone to a femoral nerve block for knee arthroplasty. The perineural dexamethasone group had a mean duration of analgesia of 1152 min, while the intravenous dexamethasone group had a mean duration of analgesia of 159 min. Since this study could have artificially skewed the results towards favoring perineural dexamethasone, a sensitivity analysis was performed with this study excluded. However, this did not result in a significant decrease in the overall heterogeneity of the studies or outcomes (MD: 2.32 h, 95% CI [1.12, 3.52], $I^2$ = 84%, P < 0.001).

Several subgroup analyses were performed to account for the significant heterogeneity of the results. When the studies involving upper limb blocks were analyzed separately, the duration of analgesia with perineural dexamethasone remained significantly longer than that with intravenous dexamethasone (MD: 2.27 h, 95% CI [1.03, 3.51], P < 0.001). Another subgroup analysis was performed that included only those studies that used interscalene blocks, which is the most common approach. However, significant differences were still not found between the groups (MD: 1.56 h, 95% CI [−0.15, 3.28], P = 0.07). A trial sequential analysis was then performed, which indicated that data were insufficient to refute a possible effect with interscalene blocks.

To determine whether dexamethasone had a dose-dependent effect, the studies using dexamethasone doses ≤ 4 mg were analyzed separately from studies using dexamethasone doses > 4 mg. Both subgroup analyses showed a significantly prolonged analgesic duration, with a mean difference of 3.01 h in the ≤ 4 mg dose group (P < 0.001) and a mean difference of 2.81 h in the > 4 mg dose group (P = 0.02).

## Secondary outcomes

*Postoperative pain scores*

The study conducted by Kahn et al. [17] reported pain scores in the post-anesthesia care unit, and the one conducted by Chun et al. [33] reported 6-h postoperative pain scores. In the study by Kahn et al. [17], no significant differences in pain scores were seen in the post-anesthesia care unit between the two groups (MD: 0.1, 95% CI [−0.6, 0.7], P = 0.999). Similarly, the study by Chun et al. [33] also did not find a significant difference in pain scores at 6 h post-operation (median [IQR]: perineural dexamethasone: 1 [0–2], intravenous dexamethasone: 1 [0–2]; P = 0.39).

A meta-analysis was performed for both the 12 and 24 h postoperative pain scores. Four trials [16,33,35,36] analyzed pain scores at 12 h post-operation, showing significantly lower pain scores in the perineural dexamethasone group (MD: −0.68, 95% CI [−1.05, −0.31]; low quality evidence, $I^2$ = 19%, P < 0.001) (Fig. 6).

Ten trials [15,16,26,28,30,31,33,35,36] compared 24 h postoperative pain scores, revealing a statistically significant reduction in pain in the perineural compared with the intravenous dexamethasone group (MD: −0.74, 95% CI [−1.40, −0.07]; low quality evi-

