A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks

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Summary
We systematically reviewed the safety and efficacy of perineural dexamethasone as an adjunct for peripheral nerve blockade in 29 controlled trials of 1695 participants. We grouped trials by the duration of local anaesthetic action (short- or medium- vs long-term). Dexamethasone increased the mean (95% CI) duration of analgesia by 233 (172–295) min when injected with short- or medium-term action local anaesthetics and by 488 (419–557) min when injected with long-term action local anaesthetics, p < 0.00001 for both. However, these results should be interpreted with caution due to the extreme heterogeneity of results, with I² exceeding 90% for both analyses. Meta-regression did not show an interaction between dose of perineural dexamethasone (4–10 mg) and duration of analgesia (r² = 0.02, p = 0.54). There were no differences between 4 and 8 mg dexamethasone on subgroup analysis.

Introduction
Moderate to severe pain after orthopaedic surgery can be reduced by regional neural blockade with local anaesthetic [1]. Interventions that increase the duration of local anaesthetic action could prolong postoperative patient comfort [2]. Perineural catheters have been used to extend the duration of analgesia but may be accompanied by catheter migration, anaesthetic leakage or pump malfunction, requiring complex logistic organisation [3], particularly following ambulatory surgery. Several adjuncts, including opioids, tramadol, clonidine and neostigmine, have been tested with single-shot regional techniques, but have failed to achieve desired results [2, 4].

Dexamethasone, a high-potency, long-acting glucocorticoid with little mineralocorticoid effect, has been shown to prolong peripheral nerve blockade in animals [5–8] and, when added to bupivacaine microspheres, to extend the duration of analgesia in humans [9, 10]. Although incompletely understood, dexamethasone’s mechanism of action may stem from decreased nociceptive C-fibre activity via a direct effect on glucocorticoid receptors [11] and inhibitory potassium channels [12]. Other authors suggest a local vasoconstrictive effect, resulting in reduced local anaesthetic absorption [13, 14], or a systemic anti-inflammatory effect [15] following vascular uptake of the drug [16]. The results of several articles support the contention that perineural dexamethasone prolongs analgesia
The objective of this meta-analysis was to define the analgesic efficacy of dexamethasone as a local anaesthetic adjunct for peripheral nerve blockade and its potential role in clinical practice.

Methods

We followed the PRISMA guideline [22]. We searched the following databases without language restriction to May 16th 2014: PUBMED; CENTRAL; Embase. We used the following search terms: (an*esthetic technique OR an*esthesia conduction OR local an*esthetics OR (peripheral) nerve block OR regional an*esthesia) AND (dexamethasone OR glucocorticoids OR steroids). We used the following keywords: anaesth*, anesth*, nerve*, dexamethas*, glucocort*, steroid*, clinical*, random*, trial*. Retrieved articles were limited with 'Clinical trials' OR 'Random allocation' OR 'Therapeutic use'. In addition, we searched by hand the references of retrieved articles for additional relevant trials. We also searched Google Scholar™ by entering the aforementioned search terms. We included randomised controlled trials (RCTs) that compared perineural local anaesthetics without vs with dexamethasone for peripheral nerve blockade. We excluded RCTs of dexamethasone: vs other adjuncts [23]; in intravenous regional anaesthesia [24, 25]; when injected in all participants [26]; when authors replicated results [27] of a previously published study [28]; or when the full article was not available and the abstract did not include the necessary information [29].

Two authors (EA and KK) independently extracted: types of surgery, regional block and injection technique; type, concentration and volume of local anaesthetic injectate; dose of dexamethasone; possible combination with neuraxial or general anaesthesia; other postoperative analgesic modalities; and duration of analgesic effect. Each used the Cochrane Collaboration’s risks of bias tool to assess retrieved RCTs [30]; a third author (CK) resolved disagreements. The primary outcome was duration of analgesia or sensory block and was defined as time from injection, or the onset of sensory blockade to pain or first analgesic request. If several doses of dexamethasone were studied against a control group, we included data from the group with the highest dose. We grouped interventions in RCTs by duration of local anaesthetic action: short- and medium- (lidocaine, mepivacaine and prilocaine) vs long-term action (bupivacaine, levobupivacaine and ropivacaine). Mixtures of anaesthetics with short- and long-term action were categorised as long-acting. We extracted the onset times of sensory and motor blockades, the duration of motor blockade and rates of block failure. We defined onset of sensory and motor blockades as the time from completion of local anaesthetic injection to complete blockade. We also analysed pain scores at rest and on movement, and cumulative intravenous morphine consumption, grouped within three postoperative periods (0–2, 8–12 or at 24 h). We also recorded: the highest rate of nausea or vomiting on the first postoperative day; the rate of pruritus; patient satisfaction; and adverse effects associated with dexamethasone, including hyperglycaemia, infection and neurological complications.

