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Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: a systematic review and meta-analysis of randomized trials

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Editor's key points

- In this systematic review of 9 studies and 801 patients, the authors demonstrate the reliable prolongation of sensory and motor block after local anaesthesia brachial plexus block via the addition of dexamethasone to the injectate.
- No adverse events of significance have been demonstrated, although it is likely that considered studies have not been powered to detect such events.
- The effect on block duration of systemic dexamethasone remains to be investigated.

Background. Brachial plexus nerve blocks (BPBs) have analgesic and opioid sparing benefits for upper extremity surgery. Single-injection techniques are limited by the pharmacological duration and therapeutic index of local anaesthetics (LAs). Continuous catheter techniques, while effective can present management challenges. Off-label use of perineural dexamethasone as an LA adjuvant has been utilized to prolong single-injection techniques. The objectives of this systematic review and meta-analysis are to assess the contemporary literature and quantify the effects of dexamethasone on BPB.

Methods. The authors searched for randomized, placebo-controlled trials that compared BPB performed with LA alone with that performed with LA and perineural dexamethasone. Meta-analysis was performed using a random effects model with subgroup analysis stratified by LA (long *vs* intermediate). The primary outcome was duration of sensory block or analgesia; the secondary outcomes were motor block duration, opioid consumption, and BPB complications.

Results. Nine trials (801 patients) were included with 393 patients receiving dexamethasone (4–10 mg). Dexamethasone prolonged the analgesic duration for long-acting LA from 730 to 1306 min [mean difference 576 min, 95% confidence interval (CI) 522–631] and for intermediate from 168 to 343 min (mean 175, 95% CI 73–277). Motor block was prolonged from 664 to 1102 min (mean 438, 95% CI 89–787). The most recent trial demonstrated equivalent prolongation with perineural or systemic administration of dexamethasone compared with placebo.

Conclusions. Perineural administration of dexamethasone with LA prolongs BPB effects with no observed adverse events. The effects of systemic administration of dexamethasone on BPB must be investigated.

Keywords: anaesthesia adjuvants; dexamethasone; nerve block

Brachial plexus nerve blocks (BPBs) for upper extremity surgery provide superior analgesia and reduce opioid consumption.[1 2] Painful procedures previously requiring inpatient hospital admission for pain control, such as shoulder surgery, are now commonly performed as ambulatory procedures facilitated by BPB analgesia. Inevitably, the effects of single-injection BPB dissipate after several hours unmasking the moderate-to-severe pain of the surgical insult. Efforts to prolong BPB duration by increasing local anaesthetic (LA) dose are limited by their narrow therapeutic window and indeed may not be effective as recent studies have demonstrated equivalent analgesic duration with volumes as low as 5 ml.[3–5] A broad cross section of surgical patients consistently rank postoperative pain as their highest concern highlighting the necessity for prolonged postoperative analgesia.[6 7] As a result, strategies to prolong BPB analgesia beyond the pharmacological duration of the LA used include placement of indwelling perineural catheters to allow prolonged infusion or the co-administration of adjuvants such as epinephrine, $\alpha 2$ agonists (i.e. clonidine and dexmedetomidine), midazolam, or the corticosteroid dexamethasone.[8–10] Indwelling catheter techniques can be very effective and provide analgesia for several days, but their utility is limited by technical

challenges with placement, inherent secondary failure rate, difficulties with catheter removal, or rarely infection.[11–13] Furthermore, not all anaesthetists have the subspecialty training required to perform advanced indwelling catheter techniques nor is there universal capability to administer and manage an outpatient perineural catheter programme.

LA adjuvants act by several mechanisms. They may cause local vasoconstriction limiting systemic uptake or they may have direct effects on peripheral nerves. In addition, they may also act systemically by anti-inflammatory effects. A meta-analysis by Pöpping and colleagues[10] determined that clonidine, as an adjuvant for peripheral nerve block (PNB), prolonged the duration of postoperative analgesia by 122 min [95% confidence interval (CI), 74–169]. This was at a cost of an increased risk of sedation [odds ratio (OR) 2.28, 95% CI 1.15–5.41], hypotension (OR 3.61, 95% CI 1.52–8.55), and bradycardia (OR 3.09. 95% CI 1.10–8.64), known side-effects of systemic clonidine. Similar results have been demonstrated with dexmedetomidine.[14]