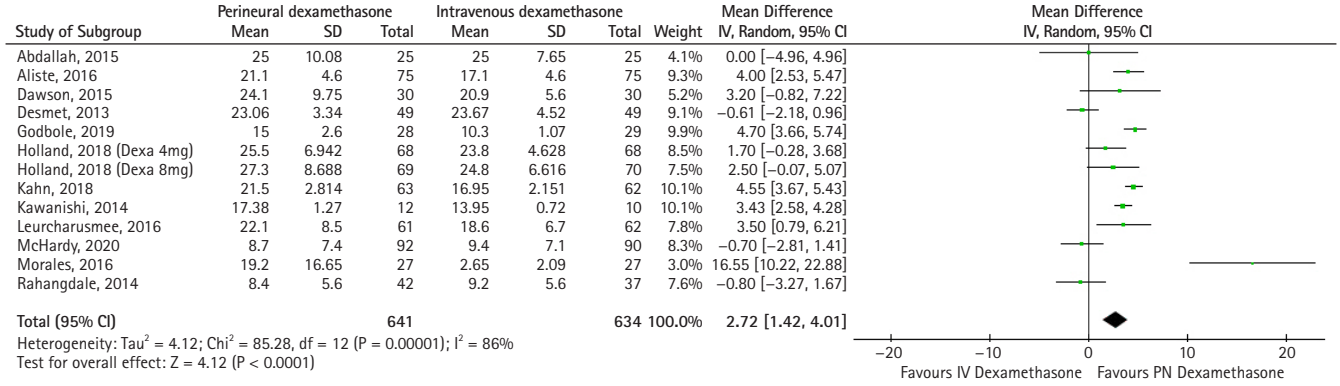


**Fig. 3.** Forest plot of perineural vs. intravenous dexamethasone; duration of analgesia in hours.

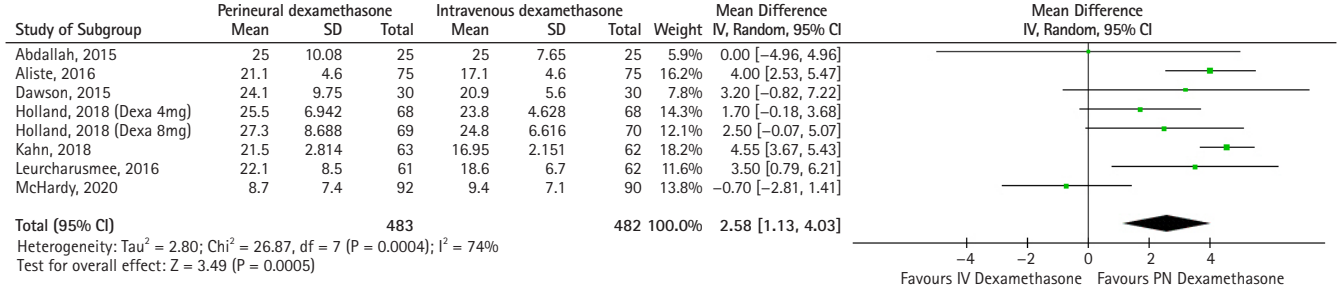


**Fig. 4.** Forest plot of subgroup analysis of time to first pain sensation in hours for perineural vs. intravenous dexamethasone.

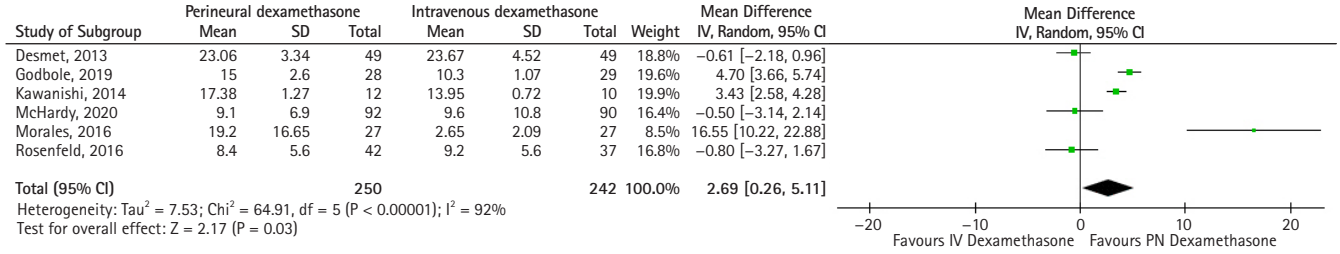


**Fig. 5.** Forest plot of subgroup analysis of time to first analgesic request in hours for perineural vs. intravenous dexamethasone.