We extracted means (SD or SEM or 95% CI) for continuous variables, or estimated their values from median (IQR) [31] when authors were unable to provide these data. We converted administered opioid into equianalgesic doses of intravenous morphine [32], while we standardised pain and satisfaction scores to a 0–100 analogue scale. We calculated pooled estimates for two or more RCTs with a random-effects model, presented as mean differences or relative risks with their 95% CI. We also analysed the primary outcome with a fixed-effect model. We employed the I² value to define low (25–49%), moderate (50–74%) and extreme (> 74%) heterogeneity [33] and applied Egger’s test to assess funnel plot asymmetry [34]. We performed meta-regression for the interaction between dexamethasone dose and duration of analgesia or sensory block, further exploring this through a subgroup analysis according to the dose of dexamethasone. The software we used for analyses was: Review Manager (RevMan version 5.2; Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration 2012); Comprehensive Meta-analysis (Version 2; Biostat, Englewood, NJ, USA) and JMP 9 statistical package (SAS Institute, Cary, NC, USA). We considered a two-sided p < 0.05 significant.

Results

We included 29 RCTs with 1695 adults – there were no paediatric studies (Fig. 1 and Table 1) [16–21, 28,
Authors of 11 RCTs provided additional data [16, 17, 19–21, 45, 50, 51, 54–56]. One RCT did not report any pre-specified outcome [35] and we were unable to generate means (SD) from a single RCT [43].

A number of RCTs were categorised as high risk or unclear risk for some bias domains (Fig. 2). All but six studies [20, 35–37, 39, 47] examined brachial plexus blockade: interscalene [16, 17, 21, 45, 46, 53]; supraclavicular [19, 28, 38, 40–44, 48–50, 52, 54, 55] or axillary [18, 51, 56]. The injection was placed under ultrasound guidance [17, 19–21, 36, 37, 45, 46, 48, 50, 54], with a nerve stimulator [16, 18, 40, 42, 49, 51–53, 55] or following anatomical landmarks [28, 35, 38, 39, 41, 43, 44, 47, 56], and was supplemented by general anaesthesia in seven RCTs [16, 17, 21, 37, 45, 46, 53] or spinal anaesthesia in one RCT [36]. The administered dose of dexamethasone was 4 mg [28, 35, 39, 45, 47, 50, 55], 5 mg [46], 8 mg [17–21, 28, 36–38, 40–44, 48, 49, 51–54, 56] or 10 mg [16]. Local anaesthetics with short-term [18, 35, 39, 40, 51, 54–56] or medium-term [19] action were injected in nine RCTs, while 20 RCTs injected local anaesthetics with long-term action [16, 17, 20, 21, 28, 36–38, 41–50, 52, 53]. With two exceptions [35, 39], RCTs used 10–50 ml of injectate.

