British Journal of Hospital Medicine

Br. J. Hosp. Med. (Lond) **2026**; 87(6): 55376
https://doi.org/10.31083/BJHM55376

Systematic Review

The Effects of Perineural Dexamethasone on Preventing Post-Surgical Rebound Pain and Effects on Hyperglycaemia: A Meta-Analysis, Meta Regression and Trial Sequential Analysis

Rahul Banerjee[1], Anindya Banerjee[2], Madhuchanda Chatterjee[3], Arnab Banerjee[4,*]

[1]School of Medicine, The University of Buckingham, MK18 1EG Buckingham, UK
[2]Department of Medicine, Goulburn Base Hospital, Goulburn, NSW 2580, Australia
[3]Department of Oncology, Betsi Cadwaladr University Health Board, LL13 7TD North Wales, UK
[4]Department of Anaesthesia, Goulburn Base Hospital, Goulburn, NSW 2580, Australia
*Correspondence: abanerjeeuk@googlemail.com (Arnab Banerjee)
Academic Editor: John Alcolado
Submitted: 24 September 2025 Revised: 27 January 2026 Accepted: 29 January 2026 Published: 28 June 2026

Abstract

Aims/Background: Rebound pain is extreme pain occurring once the effects of a regional nerve block have subsided. We undertook a meta-analysis to assess the impact of perineural dexamethasone, as an adjunct to peripheral nerve block, on post-surgical rebound pain compared to local anaesthetic alone. **Methods**: The databases PubMed, Scopus and Cochrane Library were searched for randomised controlled trials, reporting rebound pain with perineural dexamethasone used as an adjunct to peripheral nerve blocks (from inception to 28 October 2025). The primary outcome was the incidence of rebound pain post-surgically; the secondary outcomes were onset of rebound pain (hours), pain scores at 24 and 48 hours, time until first analgesic request (hours), and incidence of hyperglycaemia. **Results**: Nine studies with 764 participants were included. Perineural dexamethasone significantly reduced the incidence of rebound pain (odds ratio [OR] = 5.00, 95% confidence interval [CI] 2.69–9.29, $p < 0.00001$, $I^2 = 41\%$). The time to the first analgesic request was prolonged in the dexamethasone group (standardised mean differences [SMD] = –2.37, 95% CI –3.38– –1.36, $p < 0.00001$, $I^2 = 77\%$). Perineural dexamethasone did not delay the onset of rebound pain, reduce pain scores at 24 and 48 hours, nor did it significantly alter blood sugar levels. **Conclusion**: This meta-analysis demonstrated that perineural dexamethasone is more effective than local anaesthetic alone in reducing the incidence of rebound pain and extending the time to the patients' first analgesic request. There was no significant difference in the onset of rebound pain, pain scores at 24 and 48 hours, nor alteration of blood sugar levels. **Systematic Review Registration**: PROSPERO (CRD42024545072).

Keywords: rebound pain; dexamethasone; anaesthesia, local; adjuvants, anaesthesia; pain, postoperative; pain measurement; hyperglycaemia; meta-analysis

1. Introduction

Peripheral nerve blocks (PNBs) are widely accepted and commonly used in anaesthesia. They have been shown to decrease postoperative pain, reduce the postoperative opioid consumption and increase patient satisfaction in comparison to general anaesthesia [1]. Post-surgical rebound pain is extreme pain that occurs once the analgesic effects of the block have worn off [2]. It is a clinically significant problem, impacting patients through reduced quality of recovery, diminished ability to carry out activities of daily living and potential prolongation of recovery time [2]. It is proposed that it occurs due to unopposed nociceptive inputs that are uncovered after PNB and relates to abnormal spontaneous C-fibre hyperactivity and nociceptor hyperexcitability [3].

Perineural adjuncts are pharmacological agents that can be co-administered alongside a local anaesthetic (LA) with the aim of affecting the characteristics of the resulting block [4]. There are conflicting views on the use of dexamethasone as an adjunct, with a paucity of literature specifically recommending whether perineural dexamethasone is preferable for reducing rebound pain. Steroids also present potential complications, such as impairments in the regulation of blood glucose, prolongation of wound healing, and risk of wound infection secondary to immunosuppressant effects [5,6]. We tried to evaluate the impact of perineural dexamethasone as an adjunct to regional nerve blocks on the incidence of rebound pain post-surgery.

2. Methods

We registered this systematic review under the International Prospective Register of Systematic Reviews (PROSPERO) with the identifier CRD42024545072 (https://www.crd.york.ac.uk/PROSPERO/view/CRD42024545072). This meta-analysis adhered to the standards outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (**Supplementary Material**). Our primary outcome was to find the incidence of rebound pain, and secondary outcomes were the temporal effect of perineural

dexamethasone upon first analgesic request (hours until first request); the effect of perineural dexamethasone on pain scores at 24 and 48 hours; the onset of rebound pain (hours); and the impact of perineural dexamethasone on blood sugar levels. Search dates were from inception till 28 October 2025.

We searched using the PICO format (Population: patients receiving a peripheral nerve block during surgery; Intervention: perineural dexamethasone as an adjunct to regional nerve block; Comparison: local anaesthetic alone; Outcome: Comparative effectiveness on reducing postoperative rebound pain). The search strategy included broad terms such as: (perineural) AND (dexamethasone) AND (rebound pain). A search of the three bibliographic databases PubMed (https://pubmed.ncbi.nlm.nih.gov), Scopus (https://www.scopus.com), and the Cochrane Library (https://www.cochranelibrary.com) generated 170 citations (8, 152, and 10, from each database, respectively). Furthermore, citation tracking and searches of relevant websites were used to identify additional relevant literature beyond the initial database searches. Both backward citation tracking (reviewing the reference lists of the nine included articles) and forward citation tracking (identifying newer papers cited by these nine articles) were employed to identify further relevant articles. Studies irrespective of publication year were included if they met the following criteria: (1) were randomised controlled trials (RCTs); (2) studied dexamethasone as an adjunct to a regional nerve block; and (3) reported the incidence of rebound pain as a primary or secondary outcome. Exclusion criteria included: use of intravenous dexamethasone in the experimental or control arms of the study, and co-administration of any adjunct other than dexamethasone. Trials were included irrespective of original publication language, type of local anaesthetic (LA) and dose of LA, different types of surgery performed and patient characteristics (including those with diabetes).