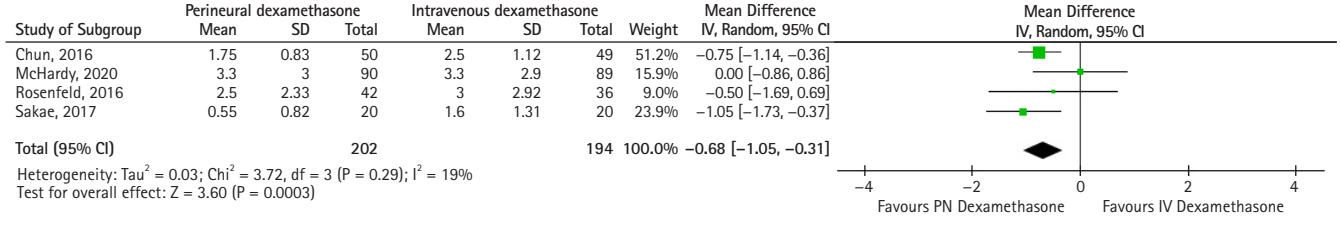


**Fig. 6.** Forest plot of 12-h postoperative pain scores for perineural vs. intravenous dexamethasone.

dence, $I^2$ = 83%, P = 0.03). However, the mean differences at both 12 and 24 h post-operation were small and not considered clinically relevant [37] (Fig. 7).

### *24 h opioid consumption*

Eight trials [15,16,26–28,31,35] examined 24 h oral morphine equivalent requirements. No significant difference was found between the groups (MD: −1.05 mg, 95% CI [−2.71, 0.61]; low quality evidence, $I^2$ = 76%, P = 0.21) (Fig. 8).


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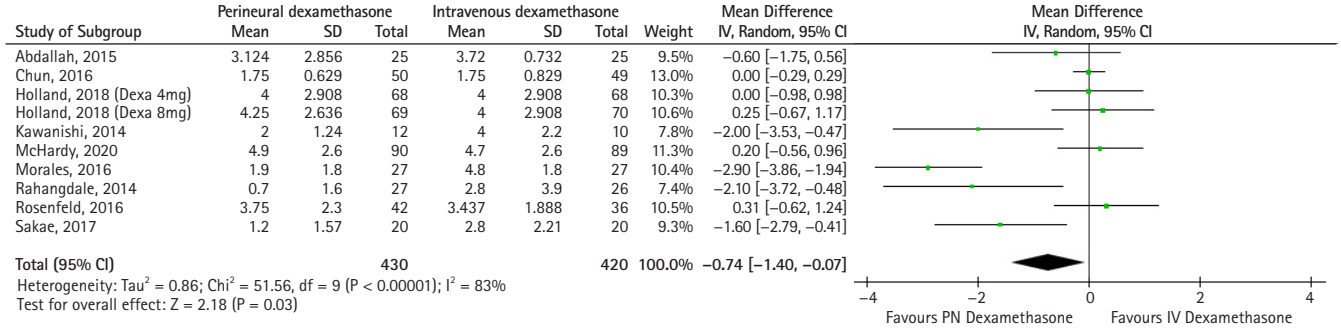


