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Corticosteroids as Adjuvants for Peripheral Nerve Blocks: A Mini Review

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ABSTRACT

Peripheral nerve blocks (PNB) have become a highly favorable anesthetic option when compared to general anesthesia for limb surgery due to the fact that they provide superior post-operative analgesia. To prolong PNB duration and postoperative analgesia a wide range of agents have been tested as adjuncts to local anesthetics (LA), corticosteroids among them, namely dexamethasone. Dexamethasone can be administrated perineurally or intravenously as additive to LA resulting in the similar effect: prolonged duration of PNB reduced post-operative pain and longer time to first analgesic request in adult patients. There is a lack of data for pediatric patients. Required dose still remains unknown for various route of administration.

Keywords: Peripheral nerve blocks, Local anesthetics, Adjuvants, Corticosteroids: dexamethasone

Abbreviations: PNB: Peripheral Nerve Block; LA: Local Anesthetic; PONV: Postoperative Nausea and Vomiting

INTRODUCTION

Any type of surgery is accompanied by acute postoperative pain which is consistent of different components (i.e., nociceptive, inflammatory and neuropathic), where applicable peripheral nerve blocks (PNB) can be used for anesthesia and analgesia. They have become a highly favorable anesthetic option when compared to general anesthesia for limb surgery due to the fact that they provide superior post-operative analgesia. In this way opioid use and its side-effects are avoided and therefore PNB are implemented in so called 'fast track' surgery and anesthesia programmes.

PNB can be performed only with single-shot injection of local anesthetic (LA) or this single-shot injection block can be prolonged by administrating continuous infusion of LA via special peripheral catheters. Single shot injection blocks are effective but time limited. A wide range of agents such as vasoactive agents (clonidine, epinephrine, dexmedetomidine), neostigmine, ketamine, midazolam, tramadol, magnesium and dexamethasone have been tested as adjuncts to LAs for PNB performance in an effort to enhance postoperative analgesia [1,2]. Some additives to LA can hasten the onset of nerve block, prolong block duration, or reduce toxicity. On the other hand, poorly selected or unnecessary additives may not have the desired effect and may even expose patients to unnecessary risks.

Primary focus of this review is on corticosteroid use as adjuvants to LA. We will discuss route of administration, analgesia duration after PNB, required dose and their safety.

CORTICOSTEROID MECHANISM OF ACTION

Corticosteroids administrated systematically are potent inhibitors of inflammatory processes and are widely used in the treatment of many conditions. They have potent anti-inflammatory effect and reduce pain and edema after surgery. To achieve anti-inflammatory effect glucocorticoids first bind to intracellular receptors, modify gene transcription and induce synthesis of proteins. Also, they inhibit many inflammation-associated molecules such as cytokines, chemokines, arachidonic acid metabolites and adhesion molecules [3,4]. The precise mechanism of action of perineurial dexamethasone added to LAs is unknown. Some studies described a direct effect of glucocorticoids on nerve conduction while others reported that dexamethasone induced perineural vasoconstriction with concomitant slower absorption of the administered LAs [5,6]. A more attractive theory holds that dexamethasone increases the activity of inhibitory potassium channels on nociceptive C-fibres (via glucocorticoid receptors), thus decreasing their activity [7].

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Therefore, 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 to PNB performed with LA alone.

ROUTE OF ADMINISTRATION AND VARIOUS TYPES OF CORTICOSTEROIDS

Additives to LA are most commonly administered perineurally. This means that the mixture of LA and additive is directly injected around peripheral nerve of interest. Preferred corticosteroid for use is dexamethasone. However, recent studies suggest that not only perineural but intravenous dexamethasone can be administered alongside with PNB performance and that it has the same clinical effects as perineurial one. Large randomized trials and meta-analysis report that patients treated with dexamethasone have prolonged PNB duration, experience less postoperative pain, require less postoperative opioids, have longer time to first analgesic dose, needless rescue analgesia and have shorter length of stay in post-anesthesia care units [8-11].

Recent meta-analysis by Pehora et al. [12] which included 35 studies involving 2702 adult patients showed prolonged duration of sensory blocks in the perineurial and intravenous dexamethasone groups when compared to placebo. When perineural and intravenous dexamethasone were compared, the duration of sensory block was longer in the perineural dexamethasone group. Postoperative pain intensity at 12 h and 24 h after surgery was lower in the perineural as well as in the intravenous dexamethasone group compared with placebo. The amount of opioid pain medication required was also lower in participants receiving perineural and intravenous dexamethasone. There was no difference in postoperative pain intensity or the amount of opioid pain medication required when perineural and intravenous dexamethasone were compared. This may lead to the conclusion that the way of dexamethasone administration does not provide better pain relief over the other.