2.1 Trial Selection

The initial database search identified 170 articles. After duplicate removal using EndNote, 150 remaining articles underwent abstract screening by two independent review authors (RB and AB). After full-text retrieval, RB and AB scored the quality of each article according to the Jadad [7] scale and assigned a final score. Disagreements were resolved through conversation with input from a third and fourth author (MC and AB) when necessary. Data were recorded independently by RB and AB to avoid transcription errors, with any discrepancies resolved by consensus after revisiting the original articles. Thirteen articles were then extracted for full-text screening, of which nine were ultimately included in the meta-analysis [8,9,10,11,12,13,14,15,16]. The selected trials were published between 2020 and 2025, enrolling a total of 764 patients, of which 438 received dexamethasone, and 326 formed the control arm. Data were extracted for statistical analysis in the programme Review Manager 5.4 (Cochrane Collaboration, Copenhagen, Denmark) and re-checked by all authors. We extracted the reporting of any adverse effects arising from the administration of perineural dexamethasone. A funnel plot and Cochrane Risk-of-Bias-2 tool (RoB 2.0, Cochrane Collaboration, London, UK) were used to assess study quality.

2.2 Statistical Analysis

The statistical analysis was carried out using Review Manager 5.4 (Cochrane Collaboration, Copenhagen, Denmark) software. Binary outcomes were extracted as odds ratio (OR) and continuous outcomes as standardised mean differences (SMD) with 95% confidence intervals. The pooled estimates were calculated using a random-effects model, presented as OR or SMD and 95% confidence intervals. We considered two-sided p-values < 0.05 significant, and the I^2 statistic was used to quantify heterogeneity. The I^2 indicates the proportion of total variation among effect sizes, which is due to heterogeneity as opposed to chance. $I^2 > 50\%$ was considered substantial. Sensitivity analysis was performed where relevant.

Where substantial heterogeneity was detected, we explored potential sources using meta-regression analysis. Potential contributors to heterogeneity included the dose and volume of local anaesthetic, types of operation, doses of dexamethasone, and Jadad score. Precision modelling included Duval and Tweedie's 'trim and fill effect' to find missing studies that might cause funnel plot asymmetry. Where applicable, the number needed to treat (NNT) and relative risk reduction (RRR) were also calculated.

Trial sequential analysis (TSA) was performed using TSA viewer (Version 0.9.5.10 Beta, Copenhagen Trial Unit, 2016, Copenhagen, Denmark). The Sidik Jonkman random effects model, which is less likely to underestimate inter-study heterogeneity, was chosen to calculate the Z-statistic (the meta-analysed intervention effect divided by its standard error). In cumulative meta-analysis, adjusted significance testing has two objectives: (1) to assess the strength of the available evidence; and (2) to control for the risk of type-1 and type-2 statistical errors due to repeated significance testing on accumulating data. The strength of the evidence is assessed by determining the required information size (IS), which reflects the sample size needed for a conclusive and reliable meta-analysis. This was calculated using a type-1 error rate of 5% and type-2 error rate of 20%, resulting in a statistical power of 80%.

3. Results

3.1 Literature Search

Following duplicate removal, 150 remaining articles underwent independent abstract screening according to the PICO and inclusion criteria, nine RCTs were selected for analysis (Fig. 1).

Table 1. Characteristics of the included studies.

Author	Study design	Surgery	Randomisation	Peripheral nerve block	Local anaesthetic	Dexamethasone dose	Number of patients		Rebound pain definition (if applicable)	Jadad
							C	D		
Fang 2021 [9]	RCT	ORIF of upper extremity closed fracture	Computer-generated random number table. Sealed envelope	Interscalene OR supraclavicular brachial plexus block OR under axillary brachial plexus block with musculocutaneous nerve block	Ropivacaine 0.375% 40 mL	8 mg	60	63	Severe pain NRS >7 that occurs suddenly and cannot be relieved after a PCIA bolus in 30 mins. If asleep—wakes up the patient and makes it difficult for them to go back to sleep	5
Woo 2021 [8]	RCT	Arthroscopic shoulder operations	Computer-generated random number table. Sealed envelope	Interscalene block (single-injection) under US guidance	Ropivacaine 0.5% 12 mL	5 mg	35	35	Severe pain NRS ≥7 at the surgical site following ISB resolution	5
Morita 2020 [10]	RCT	Arthroscopic rotator cuff repair (ARCR)	Patients assigned to arm by the day and time of surgery	Interscalene brachial plexus block (ISBPB)	Levobupivacaine 0.25% 20 mL	3.3 mg	21	33	VAS point of 5 (POD1)	5
Kim 2022 [12]	RCT	Arthroscopic rotator cuff repair (ARCR)	Determined by surgical order	Single-shot interscalene block OR interscalene indwelling catheter	0.45% Ropivacaine 12 mL + 5% Dextrose 7 mL	5 mg	36	94	None mentioned	4
Da'Meh 2021 [11]	RCT	Upper limb orthopaedic procedures	Not mentioned	Supraclavicular Brachial Plexus Block, US-guided	Bupivacaine 0.5% 35 mL	6 mg	57	59	Severe sudden pain NRS ≥7 not ameliorated in 45 min	4
Badran 2020 [13]	RCT	Upper limb orthopaedic procedures	Computer-generated random number table. Sealed envelope	Interscalene brachial plexus block (ISBPB)	Bupivacaine 0.5% 30 mL	8 mg	23	22	N/A	4
Kim 2023 [14]	RCT	Open reduction and internal fixation of distal radius fractures	Computer-generated random number table. Sealed envelope	Supraclavicular block	Ropivacaine 0.5% 16 mL	5 mg	30	30	N/A	5
Reysner 2024 [15]	RCT	Paediatric foot or ankle surgery	Computer software, 1:1:1 ratio, blocks of 6 or 9 in random order	Popliteal sciatic nerve block	Ropivacaine 0.2% 0.5 mL/kg	0.1 mg/kg or 0.05 mg/kg	30	60	N/A	5
Nobre 2025 [16]	RCT	Upper limb orthopaedic procedures	Online randomisation service. Sealed envelope	Interscalene brachial plexus block (ISBPB)	Bupivacaine 0.375% 20 mL	4 mg	34	42	Sudden onset VAS ≥7 pain without improvement with oral medication	5

ORIF, open reduction and internal fixation; PCIA, patient-controlled intravenous analgesia; POD1, postoperative day 1; RCT, randomised controlled trial; C, control group; D, dexamethasone group; NRS, Numeric Rating Scale; VAS, visual analogue scale; N/A, not applicable.

