Efficacy and Adverse Effects of Intrathecal Dexamethasone in Post-operative pain

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Abstract

The analgesic efficacy and adverse effects of a perioperative dose of dexamethasone are unclear. We performed this review to evaluate the role of dexamethasone in post-operative pain and analgesic consumption.

KeyWords:

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Introduction:

Glucocorticoids, natural and synthetic are adrenocortical steroids readily absorbed from gastrointestinal tract. They cause varied metabolic effects in addition to modifying the body's immune system to diverse stimuli. Dexamethasone is a long acting, high potency synthetic analogue of glucocorticoids and is primarily used for its anti-inflammatory effects in disorders of many organ systems (1).

At equipotent anti-inflammatory doses, Dexamethasone almost completely lacks the sodium retaining property of Hydrocortisone and its closely related derivatives. In addition to binding specific nuclear steroid receptors, it interferes with nuclear factor kappa B pathway activation (2).

Dexamethasone increases regional block associated analgesia due to either inhibitory activity of potassium channels on pain sensitive sensory neurons or by producing vasoconstriction. Dexamethasone also used as an adjuvant to local anaesthesia. It is white, odorless, crystalline powder relatively stable in air. The molecular formula is C22H29FO5 and chemically called as 9-fluoro-11-beta,17, 21 trihydroxy-16-alpha-methylpregna-1,4-diene,3,20-dione (3).

Pharmacokinetics:

Dexamethasone is water soluble ester which can be given by intravenous, intramuscular and oral route. Glucocorticoid is metabolized by microsomal enzymes present in the liver and then conjugated with glucuronic acid to get excreted through kidneys. It has a long half-life of 36 hours because of resistant to metabolism. Microsomal enzyme inducers like phenytoin decrease the efficacy of Dexamethasone (4).

Adverse effects:

1. Proximal myopathy, osteoporosis, muscle weakness, vertebral fractures.
2. Thromboembolic episodes, hypertension, decreases myocardial contractility
3. Carbohydrate intolerance, weight gain, Cushinnoid features, menstrual disturbances.
4. Increased risks of infection, decreased immunity and delayed wound healing.
5. Gastro intestinal side effects like dyspepsia, nausea, peptic ulcer, acute pancreatitis (5).
6. Neurological side effects like insomnia, depression, irritability, euphoria, psychosis, convulsions and cognitive disturbances is a 9 - Fluoro-Glucocorticoid.

Mechanism of action:

The short term effects of corticosteroids are decreased vasodilation and permeability of capillaries, as well as decreased leukocyte migration to sites of inflammation. Corticosteroids binding to the glucocorticoid receptor mediates changes in gene expression that lead to multiple downstream effects over hours to days (6).

Glucocorticoids inhibit neutrophil apoptosis and demargination; they inhibit phospholipase A2, which decreases the formation of arachidonic acid derivatives; they inhibit NF-Kappa B and other inflammatory transcription factors; they promote anti-inflammatory genes like interleukin-10. Lower doses of corticosteroids provide an anti-inflammatory effect, while higher doses are immunosuppressive. High doses of glucocorticoids for an extended period bind to the

mineralocorticoid receptor, raising sodium levels and decreasing potassium levels (6).

Dexamethasone, has anti-inflammatory and immunosuppressive characteristics can diffuse into the central nervous system (CNS). Dexamethasone inhibits the HPA axis primarily on the pituitary level by transcription mechanisms in the cells, but not obligatory for ACTH gene synthesis. It is comprehended that a harmful stimulus can suppress the HPA axis feedback information, which is a possible function of nature and intensity of the stimulus (7).

Analgesic effect of dexamethasone through variant rout:

1- Intravenous administration:

Analgesic action of dexamethasone has been found in dental surgeries (e.g., tooth extraction), ENT surgeries (e.g., mastoidectomy, tonsillectomy, adenoidectomy, etc.), ano-rectal surgeries. Even its role has been well defined in total knee arthroplasty, Samona and others (8) have used a single dose of dexamethasone and have found that there is significant reduction in narcotic consumption and significant decrease in pain scores at 24 hrs. It also appears to be a safe modality in patients undergoing total knee arthroplasty (TKA) with no increase in wound related complications.

Chalifoux et al. (9) have compared different dosage of dexamethasone and have found that 16 mg reduces post-operative pain on motion at 24 and 36 hours. Role of intravenous dexamethasone has not just confined to systemic analgesia rather its role has been defined in prolonging the peripheral nerve blockade. Addition of dexamethasone both intravenously and caudally as an adjuvant to caudal ropivacaine has been found to reduce the intensity of post-operative pain and prolonging the post-operative analgesia. Chalifoux have found that low doses of intravenous dexamethasone (4 mg and 10 mg) significantly prolong the analgesic duration of interscalene block (9).

The mean visual analog scale (VAS) was significantly lower in the Group C for up to 24 h following the caudal block. No significant hemodynamic changes were noted in any of the groups. The intravenous dexamethasone group showed higher blood glucose levels at 24 h but was not clinically relevant. These results suggest that injection dexamethasone is a safe adjunct to caudal ropivacaine in lumbosacral spine surgeries. The authors concluded that administration of dexamethasone 8 mg intravenously prolongs the duration of post-operative analgesia and sensory block in patients undergoing lower segment cesarean section under spinal anaesthesia (10).

