BJA

British Journal of Anaesthesia, 118 (2): 167–81 (2017)

doi: 10.1093/bja/aew411
Review Article

Evidence basis for using perineural dexmedetomidine to enhance the quality of brachial plexus nerve blocks: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Background. Dexmedetomidine has been proposed as a perineural local anaesthetic (LA) adjunct to prolong peripheral nerve block duration; however, results from our previous meta-analysis in the setting of brachial plexus block (BPB) did not support its use. Many additional randomized trials have since been published. We thus conducted an updated meta-analysis.

Methods. Randomized trials investigating the addition of dexmedetomidine to LA compared with LA alone (Control) in BPB for upper extremity surgery were sought. Sensory and motor block duration, onset times, duration of analgesia, analgesic consumption, pain severity, patient satisfaction, and dexmedetomidine-related side-effects were analysed using random-effects modeling. We used ratio-of-means (lower confidence interval [point estimate]) for continuous outcomes.

Results. We identified 32 trials (2007 patients), and found that dexmedetomidine prolonged sensory block (at least 57%, $P < 0.0001$), motor block (at least 58%, $P < 0.0001$), and analgesia (at least 63%, $P < 0.0001$) duration. Dexmedetomidine expedited onset for both sensory (at least 40%, $P < 0.0001$) and motor (at least 39%, $P < 0.0001$) blocks. Dexmedetomidine also reduced postoperative oral morphine consumption by 10.2mg [-15.3, -5.2] ($P < 0.0001$), improved pain control, and enhanced satisfaction. In contrast, dexmedetomidine increased odds of bradycardia (3.3 [0.8, 13.5]($P = 0.0002$)), and hypotension (5.4 [2.7, 11.0] ($P < 0.0001$)). A 50-60μg dexmedetomidine dose maximized sensory block duration while minimizing haemodynamic side-effects. No patients experienced any neurologic sequelae. Evidence quality for sensory block was high according to the GRADE system.

Conclusions. New evidence now indicates that perineural dexmedetomidine improves BPB onset, quality, and analgesia. However, these benefits should be weighed against increased risks of motor block prolongation and transient bradycardia and hypotension.

Key words: adjunct; adjuvant; axillary; brachial plexus block; infraclavicular; interscalene; nerve block; perineural dexmedetomidine; regional anaesthesia; sensory block; supraclavicular

Editor's key points

- Dexmedetomidine, an alpha-2 agonist, can be expected to extend the duration of local anaesthetic blocks but it has been unclear whether this has clinical benefit.
- This systematic review provides sufficient evidence to properly test this concept, finding enhanced onset and longer duration of block with minimal side-effects.
- The optimal local anaesthetic adjunct dose for brachial plexus block seems to be 50-60 μg.
- There is some uncertainty as to overall analgesic effectiveness and patient outcomes.

Anaesthetists have sought strategies to extend the benefits of single-shot peripheral nerve blocks beyond the duration of commonly available local anaesthetics (LA).[1] Perineural adjuncts are one technically simple strategy that can be used for this purpose.[2] Dexmedetomidine, an alpha-2 agonist,[3] has been proposed as a safe[4] and effective[5,6] adjunct capable of extending the duration of single-shot block.

Hyperpolarization-activated cation currents normally bring neurons back to the resting potential and normal functional activity during the refractory phase in an action potential. By blocking these currents, dexmedetomidine can accentuate inhibition of neuronal conduction and produce analgesia.[6] However, despite early promising evidence from animal[5,6] and human[7] studies that have signaled efficacy, our quantitative systematic review of dexmedetomidine as an adjunct to brachial plexus block (BPB), published in 2013,[8] was unable to demonstrate any clinically important benefits. Some of the trials[7,9–11] were marked by substantial clinical and statistical heterogeneities that may have undermined a precise estimation of the dexmedetomidine treatment effect. Many additional trials of dexmedetomidine as a BPB adjunct have been since published, thus prompting a re-examination specifically to assess the role of dexmedetomidine in prolonging sensory block duration.