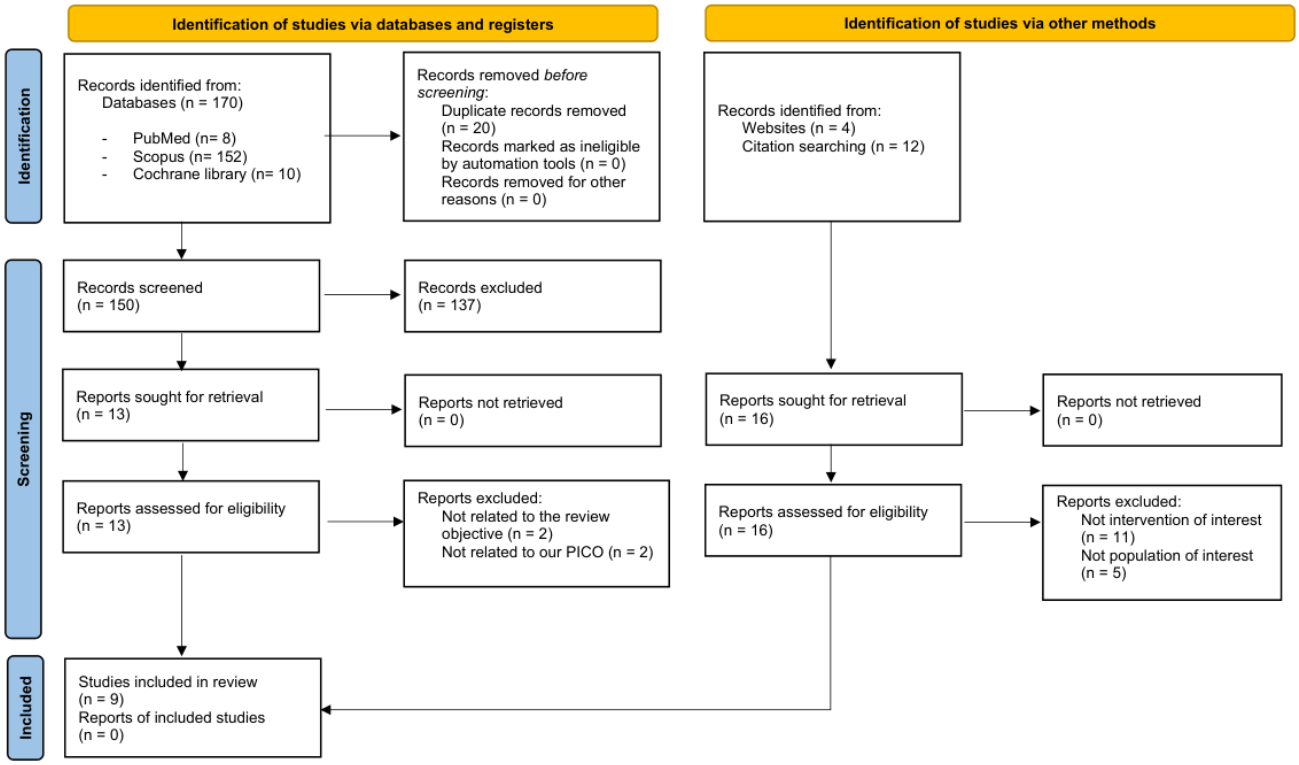

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow diagram. PICO, Population, Intervention, Comparison, Outcome.

3.2 Characteristics of the Included Studies

Nine RCTs [8,9,10,11,12,13,14,15,16] were included, with a total of 764 patients, of which 438 received dexamethasone and 326 formed the control arm. The administered dose of dexamethasone ranged from 3.3 mg to 8 mg. Of the nine included articles [8,9,10,11,12,13,14,15,16], only one declared funding, Fang et al. [9] was supported by the National Key Research and Development Program of China (NO. 2020YFC2008400). The characteristics of these studies are summarised in Table 1 (Ref. [8,9,10,11,12,13,14,15,16]).

3.3 Quality Assessment

The Cochrane Risk-of-Bias Tool (RoB 2.0, Cochrane Collaboration, London, UK) was used to assess study quality [17]. Most RCTs had a low risk of bias in all domains, indicating reliability in their findings. The overall risk of bias was 'Low risk' in seven studies and 'some concerns' in two studies, relating to issues in reporting of the randomisation process (Fig. 2).

4. Outcomes

4.1 Primary outcome – incidence of rebound pain

Incidence of rebound pain was reported in five studies (439 patients, dexamethasone: 232, control: 207). The odds ratio was 5.00 [95% CI 2.69–9.29, $p < 0.00001$]. This result indicates that the experimental groups who received dexamethasone had a lower incidence of rebound pain, favouring its use as an adjuvant to reduce the incidence of rebound pain. The $I^2 = 41\%$, and the NNT = 3.03 in favour of using dexamethasone and a corresponding RRR = 55% in favour of perineural dexamethasone. A NNT of three means that only three patients need to be treated to see a benefit in one, a finding which is further strengthened by the relative risk reduction of 55% (Fig. 3). Subgroup analysis based on varying definitions of visual analogue scale (VAS) scores and postoperative regular analgesia—opioid vs non opioid based analgesia was conducted. Based on varying definitions of VAS scores, there were not enough studies for VAS $\leq$5 to make any meaningful comparisons between the 2 groups (heterogeneity $I^2 = 0\%$). In terms of subgroup differences between the 2 groups having received regular postoperative analgesia, opioid vs non-opioid, there was no heterogeneity between the 2 groups, and $p = 0.72$ between the 2 groups showing no differences in terms of incidence of rebound pain depending upon usage/type of postoperative analgesia.

4.2 Secondary Outcomes

Secondary outcome results are summarised in Table 2.

4.2.1 Pain Scores at 24 Hours

Pain scores at 24 hours post-operatively were reported in three studies (254 patients; dexamethasone: 162, control: 92). The standardised mean difference in pain scores was

Fig. 2. Risk of bias assessment of the included studies.

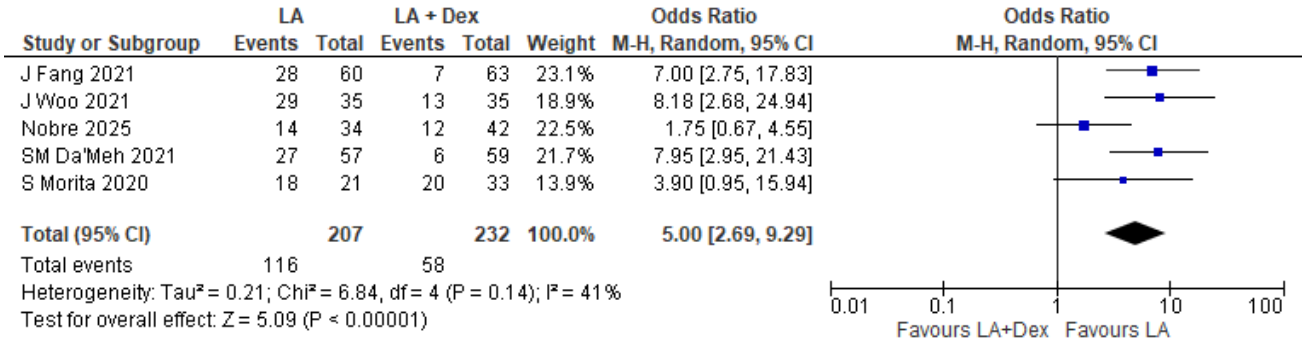

Fig. 3. Incidence of rebound pain forest plot. LA + Dex, local anaesthetic + dexamethasone; CI, confidence interval.

