EDITORIAL

Dexamethasone and peripheral nerve blocks: on the nerve or intravenous?

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In a past issue of the British Journal of Anaesthesia, Desmet and colleagues1 report that i.v. dexamethasone is equivalent to perineural dexamethasone in prolonging the analgesic duration of a single-shot interscalene block with ropivacaine.

In their study, 150 patients presenting for arthroscopic shoulder surgery with an interscalene brachial plexus block (BPB) were randomized into three groups: ropivacaine 0.5%; ropivacaine 0.5% and dexamethasone 10 mg; and ropivacaine 0.5% with i.v. dexamethasone 10 mg. The primary outcome was the duration of analgesia, defined as the time between performance of the block and the first analgesic request. The median time of a sensory block was equivalent for perineural and i.v. dexamethasone: 1405 min (inter-quartile range 1015–1710) and 1275 min (inter-quartile range 1095–2035) ropivacaine and perineural dexamethasone and ropivacaine and i.v. dexamethasone, respectively. There was a significant difference between the ropivacaine group: 757 min (inter-quartile range 635–910) and the dexamethasone groups (P = 0.0001). The authors conclude that i.v. dexamethasone is equivalent to perineural dexamethasone in prolonging the analgesic duration of a single-shot interscalene block with ropivacaine. Legitimate criticisms have been made on the design of this study such as the sample size calculation, a non-inferiority design based on a large difference in duration of analgesia for the equivalence limit (i.e. 360 min), or the reality of the intention-to-treat analysis.2 3 Although we cannot definitely say based on a single study that the duration of analgesia is equivalent with perineural or i.v. dexamethasone added to single-shot interscalene block, this study’s results should not be ignored and future studies with a larger sample of patients may conclusively answer the question.

It has been shown that continuous peripheral nerve blocks, regardless of catheter location, provided superior postoperative analgesia and fewer opioid-related side-effects when compared with opioid analgesia.4 However, painful procedures previously requiring inpatient hospital admission for pain control, such as shoulder surgery, are now commonly performed as ambulatory procedures facilitated by nerve block analgesia. Inevitably, the effects of single injection dissipate after several hours unmasking the moderate-to-severe pain of the surgical insult. A majority of surgical patients consistently rank postoperative pain as their highest concern highlighting the necessity for prolonged postoperative analgesia. Since efforts to prolong single-shot peripheral nerve block analgesia by increasing local anaesthetic dose are limited by their narrow therapeutic window, strategies include the co-administration of adjuvants such as epinephrine, α2 agonists (i.e. clonidine and dexmedetomidine),5–7 opioid,8 or more recently the corticosteroid dexamethasone.

All published prospective studies until the recent report by Desmet and colleagues1 have described a benefit of the addition of perineural dexamethasone to prolong the duration of analgesia.9–17 These data concern only single-shot BPBs with a similar number of studies using long- or intermediate-acting local anaesthetic. A recent large retrospective study suggests a similar advantage for upper and lower limb nerve block.18 A meta-analysis has confirmed this impression by analysing nine trials testing the impact of dexamethasone on BPB. These trials included 801 patients with 393 patients receiving dexamethasone (4–10 mg) and dexamethasone prolonged the analgesic duration for long-acting local anaesthetic 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 authors of this meta-analysis conclude that perineural administration of dexamethasone with local anaesthetic prolongs BPB effects with no observed adverse events. They also insist on the necessity to investigate the effects of systemic administration of dexamethasone on peripheral nerve block analgesia.

In fact, the recent study by Desmet and colleagues is the only one to have compared systemic with local administration of dexamethasone and found no clinical significant difference. We already know that i.v. dexamethasone has an analgesic effect. In a recent meta-analysis, of ~2500 patients, dexamethasone, >0.1 mg kg⁻¹, reduced postoperative pain and opioid consumption.19 The main issue is therefore to prove that perineural administration can offer an additional analgesic effect through a specific peripheral mechanism. What do we know about a selective action of dexamethasone on...
Peripheral nerve fibres? In the case of inflamed peripheral nerve after nerve damage, the local administration of dexamethasone has been proven efficient, but it only reflects the beneficial anti-inflammatory effect of dexamethasone. The mechanistic understanding regarding dexamethasone action on the normal non-inflamed peripheral nerve is quite limited.

One experimental study using electrically stimulated A-fibres and in C-fibres of the rat plantar nerve observes a direct membrane action with a suppression of the transmission in thin unmyelinated C-fibres but not in myelinated A-β fibres. In another study on isolated rat sciatic nerve, dexamethasone had no influence on the potency or duration of local anaesthetic- or midazolam-induced block of A- and C-waves of the compound action potential. In conclusion, the precise mechanism of the potential peripheral action of dexamethasone on normal peripheral nerve fibres is still unknown and should be further investigated.

Moreover, the rational for perineural administration of dexamethasone should also be based on the absence of significant neurotoxicity. Although the recent meta-analysis did not describe any complication associated with the peripheral administration of dexamethasone on the nerve, only three studies evaluated the incidence of persistent nerve palsy up to 2 weeks and 6 months after BPB (407 patients; 180 patients receiving perineural dexamethasone). No events were recorded in either arm, and therefore, no effect can be estimated. Given that the rate of persistent nerve palsy after peripheral nerve block is extremely low, we will certainly have no sufficient clinical data to exclude any neurotoxicity of perineural dexamethasone. What is the transferable evidence? The previous large use of epidural steroids including dexamethasone to treat radiculopathy pain may support the absence of local nerve toxicity. On the other hand, in an experimental study using isolated sensory neurone, results suggest that attention should be directed towards exploring the time-dependent and concentration-dependent basis for neurotoxicity associated with dexamethasone combined with ropivacaine. In addition to this issue of the potential peripheral action of dexamethasone on normal peripheral nerve fibres is still unknown and should be further investigated.

In conclusion, we presently know that i.v. dexamethasone is useful both to reduce postoperative pain and prevent postoperative nausea and vomiting without significant side-effects. The perineural administration on nerve has not been definitely shown necessary to further increase this benefit of perioperative use of dexamethasone. As dexamethasone is not licensed anywhere for perineural use and additional data are still required both on efficacy and side-effects of this route of administration, clinicians should first consider i.v. administration of dexamethasone to achieve an increased duration of analgesia after peripheral nerve block.

### References

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