Figure 1 PRISMA flow diagram showing literature search results.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Group (n)</th>
<th>Local anaesthetic</th>
<th>Surgery</th>
<th>Nerve block, technique</th>
<th>Other anaesthesia</th>
<th>Postoperative analgesia</th>
<th>Primary outcome</th>
</tr>
</thead>
</table>
| Aggarwal et al. [35] | Dexamethasone 4 mg (24)  
Control (24) | Lidocaine 2%, 1.8 ml + adrenaline 5 μg.ml⁻¹ | Dental                 | Inferior alveolar, landmark   | None              | No detail              | Rate of anaesthesia             |
| Akkaya et al. [36]  | Dexamethasone 8 mg (21)  
Control (21) | Levobupivacaine 0.25%, 30 ml                    | Caesarean section      | TAP, US                       | Spinal            | IV tramadol             | Duration of analgesia             |
| Ammar and Mahmoud [37] | Dexamethasone 8 mg (30)  
Control (30) | Bupivacaine 0.25%, 20 ml                       | Open hysterectomy      | TAP, US                       | General           | Paracetamol             | Pain on movement                 |
| Bais et al. [38]    | Dexamethasone 8 mg (25)  
Control (25) | Ropivacaine 0.5%, 30 ml                        | Hand Forearm Elbow     | Supraclavicular, landmark     | None              | No detail              | No detail                        |
| Bhargava et al. [39] | Dexamethasone 4 mg (20)  
Control (20) | Lidocaine 2%, 1.8 ml + adrenaline 5 μg.ml⁻¹ | Dental                 | Pterygomandibular, landmark   | None              | Ibuprofen              | No detail                        |
| Biradar et al. [40] | Dexamethasone 8 mg (30)  
Control (30) | Lidocaine 1.5%, 27 ml + adrenaline 5 μg.ml⁻¹ | Hand Forearm Elbow     | Supraclavicular, AC           | None              | IM diclofenac           | Onset of sensory blockade        |
| Cummings et al. [17] | Dexamethasone 8 mg (103)  
Control (106) | Bupivacaine 0.5%, 30 ml or ropivacaine 0.5%  | Shoulder Interscalene,  
AC ± US | General | Paracetamol  
Oxycodone | IV morphine,  
IM diclofenac | Duration of analgesia |
| Dar et al. [41]     | Dexamethasone 8 mg (40)  
Control (40) | Ropivacaine 0.5%, 30 ml                        | Hand Forearm Elbow     | Supraclavicular, landmark     | None              | IM diclofenac           | No detail                        |
| Desmet et al. [16]  | Dexamethasone 10 mg (49)  
Control (46) | Ropivacaine 0.5%, 30 ml                        | Shoulder Interscalene,  
AC | General | Paracetamol  
IV diclofenac | IM piritramide,  
IM diclofenac | Duration of analgesia |
| Ganvit et al. [42]  | Dexamethasone 8 mg (30)  
Control (30) | Ropivacaine 0.5%, 30 ml                        | Hand Forearm Elbow     | Supraclavicular, AC           | None              | IM diclofenac           | No detail                        |
| Golwala et al. [43] | Dexamethasone 8 mg (30)  
Control (30) | Lidocaine 2%, 15 ml + bupivacaine 0.5%, 15 ml +  
epinephrine 5 μg.ml⁻¹ | Hand Forearm Elbow     | Supraclavicular, landmark     | None              | IV diclofenac           | No detail                        |
| Islam et al. [44]   | Dexamethasone 8 mg (30)  
Control (30) | Lidocaine 2%, 15 ml + bupivacaine 0.5%, 15 ml  | Hand Forearm Elbow     | Supraclavicular, landmark     | None              | No detail              | No detail                        |
| Kawanishi et al. [45] | Dexamethasone 4 mg (12)  
Control (12) | Ropivacaine 0.75%, 20 ml                       | Shoulder Interscalene,  
AC | General | IV flurbiprofen  
Loroxiprofen | Duration of analgesia |
| Kim et al. [46]     | Dexamethasone 5 mg (20)  
Control (20) | Levobupivacaine 0.5%, 10 ml                    | Shoulder Interscalene,  
US + AC | General | IV ketorolac,  
IM morphine | Duration of analgesia |