2-Role of epidural administration:

The mechanism of action by which epidural or perineural dexamethasone acts is unknown, some believe it to be because of direct membrane stabilizing effect on nerves or direct action on spinal cord by means of transcription factors like nuclear factor kappa B (NF- κB). Hong and others (11) have used epidural dexamethasone and found that 10 mg epidural dexamethasone was more effective than lower dosage in patients undergoing gastrostomy, associated with moderate to severe intensity of pain. Total fentanyl consumption was also significantly less in dexamethasone group and no difference in adverse.

3-Perineural:

Dexamethasone prolongs the action of lignocaine 2% in dental nerve block (DNB) for third molar surgery (TMS). Study found maximum duration of DNB in study group (SG) was 248.88 min and in control group (CG) was 175.44 min.18 In a study by Zhao et al it was found that perineural dexamethasone prolongs the analgesic duration as compared to intravenous route only when epinephrine is co-administered. Without epinephrine, the two modalities show equivalent effect as adjuvants on regional anaesthesia (12).

Dexamethasone 300 µg/kg with ropivacaine intraarticular has a superior analgesic efficacy a much-prolonged post-operative pain relief, minimal post-operative analgesia requirement and better patient compliance with negligible side effects. Liu et al did a prospective observational study and used a single shot of bilateral thoracic paravertebral block (TPVB) with 25 ml of 0.2% ropivacaine and 5 mg dexamethasone in combination for both sides at the 8th thoracic transverse level (T8) performed on 201 participants who complained moderate to severe pain on arrival to post anaesthesia care unit (PACU) after laparotomy (13).

In addition to its useful effects, dexamethasone has been tried in combination to ropivacaine in ankle block and the combination has been found to improve pre-emptive ankle block by decreasing post-operative pain intensity and analgesic consumption with minimal post-operative complication. However, low dose dexamethasone 2 mg has been found to have only modest and inconsistent effect of questionable clinical relevance on block duration (14).

4- Intrathecal administration:

Dexamethasone has an effectiveness of 36-54 hours and it is a long-lasting corticosteroid. This synthetic corticosteroid administered intrathecally affects

nuclear transcription in adrenergic receptors (15).
It inhibits corticosterone binding to type II of adrenergic receptors in the pituitary gland passing through the cerebrospinal fluid (CSF) bound to proteins. Irrelevantly of the concentration, dexamethasone has a similar effect to type II of adrenergic receptors. It is possible that it resorbs somewhere in the brain without an effect on other types of receptors along the HPA axis not depending on the concentration (16).
Intrathecal addition of dexamethasone to bupivacaine for elective orthopedic surgery on lower limbs significantly prolongs duration of sensory block and decreases opioid requirements in post-operative management (17).
In several studies on peripheral nerve blocks when added to the local anaesthetic, dexamethasone prolongs sensor and motor blockade with significantly reduced post-operative analgesic requirements, which means it can inhibit phospholipase-A2 and cyclooxygenase-2 expression during inflammation decreasing prostaglandin synthesis. Prolonged block may be the result of local effect on nerve fibers. Single shot effect of intrathecal administration of dexamethasone with levobupivacaine in emergency patients with femoral fractures have not yet been evaluated in scientific literature (18).

Dexamethasone for post-operative pain and analgesic consumption:

Dexamethasone decreases total opioid consumption post-operatively Regarding this a Double-blind prospective study by as double-blind prospective study done in 2015 in West Bengal, India shows that the meperidine consumption in the Dexamethasone group was significantly reduced from the normal saline group (135.4 ± 25.7 vs. 228.8 ± 21.5) milligrams respectively. Similarly, A retrospective chart review was conducted in 2016 at Hurley Medical Center, Michigan, USA (19).

A total of 102 patients underwent TKA, 55 subjects received dexamethasone (treatment group) and 47 did not (control group) Patients who received dexamethasone required a significant smaller quantity of oral opioids (oral morphine equivalence 37.1 mg) compared to the control group (73.1 mg, P = 0.020) throughout the standard 3-day hospital stay. When we see the pain score No statistically significant difference was noted in immediate post-operative VAS pain scores upon arrival to the post-anaesthesia care unit, at 12 and 48 h. However, at 24 h the VAS pain scores were lower for the dexamethasone group (4.57) than for the control group (6.077) P = 0.003 (19).

Dexamethasone has an anti-inflammatory, analgesic effects and significantly improved the duration of sensory block in spinal anaesthesia when added to hyperbaric bupivacaine. The use of preoperative dexamethasone (8mg), with a biologic half-life of 36–72h, improved post discharge quality of recovery and decreased nausea, vomiting, pain, and fatigue in the early post-operative period (20).

As it reduces the gradient between skin and body core temperature and modifies the inflammatory response, dexamethasone has been reported to be effective in reducing shivering after cardiac surgeries. Dexamethasone may cause unpleasant symptoms following rapid IV injection (21).

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