0.23 [95% CI –0.71–1.17, p = 0.64], with the I^2 = 91%. This result indicates that there was no difference between the control and the intervention group. Sensitivity analysis by excluding the outlier/s did not alter the p-value or the direction of the overall effect. Further subgroup analysis or meta regression was not possible due to the small number of RCT's describing the outcome. Performing sensitivity analysis by excluding outlier [10] did not alter the p-value or the direction of overall results, except for the heterogeneity (I^2 = 0).

4.2.2 Pain Scores at 48 Hours

Pain scores at 48 hours post-operatively were reported in three studies (254 patients; dexamethasone: 162, control: 92). The standardised mean difference in pain scores was 0.33 [95% CI –0.17–0.82, p = 0.20], with I^2 = 70%. This shows there is no difference between the control and intervention groups. Sensitivity analysis by excluding the outlier/s did not alter the p-value or the direction of the overall effect. Further subgroup analysis or meta regression was not possible due to the small number of RCT's describing the outcome. Performing sensitivity analysis by excluding outlier [10] did not alter the p-value or the direction of overall results, except for the heterogeneity (I^2 = 0).

Table 2. Summary of secondary outcome results.

Secondary outcome	Number of studies	Number of participants		Standard mean difference (95% CI)	*p*-value	I^2
		Control	Dex			
Pain score 24 hours	3	92	162	0.23 (–0.71–1.17)	0.64	91
Pain score 48 hours	3	92	162	0.33 (–0.17–0.82)	0.20	70
First analgesic request	2	56	68	–2.37 (–3.38– –1.36)	<0.00001	77
Onset of rebound pain	3	81	75	–2.27 (–4.91– 0.37)	0.09	97
Hyperglycaemia	3	83	97	0.10 (–0.20– 0.39)	0.51	0

CI, confidence interval.

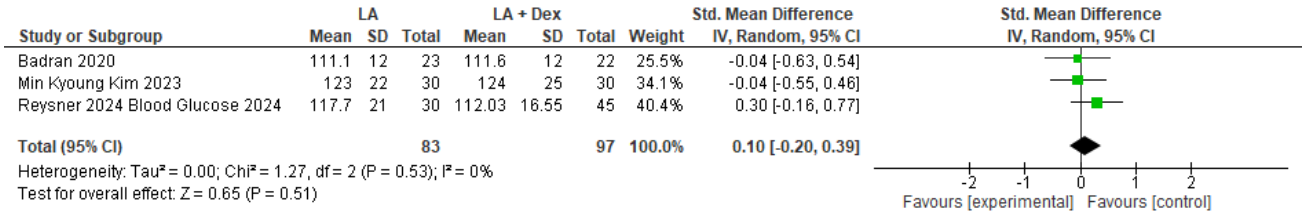

Fig. 4. Hyperglycaemia forest plot. SD, standard deviation.

4.2.3 First Analgesic Request

A first analgesic request was reported in two studies (124 patients; dexamethasone: 68, control: 56). This was used as a metric for duration of nerve block. The standardised mean difference was –2.37 [95% CI –3.38– –1.36, $p <$ 0.00001]. Meanwhile, based on the mean difference (MD) between the control and treatment groups, dexamethasone prolonged the time to first analgesic request by an average of 8.97 hours. The I^2 was 77%. This could be due to a small number of studies/participants, and therefore, the results should be treated with caution.

4.2.4 Onset of Rebound Pain

Onset of rebound pain was reported in three studies (156 patients; dexamethasone: 75, controls: 81). The standardised mean difference was –2.27 [95% CI –4.91–0.37, p = 0.09], I^2 was 97%. This result showed no significant difference between groups. However, the results need to be used with caution due to the small number of studies/participants and high heterogeneity. Sensitivity analysis excluding Morita [10] did not change the overall *p*-value or the overall direction of the results.

4.2.5 Hyperglycaemia

Hyperglycaemia was assessed in three studies (180 patients; dexamethasone: 97, control: 83). The standardised mean difference was 0.10 [95% CI –0.20–0.39, p = 0.51], I^2 = 0%. We found no difference in blood sugar levels between groups (Fig. 4).

4.3 Meta Regression and Trial Sequential Analysis (TSA)

Meta-regression was performed for the dose of dexamethasone and the type of LA used, and did not show any impact on the overall outcome (p = 0.26, 0.69, respectively) when the covariates were considered using a Z distribution (Table 3 and Fig. 5). There were not enough studies to perform meta-regression against the covariate of different doses of LA. This result was consistent when analysed with the Knapp-Hartung modification. The regression of log odds ratio on the dose of dexamethasone used had an equation Y = 1.4856 + 0.0744 × dose of dexamethasone, and 95% intervals were simultaneous based on both Z-distribution and Knapp-Hartung. The funnel plot and the precision funnel plot showed symmetry. The 'trim and fill effect' showed no unaccounted-for studies either on the left or the right of the mean using a random or fixed effects model, with Egger's intercept being p (two-tailed) = 0.21. Meta-regression could not be performed for secondary outcomes due to the small number of studies.

The TSA for the primary outcome showed that the required information size (IS) was easily reached (Fig. 6). In addition to the sensitivity analysis that excluded outliers, further analyses were conducted. These included removing one study to test the influence of individual studies, and performing cumulative analyses. Where relevant, these cumulative analyses incorporated variables such as dexamethasone dose, type of LA used, and varying doses of LA as moderators, to assess whether these factors influenced the primary outcome. It did not alter the output of the overall results for the primary outcome, nor did it demonstrate any specific correlation with the type or doses of LA used.

5. Discussion

Dexamethasone is a highly potent long-acting glucocorticoid with anti-inflammatory effects [18]. Perineural dexamethasone is proposed to provide analgesia through several mechanisms, although the exact mode of action remains unclear. It is proposed that dexamethasone reduces

Table 3. Meta regression for the primary outcome based on type of LA used and dose of dexamethasone.