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Anesthesia 2015, 70, 71–83 Albrecht et al. | Dexamethasone for peripheral nerve blocks
<table>
<thead>
<tr>
<th>Reference</th>
<th>Group (n)</th>
<th>Local anaesthetic</th>
<th>Surgery</th>
<th>Nerve block, technique</th>
<th>Other anaesthesia</th>
<th>Postoperative analgesia</th>
<th>Primary outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mahmoud et al. [47]</td>
<td>Dexamethasone 4 mg (23) Control (25)</td>
<td>Bupivacaine 0.5%, 10 ml</td>
<td>Posterior eye</td>
<td>Peribulbar, landmark</td>
<td>None</td>
<td>Paracetamol, IV pethidine</td>
<td>Duration of block</td>
</tr>
<tr>
<td>Movafegh et al. [18]</td>
<td>Dexamethasone 8 mg (20) Control (20)</td>
<td>Lidocaine 1.5%, 34 ml</td>
<td>Hand Forearm</td>
<td>Axillary, AC</td>
<td>None</td>
<td>No detail</td>
<td>Duration of sensory blockade</td>
</tr>
<tr>
<td>Parrington et al. [19]</td>
<td>Dexamethasone 8 mg (24) Control (21)</td>
<td>Mepivacaine 1.5%, 30 ml</td>
<td>Hand Forearm</td>
<td>Supraclavicular, US</td>
<td>None</td>
<td>IV fentanyl</td>
<td>Duration of analgesia</td>
</tr>
<tr>
<td>Patel et al. [48]</td>
<td>Dexamethasone 8 mg (30) Control (30)</td>
<td>Lidocaine 2%, 15 ml + bupivacaine 0.5%, 15 ml + adrenaline 5 μg.ml⁻¹</td>
<td>Hand Forearm</td>
<td>Supraclavicular, US</td>
<td>None</td>
<td>No detail</td>
<td>No detail</td>
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<tr>
<td>Pathak et al. [49]</td>
<td>Dexamethasone 8 mg (25) Control (25)</td>
<td>Lidocaine 2%, 20 ml + bupivacaine 0.5%, 16 ml + adrenaline 5 μg.ml⁻¹</td>
<td>Hand Forearm</td>
<td>Supraclavicular, AC</td>
<td>None</td>
<td>No detail</td>
<td>No detail</td>
</tr>
<tr>
<td>Persec et al. [50]</td>
<td>Dexamethasone 4 mg (35) Control (25)</td>
<td>Levobupivacaine 0.5%, 25 ml</td>
<td>Hand Forearm</td>
<td>Supraclavicular, AC + US</td>
<td>None</td>
<td>IV diclofenac</td>
<td>Duration of analgesia</td>
</tr>
<tr>
<td>Rahangdale et al. [20]</td>
<td>Dexamethasone 8 mg (27) control (27)</td>
<td>Bupivacaine 0.5%, 0.45 ml.kg⁻¹ + adrenaline 3.3 μg.ml⁻¹</td>
<td>Ankle Foot</td>
<td>Sciatic, US</td>
<td>None</td>
<td>Paracetamol, Hydrocodone</td>
<td>Quality of recovery</td>
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<tr>
<td>Saritas and Sabuncu [51]</td>
<td>Dexamethasone 8 mg (15) Control (15)</td>
<td>Prilocaine 2%, 5 ml.kg⁻¹</td>
<td>Hand Forearm</td>
<td>Axillary, US</td>
<td>None</td>
<td>IM diclofenac</td>
<td>No detail</td>
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<tr>
<td>Shaikh et al. [52]</td>
<td>Dexamethasone 8 mg (27) Control (27)</td>
<td>Bupivacaine 0.25%, 38 ml</td>
<td>Hand Forearm</td>
<td>Supraclavicular, AC</td>
<td>None</td>
<td>IM diclofenac</td>
<td>No detail</td>
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<tr>
<td>Shrestha et al. [28]</td>
<td>Dexamethasone 4–8 mg (20) Control (20)</td>
<td>Lidocaine 2%, 20–25 ml + bupivacaine 0.5%, 20–25 ml + adrenaline 5 μg.ml⁻¹</td>
<td>Hand Forearm</td>
<td>Supraclavicular, landmark</td>
<td>None</td>
<td>No detail</td>
<td>No detail</td>
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<tr>
<td>Tandoc et al. [53]</td>
<td>Dexamethasone 8 mg (30) Control (28)</td>
<td>Bupivacaine 0.5%, 40 ml + epinephrine 5 μg.ml⁻¹</td>
<td>Shoulder</td>
<td>Interscalene, AC</td>
<td>General</td>
<td>Paracetamol, Ibuprofen, Hydrocodone</td>
<td>Duration of analgesia</td>
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<tr>
<td>Trabelsi et al. [54]</td>
<td>Dexamethasone 8 mg (20) Control (20)</td>
<td>Lidocaine 2%, 15 ml</td>
<td>Hand Forearm</td>
<td>Supraclavicular, US</td>
<td>None</td>
<td>IV paracetamol, SC morphine</td>
<td>Duration of analgesia</td>
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<tr>
<td>Vieira et al. [21]</td>
<td>Dexamethasone 8 mg (44) Control (44)</td>
<td>Bupivacaine 0.5%, 20 ml + adrenaline 5 μg.ml⁻¹ + clonidine 75 mg</td>
<td>Shoulder</td>
<td>Interscalene, US</td>
<td>General</td>
<td>Hydrocodone, Oxycodone, Hydromorphone</td>
<td>Duration of analgesia</td>
</tr>
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</table>
### Table 1 (continued)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Group (n)</th>
<th>Local anaesthetic</th>
<th>Surgery</th>
<th>Nerve block, technique</th>
<th>Other anaesthesia</th>
<th>Postoperative analgesia</th>
<th>Primary outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yadav et al. [55]</td>
<td>Dexamethasone 4 mg (30)</td>
<td>Lidocaine 1.5%, 24 ml + adrenaline 5 μg.ml⁻¹</td>
<td>Hand forearm</td>
<td>Supravacicular, AC</td>
<td>None</td>
<td>IM diclofenac</td>
<td>No detail</td>
</tr>
<tr>
<td>Yaghoobi et al. [56]</td>
<td>Dexamethasone 8 mg (21)</td>
<td>Lidocaine 1%, 40 ml</td>
<td>Forearm</td>
<td>Axillary, landmark</td>
<td>None</td>
<td>IV pethidine</td>
<td>Duration of analgesia</td>
</tr>
</tbody>
</table>

