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Perineural *Versus* Intravenous Dexamethasone as an Adjuvant for Peripheral Nerve Block: A Prospective Study Conducted in a Tertiary Care Institution in South India

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Abstract

Perineural dexamethasone appears to prolong the duration of analgesia after brachial plexus block when combined with local anaesthetics. Several studies have compared intravenous with perineural dexamethasone in upper extremity surgeries, however there is concern regarding potential neural toxicity of perineural dexamethasone; Therefore we aimed to find out whether intravenous dexamethasone compared to perineural dexamethasone had similar or superior effects in prolonging the duration of nerve block, as adjuvant to local anaesthetic brachial plexus block.

This randomized, prospective observational study was conducted on 222 patients, in government. medical college hospital, thiruvananthapuram, posted for upperlimb forearm surgeries under supraclavicular brachial plexus block with duration of analgesia as the primary outcome. The Study period was from December 2016 to June 2018 (1.5 years) after getting clearance from Institutional Ethics Committee and study duration was 1½ years. Analysis was done using Excel 2007 worksheet and SPSS 16 statistical software Qualitative data were expressed in proportion and percentage. Quantitative data expressed as mean and SD. Bivariable analysis was done using students t-test and chi-square test. The supraclavicular block lasted significantly longer in patients who received intravenous dexamethasone compared with perineural dexamethasone (p=0.001).With respect to secondary outcomes, there was a reduction in total post-operative morphine equivalent administration in perineural dexamethasone compared with intravenous dexamethasone (p= 0.002). We have concluded that 8 mg of intravenous dexamethasone extended the duration of analgesia and reduced pain scores. We suggest that intravenous dexamethasone be preferred, as its use is licensed and the possibility of neurotoxicty is avoided.

Keywords: Intravenous dexamethasone • Brachial plexus block • Perineural dexamethasone

Introduction

Postoperative pain, an unpleasant experience negatively affects postoperative recovery; it delays hospital discharge and can increase the risk of postoperative complications and development of chronic pain [1]. Optimization of postoperative pain control plays an important role in the outcome of orthopaedic surgeries, permitting early rehabilitation [2]. Preoperative local anesthetic brachial plexus blockade significantly reduces postoperative discomfort, and can reduce opioid consumption [3]. Dexamethasone has been evaluated as an adjunct to regional anaesthesia compared to placebo. Perineural dexamethasone appears to prolong the duration of analgesia after brachial plexus block when combined with local anaesthetics lidocaine and bupivacaine [4-5]. Several studies have compared intravenous with perineural dexamethasone in upper extremity surgeries [6]. There is concern regarding potential neural toxicity of perineural dexamethasone; however, the evidence is not conclusive, and in fact some data suggest that dexamethasone may actually protect against local anesthetic neuronal toxicity [7-8]. Studies have shown intravenous dexamethasone when combined with brachial plexus block has prolonged block effect equivalent to or more than perineural dexamethasone.

Mechanism of action of dexamethasone 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 [9]. Dexamethasone as a single drug is not neurotoxic in cell culture, but there is a dose-response worsening of ropivacaine-induced neurotoxicity in cell culture [10]. The primary focus of Brummett CM is the effect of the additive on the duration of analgesia, neurotoxicity and other safety concerns [6]. More recent publications since the aforementioned review indicate that 8 mg dexamethasone added to perineural local anesthetic injections augment the duration of peripheral nerve block analgesia.

This observational study aimed to find out whether intravenous dexamethasone compared to perineural dexamethaone had similar or superior effects in prolonging the duration of nerve block, as adjunct to local anaesthetic brachial plexus block in forearm surgeries. The primary outcome of our study was duration of analgesia and secondary outcomes were amount of post-operative opioid dose at 24 hours in mg morphine equivalents and time until first dose of analgesic in hours.

Methods

The study was conducted on 222 patients, in the age group 18-65, posted for upper limb forearm surgeries under supraclavicular brachial plexus block in the Department of Anaesthesiology, Government Medical College, and Thiruvananthapuram.

Informed written consent was taken. Result values were recorded using a preset profoma. A prospective cohort study to compare the effectiveness of perineural dexamethasone 8 mg with 0.5% ropivacaine versus intravenous dexamethasone 8mg with 0.5% ropivacaine in supraclavicular brachial plexus block in upper limb orthopaedic surgeries.

Inclusion criteria

- Patients in the age group of 18 years till 65 years weighing 60 to 80 kg of either sex
- Patients willing to provide written informed consent
- Patients scheduled to undergo elective forearm surgeries

Exclusion criteria

- Patient refusing block

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- Inability to give consent
- Pregnancy
- Diabetes mellitus.
- Patient with an allergy to amide local anaesthetic or dexamethasone
- Contraindication to brachial plexus block

Method

After Research Methodology and Ethical Committee approval for the study, study subjects were selected from among those coming for orthopaedic surgery of forearm or hand during the period of study at Medical college hospital. Subjects were assessed in the pre-anaesthetic assessment clinic and categorized into ASA classes. Only patients belonging to ASA class 1, 2 and satisfying the inclusion and exclusion criteria were considered for the study. Selected patients were asked about their willingness to participate in the study after explaining the details of the study to them.