It is widely believed that dexamethasone improves the quality and duration of PNB over LA alone. This is thought to be mediated by attenuating the release of inflammatory mediators, reducing ectopic neuronal discharge, and inhibiting potassium channel-mediated discharge of nociceptive C-fibres.[15–17] The addition of dexamethasone may provide patients who are otherwise not eligible for extended, continuous perineural techniques, to experience an extended period of analgesia compared with LA BPB alone. However, dexamethasone is not approved for perineural administration by the United States Food and Drug Administration (FDA), Health Canada (HC), the European Union (EU), nor any other regulatory body. There are no systematic reviews or meta-analyses estimating the effect of dexamethasone on BPB duration and the incidence of complications (prolonged nerve palsy, hyperglycaemia, and infection) associated with its use in the contemporary literature. If anaesthesiologists are to be confident in utilizing off-label dexamethasone as a BPB adjuvant, a good estimate of the expected positive and negative effects must be available to make informed decisions.

Methods

Reconciliation of study procedures

All activities including the literature search, inclusion of studies, grading study quality, and extraction of data were carried out independently and in duplicate by two authors (S.C. and R.R.). Disagreements between reviewers were resolved through discussion with a third reviewer experienced in the field of regional anaesthesia (C.J.L.M.).

Search strategy

The following electronic databases were searched: (i) MEDLINE (1946–April 2013), (ii) EMBASE (1980–April 2013), and (iii) Cochrane Central Register of Controlled Trials (2005–April 2013). The initial search terms with the keywords *regional anaesthesia, brachial plexus*, *interscalene, supraclavicular, infraclavicular, axillary*, or *nerve block* with the definition exploded were utilized. The 'and' function was used to combine these terms with *dexamethasone, corticosteroid, or steroid* with the definition exploded. The identified abstracts were screened and full-text articles meeting the selection criteria were retrieved. The references of all retrieved articles were manually searched to identify any other studies not found in the electronic search. All available abstracts from major international meetings including the American Society of Regional Anesthesia (ASRA—2005–2012), the European Society of Regional Anaesthesia (ESRA—2007–2012), and the American Society of Anesthesiologists (ASA—2000–2012) annual meetings were examined and published protocols on the trial registration site www.clinicaltrials.gov.

Selection criteria

Studies meeting the following criteria were included: (i) prospective study with randomized allocation; (ii) comparison of LA with perineural dexamethasone (intervention) with that without (control) in single-injection BPB regional analgesia or anaesthesia for upper extremity surgery; and (iii) studies only assessing adult (>18 yr old) patients. Attempts were made to contact study authors, particularly for meeting abstracts, to elicit information regarding methodology, missing data, and other study details relevant to this review. Abstracts were planned for inclusion if they were low risk of bias. Studies were planned for inclusion regardless of whether regulatory approval (United States Investigational New Drug or national equivalent) was sought by authors.

Data extraction

Two reviewers performed data extraction independently and in duplicate. The following patient characteristic data were extracted: primary author, year of publication, specific surgical population, sample size, specific type of BPB, nerve localization technique, type and dose of LA, and dose of perineural dexamethasone. Specific extracted outcomes and risk of bias assessments are detailed in the following sections. Where data were reported as median and interquartile range (IQR), authors were contacted to obtain raw data and the mean and standard deviation (SD) were determined to enable meta-analysis. If this was not possible, the mean and SD were estimated from the median and range according to the method described by Hozo and colleagues.[18] As a last resort, the SD was estimated from the IQR by the method described by the Cochrane Handbook for Systematic Reviews (IQR=1.35SD).[19] In the case of multiple groups with differing doses of perineural dexamethasone, these groups were combined and compared with patients receiving no perineural dexamethasone. In the case where systemic dexamethasone was administered, these patients were included in the control or no perineural dexamethasone group.

Outcomes to be assessed

The important patient outcomes extracted were: (i) duration of analgesia or sensory block; (ii) duration of motor block; (iii) cumulative 72 h opioid consumption; and (iv) complications associated with BPB or dexamethasone including persistent nerve palsy lasting >1 week, infection at the site of BPB, and