AC, alternating current nerve stimulation; GA, general anaesthesia; IM, intramuscular; IV, intravenous; PCA, patient-controlled analgesia; SC, subcutaneous; TAP, transversus abdominis plane; US, ultrasound.
Dexamethasone shortened the onset of sensory blockade (Fig. 3) and motor blockade (Fig. 4). Dexamethasone prolonged the duration of analgesia or sensory block (Fig. 5, random-effects model). With a fixed-effect model, dexamethasone increased the mean (95% CI) duration of analgesia by 136 (127–145) min, when injected with local anaesthetics with short- or medium-term action, p < 0.00001, and by 406 (400–413) min when injected with local anaesthetics with long-term action, p < 0.00001. The funnel plot (Fig. 6) was asymmetric with a regression line intercept (95% CI) of 11.14 (9.53–12.75), p < 0.00001. During the meta-regression analysis, one study was excluded as the authors used doses of 4 and 8 mg indiscriminately [28]. There was no association between the total dose of perineural dexamethasone and the mean increase in duration of analgesia: r² = 0.02, p = 0.54. This was confirmed by subgroup analysis, in which the mean (95% CI) durations of analgesia with 4 mg and 8 mg dexamethasone were not different with local anaesthetics of short- or medium-term action (200 (51–350) min vs 251 (175–327) min, respectively, p = 0.55) or long-term action (461 (240–682) min vs 480 (403–557) min, respectively, p = 0.88). Dexamethasone prolonged motor blockade (Fig. 7). The relative rate (95% CI) of block failure was not significant, 0.72 (0.43–1.20), p = 0.21.

Table 2 presents secondary outcomes of the effect of perineural dexamethasone on postoperative pain. Perineural dexamethasone reduced the rate of postoperative nausea and vomiting (Fig. 8).

One RCT reported a single case of superficial wound infection treated by local incision and drainage and also reported that dexamethasone increased mean (SD) serum glucose concentrations by 3.8 (1.2) mg.dl⁻¹. Seven RCTs recorded the rate of neurological complications [16, 17, 19, 28, 40, 53, 55]: one of 286 participants who had perineural dexamethasone reported symptoms, with persistent paraesthesia related to cervical disc herniation [16]. No other complications related to perineural dexamethasone were reported.

Discussion

We found that perineural dexamethasone prolonged the durations of analgesia and motor blockade from short-, medium- and long-term action local anaesthetics. Similarly, dexamethasone was associated with a reduction in pain scores at rest during the intermediate (8–12 h) and late (24 h) postoperative periods and in movement at all times. At 24 postoperative hours, cumulative morphine consumption and the rate of nausea or vomiting were also reduced. Dexamethasone slightly reduced the onset times of sensory and motor blockades, which we think is clinically unimportant.

**Figure 3** Effect of perineural dexamethasone on the onset time of sensory blockade. LA, local anaesthetics.
Figure 4 Effect of perineural dexamethasone on the onset time of motor blockade. LA, local anaesthetics.