Besides dexamethasone, methylprednisolone can be added as adjuvant for PNB. Eker et al. [13] studied its analgesic effects in treatment of neuropathic pain. They suggest that corticosteroids improve 3 month outcomes in patients with neuropathic pain following nerve injury. However, they must be administered in the early period after injury in high doses, in their case 80 mg of methylprednisolone, which is equivalent to 16 mg of dexamethasone.

Until now only one trial has been conducted by using oral corticosteroid, namely prednisone, in ultrasound-guided supraclavicular nerve block [14]. Investigators used 20 mg of oral prednisone, which is equivalent to 3 mg of dexamethasone, as an addition to PNB performance. As a result, PNB duration among groups was comparable but the postoperative pain score was significantly improved. This can be related to the fact that corticosteroids modulate the response of nerve fibers and nociceptors. The efficacy of oral prednisone for this purpose remains incompletely studied, calling for prospective, double-blind controlled trials.

DOSE

In the last decade fair amount of clinical trials on PNBs for upper and lower extremity has be performed using either intravenous or perineurial dexamethasone. Regardless on the route of administration, dexamethasone significantly prolonged sensory and motor block. It also has a greater absolute effect on long-lasting LAs [15]. Prolonged analgesia without prolonged motor block is desirable both for the surgeons and for the anesthesiologist. But the optimal dose of dexamethasone and ratio in the LA mixture has yet to be determined.

There are no pharmacokinetic data on the absorption of perineurally administered dexamethasone. Direct comparisons among trials are difficult because of the variety of LA mixtures used, different blocks studied, and different methods of evaluating block duration. Common to all these trials is the fact that addition of dexamethasone to PNB resulted in prolonged motor block and duration of analgesia regardless on route of administration and dose (low or high).

One of the first trials used relatively high doses of dexamethasone for nowadays standards, up to 10 mg [9]. However, the administration of dexamethasone is not without risk and may lead, in a dose-dependent manner, to complications including hyperglycemia, infection, suppression of the hypothalamic–pituitary axis, and impaired wound healing, among others. It is therefore important to define the optimal dose of perineural dexamethasone that maximizes the analgesic benefit while minimizing associated risk. Unfortunately, dose-finding studies have presented conflicting conclusions. While, Liu et al. [16] suggested a ceiling effect is reached with a dose as low as 1 mg, Woo et al. [17] demonstrated a dose-dependent effect up to a maximum of 5 mg.

Most recent meta-analysis by Kirkham et al. [18] based on 33 randomized controlled trials, including a total of 2138 patients, suggests that 4 mg of perineural dexamethasone represents a ceiling dose and prolongs analgesia by a mean period of 6 h and 8 h, when combined with short/intermediate/long acting LAs, respectively. Higher doses failed to provide additional analgesic duration. The risk of neurologic complications was not increased.

It is of most importance that we aim further research towards the ideal dose and timing of dexamethasone administration.

ADVERSE EFFECTS

There is ongoing debate about intravenous vs. perineurial dexamethasone administration and its safety. Their main argument is that the dexamethasone is still "off-label" for perineural administration and that there has not been fully

defined its neurotoxicity. However, many clinical trials have been conducted in patients that received perineural dexamethasone as an adjunct to LA [19,20]. None of them reported an increased incidence of serious adverse effects or neurotoxicity compared with the control groups [18]. So far no safety trial on the use of perineural dexamethasone has been performed and it is highly unlikely that such a trial will ever be conducted; because it had to involve thousands of patients (a total sample size of roughly 16,000 patients would be required). However, local perineural steroid injection has been used for many years in the treatment of carpal tunnel syndrome and is acknowledged to be an effective and safe therapy [21].

Additionally, corticosteroids have a long history of safe use in the epidural space for the treatment of radicular pain arising from nerve root irritation and dexamethasone specifically has been studied as an adjuvant to epidural LAs [22]. The neurological risk, if any, of dexamethasone thus appears to be small when used in clinical relevant concentrations. In fact, the use of dexamethasone as an adjunct to local anesthesia for nerve blocks is discussed in prominent textbooks [23,24].

Systemic toxicity from a single dose of dexamethasone is also unlikely. It is effective and widely administered intravenously by anesthesiologists for prophylaxis against postoperative nausea and vomiting (PONV) [25]. Concerns about steroid-induced hyperglycemia have been borne out in high-dose intravenous regimens, but have not been problematic in clinical practice [26].

CONCLUSION

Corticosteroids whether administrated intravenously or perineurally can be safely used as additive to PNB. Regardless on the route of administration, sensory and motor block, as well as the time to first analgesic request in upper or lower extremity blocks is significantly prolonged in adult patients. There is a lack of data for pediatric patients. Optimal dose still remains unknown for various route of administration. Further research should be aimed towards the ideal dose and timing of dexamethasone administration.

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