Meta regression: incidence of rebound pain	Type of LA	Dose of dexamethasone
2-sided *p*-value	0.69	0.26

LA, local anaesthetic.

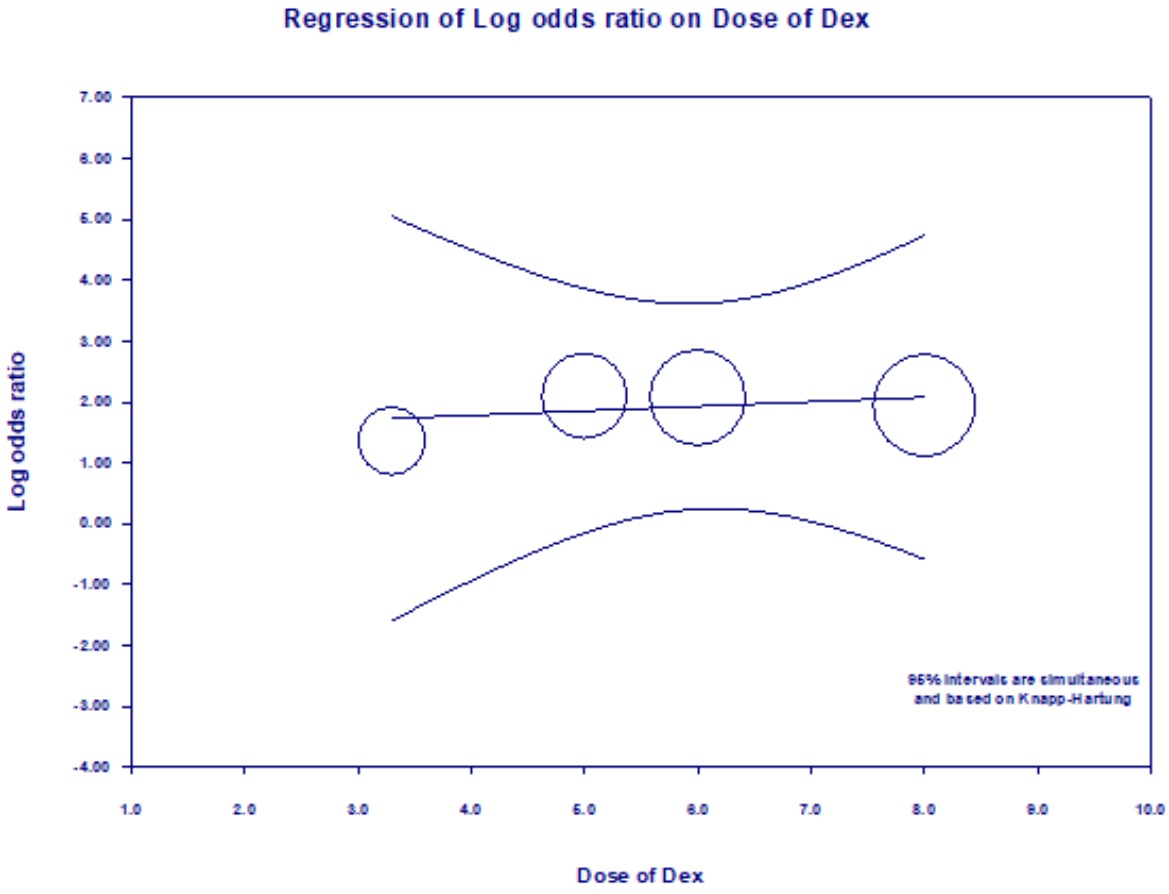

Fig. 5. Meta regression of the log odds ratio on the dose of dexamethasone.

ectopic neuronal discharge from potassium-mediated nociceptive C-fibres, reducing pain transmission [5,9]. This C-fibre inhibition is dependent upon an increase in the expression of inhibitory K^+ channels with a reduction in nociceptive neuronal transmission [5]. It may also induce vasoconstriction around the nerve, slowing the absorption of local anaesthetics and thereby extending their duration of action [4]. It may also exert systemic anti-inflammatory effects, reducing inflammation and associated pain [10].

Experimental studies suggest that local anaesthetics have proinflammatory effects and it changes the nerve permeability, resulting in abnormal conduction. This is thought to contribute to the occurrence of rebound pain. In these experimental models, dexamethasone prevents local anaesthetic-induced neurotoxicity and mitigates rebound hyperalgesia [9].

A meta-analysis was performed with the principal aim of examining the role of dexamethasone as an adjunct to a regional nerve block upon rebound pain incidence after surgery. The secondary aims were to define the time in hours to the first analgesic request, pain scores at 24 and 48 hours, the onset of rebound pain and hyperglycaemia post perineural dexamethasone. Nine papers fulfilled the inclusion criteria [8,9,10,11,12,13,14,15,16]. There is a relative paucity of prior research focused specifically on rebound pain following administration of perineural dexamethasone as an adjunct to local anaesthetic. This work sought to quantify the basis of evidence for its role in clinical practice.

Our primary finding was that dexamethasone, when used as an adjunct with a peripheral nerve block, reduced the incidence of post-surgical rebound pain. This finding reached significance and is corroborated by a meta-analysis from Singh et al. [19], in which dexamethasone reduced rebound pain incidence with an odds ratio of 0.16, but their study included both peripheral and perineural administration of dexamethasone. Our study showed an OR = 5.00 compared to theirs of 0.16. Our NNT = 3.03, which is slightly different to that of Singh et al. [19] at 2.8, may be ascribed to the higher number of included trials in our study. This therefore shows that perineural dexamethasone is a