Figure 5 Effect of perineural dexamethasone on duration of analgesia according to type of local anaesthetics used. LA, local anaesthetics.
Although inconsistently reported, neither neurological complications nor infections were described, while a single study found increased blood glucose concentrations after dexamethasone administration [16]. Our evaluation of the relationship between the dose of dexamethasone and duration of analgesia was inconclusive. We did not find evidence that a dexamethasone dose of 4 mg was less effective than 8 or 10 mg, which most RCTs administered without justification. Dose-finding studies are needed to define better the optimal balance between dose, effects and side-effects, particularly at doses lower than 4 mg.

Fewer than 300 participants were monitored for neurological complications, so we cannot conclude that dexamethasone has no effect. Cummings et al. calculated that 16,000 patients would be required to demonstrate a doubling of the baseline complication rate of 0.4% [17]. Although caution is warranted, animal studies have provided encouraging results, concluding that neurological injury is absent [7, 14, 57]. During in-vitro studies, Ma et al. demonstrated a potential protective effect of dexamethasone against local anaesthetic-induced cell injury [58] and a series of 2000 intrathecal injections of 8 mg dexamethasone for the treatment of post-traumatic visual disturbance in 200 patients failed to demonstrate any neurological sequelae [59]. Nevertheless, clinicians must be aware that perineural dexamethasone represents off-label use and solutions free of neurotoxic preservatives should be used [60, 61]. Finally, although the safety profile of perineural dexamethasone is promising, it should be noted that intravenous dexamethasone at a dose of 0.1–0.2 mg.kg\(^{-1}\) could have a comparable analgesic effect [16, 20, 62] and could obviate the need for perineural injection. Further comparative evaluation of these routes for administration is warranted.

This meta-analysis is limited by the absence of systematic definitions for certain endpoints, such as duration of analgesia. Although we acknowledge that duration of analgesia, duration of sensory blockade and time to first analgesic request are not synonymous, they are surrogate markers of a meaningful clinical concept of a pain-free period after surgery.

### Table 1

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Dexamethasone-LA Mean (minutes) SD (minutes) Total</th>
<th>LA Mean (minutes) SD (minutes) Total</th>
<th>Weight</th>
<th>Mean Difference IV, Random, 95% CI (minutes)</th>
<th>Mean Difference IV, Random, 95% CI (minutes)</th>
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<tbody>
<tr>
<td>1.2.1 LA with short or medium term action</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bais et al. 2014</td>
<td>496 ± 42</td>
<td>25</td>
<td>436.8</td>
<td>48</td>
<td>25</td>
</tr>
<tr>
<td>Dar et al. 2013</td>
<td>492 ± 30</td>
<td>40</td>
<td>354</td>
<td>24</td>
<td>40</td>
</tr>
<tr>
<td>Gamelt et al. 2013</td>
<td>501 ± 48.6</td>
<td>30</td>
<td>445.3</td>
<td>46</td>
<td>30</td>
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<tr>
<td>Mahmoud et al. 2013</td>
<td>188.2 ± 12.4</td>
<td>23</td>
<td>179</td>
<td>11.6</td>
<td>25</td>
</tr>
<tr>
<td>Paeli et al. 2013</td>
<td>653.3 ± 57.6</td>
<td>30</td>
<td>321.3</td>
<td>36.4</td>
<td>30</td>
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<tr>
<td>Patel et al. 2012</td>
<td>376.4 ± 40</td>
<td>25</td>
<td>171.2</td>
<td>26.9</td>
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<td>Persec et al. 2013</td>
<td>1,243.4 ± 333.5</td>
<td>35</td>
<td>714.8</td>
<td>187.7</td>
<td>25</td>
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<tr>
<td>Rahangdale et al. 2014</td>
<td>1,794 ± 438</td>
<td>27</td>
<td>1,146</td>
<td>486</td>
<td>27</td>
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<tr>
<td>Shams et al. 2013</td>
<td>846.7 ± 102.3</td>
<td>27</td>
<td>544.1</td>
<td>59.4</td>
<td>27</td>
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<tr>
<td>Tardoc et al. 2011</td>
<td>2,312 ± 234</td>
<td>30</td>
<td>1,476</td>
<td>198</td>
<td>28</td>
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<tr>
<td>Vieria et al. 2010</td>
<td>1,346 ± 344.7</td>
<td>44</td>
<td>913.6</td>
<td>307.3</td>
<td>44</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>336</td>
<td></td>
<td></td>
<td>326</td>
<td>70.8%</td>
</tr>
</tbody>
</table>