**Fig. 7.** Forest plot of 24 h postoperative pain scores for perineural vs. intravenous dexamethasone.

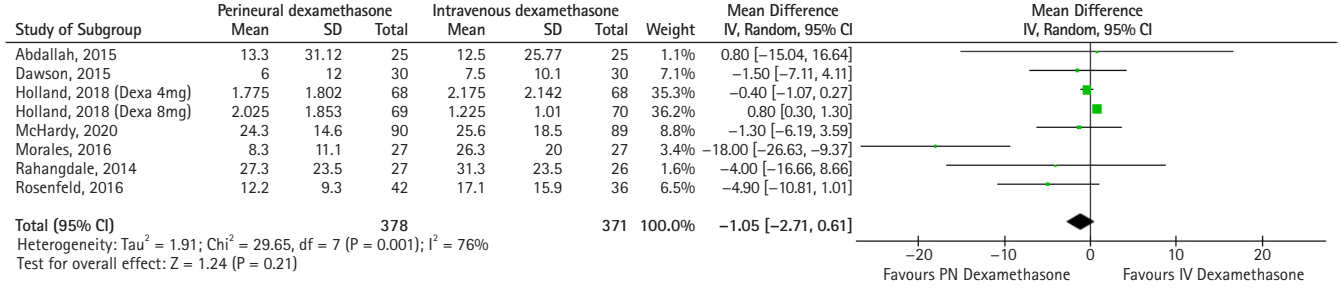


**Fig. 8.** Forest plot of 24 h oral morphine equivalent consumption in mg for perineural vs. intravenous dexamethasone.

### *Duration of sensory and motor block*

Six studies [14,27,32,34–36] reported on the sensory block duration. The perineural dexamethasone group showed a longer duration compared to the intravenous dexamethasone group (MD: 3.45 h, 95% CI [1.36, 5.54]; moderate quality evidence, $I^2$ = 82%, P = 0.001).

Additionally, six trials [14,16,31,32,34,36] analyzed the motor block duration; however, no significant difference between the groups was found (MD: 2.01 h, 95% CI [−0.92, 4.94]; low quality evidence, $I^2$ = 93%, P = 0.18).

### *Postoperative nausea and vomiting*

Six studies [16,26,27,30,31,36] compared the incidence rates of postoperative nausea and vomiting. No significant differences were observed between the groups, with a pooled incidence of 17.15% in the perineural dexamethasone group and 20.4% in the intravenous dexamethasone group (odds ratio: 0.78, 95% CI [0.46, 1.34], $I^2$ = 0%, P = 0.37).

### *Postoperative blood glucose levels*

Postoperative blood glucose levels were reported in three studies. Both Desmet et al. [29] and McHardy et al. [16] reported a statistically (but not clinically) significantly higher mean postoperative blood glucose level in the intravenous dexamethasone group than in the perineural dexamethasone group. Desmet et al. showed a mean increase of 0.3 mmol/L in the intravenous group and 0.2 mmol/L in the perineural group (P < 0.05), while McHardy et al. demonstrated a mean difference of 0.34 mmol/L (P = 0.02) in the intravenous group compared to the perineural group. Another study, conducted by Chun et al. [33], reported no significant differences between the two groups (mean [95% CI] 0.5 mmol/L [0.2, 0.8] vs. 0.4 mmol/L [0.2, 0.6], P = 0.55).

### *Neurological complications*

Six studies [15,28,29,32–34] reported the neurological outcomes of the participants. The studies conducted by Desmet et al. [29], Aliste et al. [32], Chun et al. [33] and Rahangdale et al. [28] found no significant short-term or long-term neurological deficits. However, two studies [15,34] reported longer-lasting neurological outcomes in their participants. Leurcharusmee et al. [34] reported paresthesia in one patient in the perineural dexamethasone group that resolved within a week, while no neurological complications were reported in the intravenous dexamethasone group. The study conducted by Holland et al. [15] reported a higher incidence of neurological issues in the perineural dexamethasone group. In that study, the incidence of paresthesia was 13% and 14% in the 4 mg and 8 mg perineural dexamethasone groups, respectively, while for the intravenous dexamethasone groups, the incidence was 6% (4 mg group) and 11% (8 mg group). These differences, however, were not statistically significant, and an in-depth review of the cas-

es resulted in the conclusion that paresthesia was unlikely to be related to the use of dexamethasone.

*Satisfaction scores*

Satisfaction scores were recorded in seven studies [17,26,28–31,35], of which five [17,28,29,31,35] reported similar mean satisfaction scores between the groups, one [26] reported better patient satisfaction scores with perineural dexamethasone, and another [30] showed better satisfaction scores with intravenous dexamethasone.

## Discussion

Compared to placebo, perineural dexamethasone as an adjunct to local anesthetics has been estimated to increase the duration of analgesia by 6.7 h [6]. However, it is unclear whether this is a result of systemic dexamethasone absorption. This meta-analysis, which included 15 RCTs and at total of 1,467 patients, suggests that local effects might explain this difference, considering that the duration of analgesia was longer in the perineural dexamethasone group compared to the intravenous dexamethasone group. The results of this study are similar to those of a previous meta-analysis performed in 2017 [11]. However, the impact of perineural dexamethasone on the duration of analgesia was found to be more modest than previously estimated [11].