Methods

We followed PRISMA statement guidelines[12] in the preparation of this manuscript. Randomized trials examining the effect of dexmedetomidine on the duration of sensory block after single-shot BPB were evaluated using a predefined protocol, but this was not previously published.

Literature search

Two of the authors (LV and FWA) independently sought and retrieved relevant studies from electronic databases including the US National Library of Medicine database, MEDLINE; the Excerpta Medica database, EMBASE; the Cochrane Databases of systematic reviews; the Cochrane central register of controlled clinical trials; Cumulative Index of Nursing and Allied Health Literature (CINAHL); Scopus; Web of Science; MEDLINE In-Process; and other non-indexed citations. The medical subject headings (MeSH), text words, and controlled vocabulary terms relating to Dexmedetomidine and Medetomidine were sought. Results were combined using the Boolean operator "AND" with the search terms analgesia, anaesthesia, adjunct, adjuvant, anaesthetics local, nerve block, perineural, regional anaesthesia and terms designating upper extremity such as arm, brachial plexus, forearm, elbow, hand, humerus, radius, shoulder, and wrist. Additional non-indexed articles were retrieved using Google Scholar; and the bibliographies of retrieved trials were hand-searched for additional relevant studies. Our search was limited to randomized trials published in the English language. Only trials including adults (age > 18 yr) published in full-manuscript form between January 1985 and February 2016 were considered. Abstracts were excluded.

Inclusion criteria

We included randomized trials with parallel group design examining the effects of adding perineural dexmedetomidine as an adjunct to LA (Dex group), compared with LA alone (Control group) on BPB characteristics, postoperative analgesia and dexmedetomidine-related side-effects, in patients undergoing upper extremity surgery with BPB. Specifically, interscalene (ISB), supraclavicular (SCB), infraclavicular (ICB) and axillary (AXB) level blocks of the brachial plexus performed for either anaesthesia or postoperative analgesia were considered. Randomized and quasi-randomized, and single- and double-blinded trials were included. Randomized trials without a control group were excluded. We also excluded trials if non-perineural routes of dexmedetomidine administration were used (e.g. intra-articular injection);[13] if surgeries involved anatomical areas other than the upper extremity (e.g. abdominal);[14] and if blocks other than BPB were performed.[15] Studies of i.v. regional anaesthesia[16,17] and distal peripheral nerve blocks (e.g. medial, radial or ulnar blocks)[18,19] were also excluded.

Trial selection and methodological assessment

The two authors (LV and FWA) independently evaluated the identified abstracts. Inclusion of qualifying studies in the review was taken by consensus between the two authors. Disagreements were resolved by re-evaluating the full manuscript of the source studies and consulting with the third author (RB). Trials that failed to meet the inclusion criteria were excluded.

The quality of the reviewed trials was independently assessed using the Cochrane Collaboration Risk of Bias tool[20] by two of the authors (LV and FWA). The tool evaluates trials for biases, among which are selection (randomization and allocation), performance and detection (blinding), attrition, reporting, and other forms of bias. A score was assigned to each trial by consensus; if an agreement could not be reached, the third author (RB) was consulted. Considering the limited number of studies and that our earlier meta-analysis failed to demonstrate the effects of dexmedetomidine on nerve blocks, we decided not to exclude studies based on the quality scores, but rather to take an inclusive approach towards studies with a view towards answering the question of interest. However, trials were excluded if they had fewer than 10 subjects per group, to reduce the possibility of chance in estimating a treatment effect.

Data extraction

The authors independently extracted relevant data using a standardized data sheet; discrepancies were resolved by re-examining the source data as a first resort, then consulting with the third author. Data extracted included primary author, yr of publication, comparative groups, sample size, nature of primary outcome, surgical site, nature of surgical anaesthetic, level of BPB, nerve localization technique, type and dose of LA, dose of perineural dexmedetomidine, block characteristics, analgesic effects, and dexmedetomidine-related side-effects. Data on additional study arms examining other perineural additives