**Heterogeneity:** Tau\(^2\) = 3561.44, \(I^2 = 1500.20\), df = 10 \(P < 0.00001\); \(I^2 = 99%\) Test for overall effect: \(Z = 7.15 \(P < 0.00001\)\)

**Total (95% CI)**

| 431 | 419 | 100.0% | 241.18 \(Z = 183.23, P < 0.00001\) | |

**Heterogeneity:** Tau\(^2\) = 1177.97, \(I^2 = 1522.91\), df = 14 \(P < 0.00001\); \(I^2 = 99%\) Test for overall effect: \(Z = 8.16 \(P < 0.00001\)\)

**Test for subgroup differences:** \(I^2 = 9.44, df = 1 \(P < 0.00001\); \(I^2 = 89.4\%\)

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**Figure 6** Funnel plot of the effect of perineural dexamethasone on duration of analgesia.

**Figure 7** Effect of perineural dexamethasone on the duration of motor blockade. LA, local anaesthetics.
Table 2 Secondary outcomes after perineural dexamethasone injection.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group</th>
<th>RCT Mean</th>
<th>SD</th>
<th>n</th>
<th>Control Mean</th>
<th>SD</th>
<th>n</th>
<th>Mean difference (95% CI)</th>
<th>I² (%)</th>
<th>p value</th>
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<td>0–2 h</td>
<td>[37]</td>
<td>0.6</td>
<td>2.2</td>
<td>24</td>
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<tr>
<td>8–12 h</td>
<td>[19]</td>
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<td>2.4</td>
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<tr>
<td>24 h</td>
<td>[37]</td>
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<td>3.3</td>
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<td>20</td>
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RCT, randomised controlled trial; VAS, visual analogue scale.
*Intravenous equivalent dose (mg).

Figure 8 Effect of perineural dexamethasone on the rate of postoperative nausea and vomiting. LA, local anaesthetics.
The asymmetry of the funnel plot, along with a significant Egger’s test, indicate the presence of small studies effects, possible causes of which include publication bias, selective outcome reporting or poor methodological design. Another limitation is the variability in anaesthetic strategies employed in the included studies. For example, peripheral nerve blocks were combined with general anaesthesia in about 25% of the articles. The method of nerve location varied (anatomical landmarks, nerve stimulator or ultrasound-guided), as did the volume of local anaesthetics and the addition of other perineural adjuncts, such as adrenaline [20, 28, 35, 39, 40, 43, 48, 49, 53, 55] or adrenaline and clonidine [21]. Each of these factors may contribute to the substantial heterogeneity observed in the primary outcome. All RCTs blocked the brachial plexus, with six exceptions [20, 35–37, 39, 47]. We are therefore unable to draw conclusions regarding the potential efficacy of perineural dexamethasone in other peripheral nerve blocks, such as those in the distribution of the lumbar or sciatic plexus, and further research in this area is warranted. Finally, a number of pre-defined endpoints could not be assessed, as the required data were not captured by the included trials.

In summary, perineural dexamethasone at a dose of 4 mg prolongs the duration of analgesia after local anaesthetic peripheral nerve blockade with efficacy similar to a dose of 8 mg and without any reported serious adverse effects. Dexamethasone is an efficacious adjunct to local anaesthetics, but clinicians should be aware that dose-ranging studies are needed.

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Competing interests
No external funding or competing interests declared.

References
19. Parrington SJ, O’Donnell D, Chan VW, et al. Dexamethasone added to mepivacaine prolongs the duration of analgesia...


38. Bais DS, Geetha C, Kawale A. Effectiveness of addition of dexamethasone to 0.5% ropivacaine in providing perioperative analgesia for supraclavicular brachial plexus block. *Journal of Evolution of Medical and Dental Sciences* 2014; 3: 2456–64.


51. Saritas A, Sabuncu C. Comparison of clinical effects of prilocaine, dexamethasone added to prilocaine and levobupivacaine on brachial plexus block. *Journal of the Pakistan Medical Association* 2014; **64**: 433–6.