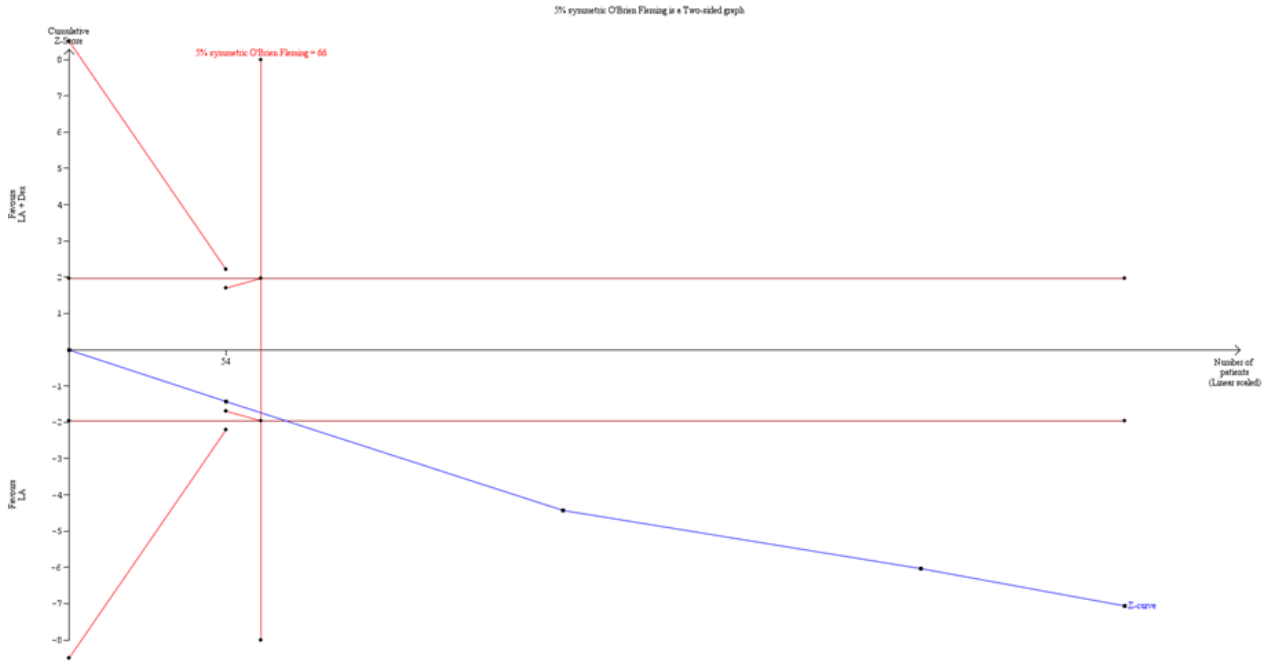

Fig. 6. Trial sequential analysis for incidence of rebound pain. The blue z curve represents the number of studies; the vertical red line represents the required information size (IS); the outer inward sloping red coloured lines represent the monitoring boundaries; the inner sloping lines demonstrate the futility boundary; the brown upper and lower horizontal lines represent the conventional boundary.

useful adjunct, as by decreasing the incidence of rebound pain, greater patient satisfaction will be achieved. This is clinically significant, as poor pain management has been shown to increase complications, impact hospital length of stay, leading to increased associated costs [20].

One of the secondary findings in this study was that perineural dexamethasone as an adjunct was associated with a significant increase in the first analgesic request. Furthermore, the required IS (n = 168) was reached, supporting the utility of adding dexamethasone to perineural blocks, by further reducing the need for post-operative analgesia.

Another secondary finding was that there was no statistically significant difference in pain scores at 24 and 48 hours with the use of perineural dexamethasone as an adjunct to peripheral nerve blockade. This is corroborated by the findings of De Oliveira et al. [21], who performed a meta-analysis which showed that perineural dexamethasone conferred no advantage on late pain at 24 and 48 hours when compared to control groups. The results should be carefully considered due to the small number of studies and participants, along with the limited reporting of the same in other studies.

There was no difference between the two groups for the onset of rebound pain, pain scores at 24 hours, 48 hours, nor blood sugar levels. However, for these outcomes which showed no difference, it could be that the sample sizes were too small to conclude. We would suggest exercising caution in interpreting these results due to the small number of studies involved.

From an anaesthetic perspective, rebound pain refers to a surge in pain intensity following the resolution of a peripheral nerve block, often described by patients as intense and disproportionate. In this meta-analysis, we evaluated three distinct yet related outcomes: incidence, onset, and time to first analgesic request. Incidence measures how frequently patients experienced rebound pain, while onset refers to the time (in hours) after nerve block resolution when pain began. Time to first analgesic request represents how long patients remained comfortable before requiring further pain relief. Our results showed that perineural dexamethasone significantly reduced the incidence of rebound pain and prolonged the time to first analgesic request, but did not significantly alter the onset of rebound pain. These findings are not contradictory- they reflect that dexamethasone effectively prevents rebound pain in some patients and extends the duration of analgesia, but among those who still experience rebound pain, the timing of its onset does not appear substantially delayed.

Although the overall analysis found no statistically significant difference in the onset of rebound pain, a sensitivity analysis excluding Morita did not alter the direction or significance of the pooled estimate. However, in an exploratory sensitivity analysis to investigate the source of substantial heterogeneity (I^2 = 97%), excluding the outlier study by Nobre et al. [16] revealed a significant difference ($p < 0.00001$), suggesting that this study had a substantial influence on the pooled result. Trial sequential analysis (TSA) confirmed that the required information size was reached (n = 105), strengthening the reliability of this find-

ing. However, given the small number of studies contributing to this outcome, we could not perform a meta-regression to explore potential sources of heterogeneity. Thus, while the results suggest that perineural dexamethasone may impact the timing of rebound pain in specific contexts, these conclusions should be interpreted with caution.

As mentioned in Zufferey et al. [22], 4 mg perineural dexamethasone versus 8 mg intravenous dexamethasone increased the mean duration of analgesia. In our analysis, although constrained by the limited number of studies, the duration of analgesia or time to first request for analgesia was significantly extended to 8.97 hours for the dexamethasone group compared to the control group. However, there was a minimum requirement of three studies to run a meta-regression to justify the goodness of fit plot. Only two studies on this domain were found, and so we were unable to compute the goodness-of-fit plot. In contrast to Singh et al. [19], we found that the regression of log odds ratio on the dose of dexamethasone demonstrated an almost linear response to the different doses of dexamethasone using the Knapp-Hartung computational effect.

The incidence of perioperative hyperglycaemia with the use of perineural dexamethasone was also not significant ($p = 0.51$ with $I^2 = 0$), which is promising and echoed by Fang et al. [9] and Xu et al. [23], but the results should be treated with caution due to the small number of trials involved.