Compared with intravenous dexamethasone, perineural dexamethasone was found to only increase the duration of analgesia by 2.72 h. The study conducted by Morales-Muñoz et al. [26] thus appears to be an outlier. Although efforts were made to determine why their results differed so considerably from those of the rest of the studies, no reasonable explanation was found. After this study was excluded from the analysis, an even more modest difference of 2.32 h was found. We believe that 2.32 h is likely to be closer to the true effect size.

Although the subgroup analysis that included only those patients undergoing interscalene blocks demonstrated no statistically significant differences between the perineural and intravenous dexamethasone groups, there was a trend towards a longer duration of analgesia in the perineural group. A trial sequential analysis confirmed that this may have been due to an inadequate sample size. Importantly, there were no clinically relevant differences in the 24 h postoperative pain scores, 24 h opioid consumption, or satisfaction scores.

A potential concern regarding the use of perineural dexamethasone is neurotoxicity. Animal studies have raised concerns regarding the potential neurotoxic effects of dexamethasone [38]. Despite this, we caution against labelling dexamethasone as neurotoxic based on animal cell culture studies with methodological flaws. Perineural dexamethasone has been used in the past for many causes of acute and chronic pain with no indication of increased neurotoxicity [39,40]. Consistent with other meta-analyses examining perineural steroids [16,33], no concerns linking the use of perineural steroids with poor neurological outcomes were found in our study.

This study has certain limitations. The most significant limitation was the heterogeneity of the included studies. Although the primary outcome (duration of analgesia) was assessed in all the studies, there was a lack of standardization regarding how this was defined or assessed. For example, some studies defined it as the time to the first pain sensation, while others defined it as the time to the first analgesia request. Furthermore, the methods of collecting the data were different between the studies; for example, some utilized retrospective telephone interviews, while others utilized patient self-report diaries. Heterogeneity may have also resulted from differences in the exact nature of the surgery as well as differences in surgical techniques.

Another limitation of this study was the lack of clarity on how researchers handled the time to first analgesia for the patients did not require rescue analgesia. Apart from the study by Desmet et al. [29], which reported no significant differences in the number of patients who did not require rescue analgesia at 48 h post-surgery (4 out of 49 patients in the perineural dexamethasone group compared to 5 out of 49 in the intravenous dexamethasone group), the remaining studies did not report the number of patients who did not require rescue analgesia and did not discuss how these data were handled.

Taken together, this systematic review and meta-analysis offers a weak recommendation that perineural dexamethasone not be routinely administered as an adjunct to local anesthetics. Rather, intravenous dexamethasone should be considered, as it may be able to extend the duration of analgesia and can also be used to prevent postoperative nausea and vomiting [41]. The basis for this recommendation is that an increase in the duration of analgesia of 2.32 h is unlikely to be clinically relevant. Furthermore, perineural dexamethasone did not improve other pain-related parameters, such as pain scores or opioid consumption. The lack of standardization regarding how the primary outcome was defined and assessed in many of the studies also affects the reliability of the pooled results. Nevertheless, this review does not recommend further studies be conducted on this topic, given that they are unlikely to drastically change the results of this meta-analysis or lead to a change in the recommendations.

In conclusion, this systematic review and meta-analysis showed that perineural dexamethasone, when used as an adjunct to local


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anesthetics, results in a longer duration of analgesia than intravenous dexamethasone. However, the effect size was small and may not be clinically meaningful. Perineural dexamethasone was also not associated with a clinically significant reduction in 24 h pain scores or opioid consumption. We therefore make a weak recommendation that perineural dexamethasone not be routinely administered to patients to prolong the duration of analgesia following peripheral nerve blocks. Instead, intravenous dexamethasone should be considered.

## Funding

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## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

## Author Contributions

Elizabeth Sein Jieh Tan (Conceptualization; Formal analysis; Investigation; Methodology; Writing – original draft)
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