One of the indications for using peripheral nerve blocks in contrast to general anaesthesia is to improve patient-reported satisfaction after surgery by decreasing postoperative pain and reducing opioid associated comorbidity. It is, therefore, important to take measures to reduce the incidence and intensity of rebound pain to justify the use of peripheral nerve blocks. Dexamethasone administered perineurally is an off-label use of the drug without current approval by the European Union or the United States Food and Drug Administration [4]. Anaesthetists should have access to information on predicted positive and negative effects when making informed decisions around this adjunct. The value of increased duration of sensory blockade and reduced rebound pain scores by the addition of perineural dexamethasone should therefore be weighed against the potential complications of its use, such as the potential for neurotoxicity. To date, no papers have established a causal link between dexamethasone and neuronal damage. In contrast, an *in vitro* study has shown that dexamethasone can protect neurones from bupivacaine-induced injury [24]. From the studies we considered, no patients experienced an adverse outcome associated with the use of dexamethasone perineurally; however, this absence of evidence is not evidence of absence. The practicality of dexamethasone use clinically should also be considered. Introducing additional agents into regional anaesthesia protocols increases the potential for medication errors, which can negatively affect patients. It may also be tricky to change the practise of current anaesthetists who feel more comfortable administering dexamethasone intravenously and have done so for a long period. Cannulas will routinely be in place and allow for seamless administration intravenously, but perineural dexamethasone requires an injection that may interrupt the workflow of an anaesthetist and mean more time in the anaesthetic room.

This paper's limitations should be considered when applying its findings to a clinical context. There are a small number of studies, with varying Jadad scores; however, through Egger's regression test and 'trim and fill method', we could not find any outlying studies that could have had an impact. The regression of the log odds ratio on the dose of dexamethasone showed no significant variation across the different doses of dexamethasone used. The NNT of 3.03 overwhelmingly points towards the benefit of reduction of rebound pain with the use of dexamethasone. Furthermore, for some of our data, heterogeneity was high with I^2 values of 77%, 91%, 70% and 97% for the time to first analgesic request, pain scores at 24 hours, pain scores at 48 hours and onset of rebound pain, respectively. This could be ascribed more to intra-study differences than inter-study, as sensitivity analysis did not alter the overall results or the direction of the *p*-value, neither did meta regression, trim and fill effect or precision modelling reveal any discrepancies. Reasons for heterogeneity could include differences in surgical procedures; dosages of dexamethasone; administration techniques for peripheral nerve blocks, such as indwelling catheters; and the use of ultrasound guidance. Subgroup analyses may have proved useful in better understanding this variability in effect sizes among studies, but there were not enough studies to perform a subgroup analysis. From the qualitative perspective, there was Fang et al. [9], who reported elevated blood sugar levels at 8 hours after the surgery, but no statistically significant difference was found between the two groups, and our analysis did not demonstrate any differences between the groups either ($p = 0.51$). There seems to be a discordance between the incidence of rebound pain and the onset described by the respective authors in their trials. We postulated that it could be due to a variety of reasons, including the way the authors have described their findings and the way it has been measured as described by Fang et al. [9], Nobre et al. [16] and Kurdi et al. [25].

It is impossible to evaluate the glucose safety in diabetic patients, and future studies should focus on this population. There was also a lack of long-term safety data; the follow-up duration of all included studies is $\leq$72 hours, which prevents the evaluation of the long-term impact of dexamethasone on nerve function (e.g., delayed neuritis). Future studies should extend the follow-up period to 3–6 months to assess sensory and motor function.

It can be deduced from the included trials in this meta-analysis that there is a relative paucity of literature surrounding perineural dexamethasone, pain scores and inci-

dence of hyperglycaemia, along with long-term follow-up of any steroid-induced perineural complications. Future work should be focussed on randomised controlled trials looking at the effect of standardised dosage of perineural dexamethasone on pain scores, including duration of analgesia. Of specific note, there should be consideration of the negative effects of dexamethasone usage and its impact on wound healing and neurotoxicity [26]. This study found that dexamethasone, when used as an adjunct to peripheral nerve block, significantly reduced the incidence of rebound pain and extended the time until patients' first analgesic request (8.97 hours), indicating an extended duration of the local anaesthetic effect compared to the control group. However, analysis found that perineural dexamethasone did not confer a significant improvement on patient self-reported pain scores at 24 and 48 hours. Additionally, it showed no difference in delaying the onset of rebound pain. Dexamethasone was not found to significantly affect blood sugar levels.

6. Conclusion

These findings contribute valuable evidence to the ongoing debate regarding the role of perineural dexamethasone as an adjunct in peripheral nerve blockade. Future RCTs should address these issues in a robust manner, particularly the effect of dexamethasone on diabetic patients' glucose levels perioperatively, and blood glucose monitoring should be considered in the perioperative period when dexamethasone is used in diabetic patients. This should be done with consistent dosages so future informed analyses can be performed using robust results.

Key Points

• Perineural dexamethasone reduces the incidence of rebound pain.

• Extends the duration of analgesia when used as an adjunct along with local anaesthetics.

• No significant difference in the onset of rebound pain, pain scores at 24 and 48 hours.

• No alteration of blood sugar levels.

Availability of Data and Materials

All data included in this study are available from the corresponding author upon reasonable request.

Author Contributions

RB, Anindya B, MC and Arnab B designed the work. RB drafted the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/BJHM55376.

References

[1] Jogie J, Jogie JA. A Comprehensive Review on the Efficacy of Nerve Blocks in Reducing Postoperative Anesthetic and Analgesic Requirements. Cureus. 2023; 15: e38552. https://doi.org/10.7759/cureus.38552.

[2] Muñoz-Leyva F, Cubillos J, Chin KJ. Managing rebound pain after regional anesthesia. Korean Journal of Anesthesiology. 2020; 73: 372–383. https://doi.org/10.4097/kja.20436.

[3] Admassie BM, Tegegne BA, Alemu WM, Getahun AB. Magnitude and severity of rebound pain after resolution of peripheral nerve block and associated factors among patients undergoes surgery at university of gondar comprehensive specialized hospital northwest, Ethiopia, 2022. Longitudinal cross-sectional study. Annals of Medicine and Surgery (2012). 2022; 84: 104915. https://doi.org/10.1016/j.amsu.2022.104915.

[4] Choi S, Rodseth R, McCartney CJL. Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: a systematic review and meta-analysis of randomized trials. British Journal of Anaesthesia. 2014; 112: 427–439. https://doi.org/10.1093/bja/aet417.

[5] Desai N, Albrecht E, El-Boghdadly K. Perineural adjuncts for peripheral nerve block. BJA Education. 2019; 19: 276–282. https://doi.org/10.1016/j.bjae.2019.05.001.

[6] Polderman JAW, Farhang-Razi V, van Dieren S, Kranke P, DeVries JH, Hollmann MW, et al. Adverse side-effects of dexamethasone in surgical patients - an abridged Cochrane systematic review. Anaesthesia. 2019; 74: 929–939. https://doi.org/10.1111/anae.14610.

[7] Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clinical Trials. 1996; 17: 1–12. https://doi.org/10.1016/0197-2456(95)00134-4.

[8] Woo JH, Lee HJ, Oh HW, Lee JW, Baik HJ, Kim YJ. Perineural dexamethasone reduces rebound pain after ropivacaine single injection interscalene block for arthroscopic shoulder surgery: a randomized controlled trial. Regional Anesthesia and Pain Medicine. 2021; 46: 965–970. https://doi.org/10.1136/rapm-2021-102795.

[9] Fang J, Shi Y, Du F, Xue Z, Cang J, Miao C, et al. The effect of perineural dexamethasone on rebound pain after ropivacaine single-injection nerve block: a randomized controlled trial. BMC Anesthesiology. 2021; 21: 47. https://doi.org/10.1186/s12871-021-01267-z.

[10] Morita S, Oizumi N, Suenaga N, Yoshioka C, Yamane S, Tanaka Y. Dexamethasone added to levobupivacaine prolongs the duration of interscalene brachial plexus block and decreases rebound pain after arthroscopic rotator cuff repair. Journal of Shoulder and Elbow Surgery. 2020; 29: 1751–1757. https://doi.org/10.1016/j.jse.2020.04.019.

[11] Da'meh SM, Qabaha AH, Beidas MJ, Al Awamreh TO, Adaileh MA, Al Soud NM, et al. PERINEURAL DEXAMETHASONE AND REBOUND PAIN FOLLOWING BUPIVACAINE SUPRACLAVICULAR BRACHIAL PLEXUS BLOCKADE. European Journal of Biomedical and Pharmaceutical Sciences. 2021; 8: 140–144.

[12] Kim YS, Park Y, Koh HJ. Is There a Difference between Perineural Dexamethasone with Single-Shot Interscalene Block (SSIB) and Interscalene Indwelling Catheter Analgesia (IICA) for Early Pain after Arthroscopic Rotator Cuff Repair? A Pilot Study. Journal of Clinical Medicine. 2022; 11: 3409. https://doi.org/10.3390/jcm11123409.

[13] Badran MA, Kamaly AM, Abdel Hamid HM, Mostafa RH. Dexamethasone as a bupivacaine adjuvant for ultrasound-guided interscalene brachial plexus block: a prospective randomized study. Ain-Shams Journal of Anesthesiology. 2020; 12: 61. https://doi.org/10.1186/s42077-020-00113-7.

[14] Kim MK, Park YH, Lee JS, Jung HS. How Does the Addition of Dexamethasone to a Brachial Plexus Block Change Pain Patterns After Surgery for Distal Radius Fractures? A Randomized, Double-blind Study. Clinical Orthopaedics and Related Research. 2023; 481: 1966–1974. https://doi.org/10.1097/CORR.0000000000002640.

[15] Reysner M, Reysner T, Janusz P, Kowalski G, Shadi M, Daroszewski P, et al. Dexamethasone as a perineural adjuvant to a ropivacaine popliteal sciatic nerve block for pediatric foot surgery: a randomized, double-blind, placebo-controlled trial. Regional Anesthesia and Pain Medicine. 2024; 50: 970–976. https://doi.org/10.1136/rapm-2024-105694.

[16] Nobre LV, Ferraro LHC, Júnior JADO, Winkeler VLL, Muniz LFFV, Braga HP, et al. Efficacy of dexamethasone or clonidine as adjuvants in interscalene brachial plexus block for preventing rebound pain after shoulder surgery: a randomized clinical trial. Brazilian Journal of Anesthesiology (Elsevier). 2025; 75: 844575. https://doi.org/10.1016/j.bjane.2024.844575.

[17] Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ (Clinical Research Ed.). 2019; 366: l4898. https://doi.org/10.1136/bmj.l4898.

[18] Johnson DB, Lopez MJ, Kelley B. Dexamethasone. StatPearls. StatPearls Publishing: Treasure Island (FL). 2023.

[19] Singh NP, Makkar JK, Chawla JK, Sondekoppam RV, Singh PM. Prophylactic dexamethasone for rebound pain after peripheral nerve block in adult surgical patients: systematic review, meta-analysis, and trial sequential analysis of randomised controlled trials. British Journal of Anaesthesia. 2024; 132: 1112–1121. https://doi.org/10.1016/j.bja.2023.09.022.

[20] Córcoles-Jiménez MP, Ruiz-García MV, Cervera-Monteagudo B, Bernal-Celestino R, Herreros-Saez ML, Flores-Bautista AB. Postoperative pain intensity and patient satisfaction: A multicentre observational study. Applied Nursing Research. 2025; 81: 151898. https://doi.org/10.1016/j.apnr.2024.151898.

[21] De Oliveira GS, Jr, Castro Alves LJ, Nader A, Kendall MC, Rahangdale R, McCarthy RJ. Perineural dexamethasone to improve postoperative analgesia with peripheral nerve blocks: a meta-analysis of randomized controlled trials. Pain Research and Treatment. 2014; 2014: 179029. https://doi.org/10.1155/2014/179029.

[22] Zufferey PJ, Chaux R, Lachaud PA, Capdevila X, Lanoiselée J, Ollier E. Dose-response relationships of intravenous and perineural dexamethasone as adjuvants to peripheral nerve blocks: a systematic review and model-based network meta-analysis. British Journal of Anaesthesia. 2024; 132: 1122–1132. https://doi.org/10.1016/j.bja.2023.12.021.

[23] Xu C, Wang C, Hu Y, Gu F, Lu J, Zhou Q. Comparing preoperative and postoperative dexamethasone effects on analgesia duration in shoulder surgery. iScience. 2024; 27: 109019. https://doi.org/10.1016/j.isci.2024.109019.

[24] Ma R, Wang X, Lu C, Li C, Cheng Y, Ding G, et al. Dexamethasone attenuated bupivacaine-induced neuron injury in vitro through a threonine-serine protein kinase B-dependent mechanism. Neuroscience. 2010; 167: 329–342. https://doi.org/10.1016/j.neuroscience.2009.12.049.

[25] Kurdi MS, Abinaya K, Ladhad DA, Theerth KA, Mitragotri MV. Comparison of perineural dexamethasone and dexmedetomidine as adjuvants in reducing rebound pain in patients undergoing peripheral nerve block: A double blind randomized controlled study. Journal of Anaesthesiology, Clinical Pharmacology. 2025; 41: 664–670. https://doi.org/10.4103/joacp.joacp_598_24.

[26] Zhu N, Xiang B, Shi J, Yang P, Dai Y, Wang S. The effect of perineural dexamethasone on nerve injury and recovery of nerve function after surgery: A randomized controlled trial. Heliyon. 2024; 10: e35612. https://doi.org/10.1016/j.heliyon.2024.e35612.