Pre-Operative Evaluation:

- Detailed history
- Age and weight

Investigations:

- Hemoglobin
- Total and differential count
- Blood urea
- Routine urine examination
- Chest Xray
- ECG

Type of surgeries: ORIF/External fixation/ debridement/ tendon repair

Procedure

- Both perineural dexamethasone and intravenous dexamethasone were routinely used as adjuvancts to local anaesthetic for brachial plexus block in the Dept of anaesthesia, Medical college, Thiruvananthapuram for forearm surgery. The regimen was chosen and patients were allocated randomly. 222 patients satisfying the inclusion criteria were included in the study.The anaesthesiologists in charge, allocated patients alternatively to receive either perineural dexamethasone with local anesthetic (Group A), or intravenous dexamethasone with local anesthetic (Group B) in the brachial plexus block.
- All patients received supraclavicular brachial plexus block using ultrasound guided technique using 6-13 MHz 38-mm linear array transducer (M-Turbo; Sonosite Inc, USA), performed by one of the two anaesthesiologist. All were highly experienced in the technique. Sedation for block insertion was achieved using intravenous fentanyl upto 100 microgram and midazolam upto 2 milligram. Patients in the perineural dexamethasone group (Group A) received a block injection with 28 ml ropivacaine 0.5% mixed with 2 ml of 8 mg preservative free dexamethasone in saline 0.9% to a volume of 30 ml. We gave 5 ml saline 0.9% intravenously over 3 min at the time of the block. Patients in the intravenous dexamethasone group (Group B) received block injection with 28 ml ropivacaine 0.5% mixed with 2 ml saline 0.9% to a volume of 30 ml, and 8 mg intravenous dexamethasone mixed with saline 0.9% to a total volume of 5 ml administered as above. The dose of dexamethasone was chosen in line with recent studies [11]. Block success was taken as the patient's inability to flex the forearm and profound forearm numbness.
- All patients subsequently underwent standardized general anesthesia in supine position using propofol, fentanyl, succinylcholine, sevoflurane or isoflurane and ondansetron; a neostigmine/glycopylorate mixture was used to reverse residual neuromuscular blockade. Intra-operative fentanyl was limited to 100 microgram; no long acting opioids were given. Patients had standardised postoperative pain management regimen for 24 h after block placement.
- The duration of analgesia, onset and duration of sensory block, onset and duration of motor block were recorded at the first minute and at 30 min, 480 min, 720 min, and 920 min after completion of injection. Nausea score were recorded after the block at 480 min, 720 min and 920 min.
- Data collection was by means of a patient diary completed either with assistance from nursing staff or with assistance from patient's bystanders. The analgesic regimen for the first 24 hours after arrival in the Ortho-ICU consisted of intravenous diclofenac sodium aqua 75 mg every 8 h and intravenous morphine as required. Opioid consumption was tabulated using patient diary and converted to morphine equivalents using standard conversions.

Discussion

Brachial plexus blockade for upper limb surgeries is one of the most common major peripheral nerve block techniques. This study builds on a limited number of studies examining the efficacy of systemic dexamethasone administered at the time of upper extremity regional block compared with perineural administration of dexamethasone in the block local anaesthetic solution [12].

Choi concluded that perineural dexamethasone prolonged the effects of brachial plexus block with no observed side-effects. We were able to confirm that block duration is increased with intravenous dexamethasone compared with perineural dexamethasone. However pain scores are reduced by dexamethasone by both the perineural and intravenous routes. We observed that an opiod-sparing effect in both dexamethasone groups 24 hour after Ortho-ICU arrival, however perineural dexamethasone demonstrated superior and decreased mean opiod dose 24 hour after Ortho-ICU arrival compared to intravenous dexamethasone.

Fewer patients were given anti-emetics in both perineural and intravenous dexamethasone groups, and this is consistent with previous reports of the drug's anti-emetic effect [13]. In our study we have observed that Intravenous dexamethasone has slightly better than perineural dexamethasone, although their effects were not statistically significant.

Rosenfeld showed similar effects of perineural and systemic dexamethasone, with 120 patients undergoing shoulder surgeries with interscalene block randomized similarly to our study except for supraclavicular block technique and forearm surgeries using 0.5% ropivacaine and 8mg dexamethasone [14].

Their study arrived at the same conclusion as ours that block duration is prolonged in intravenous group than perineural dexamethasone group, postoperative opioid dose at 24 hours requirement is more in intravenous dexamethasone group compared to perineural dexamethasone group, time until first dose of analgesic also does not conflict with our results. Rosenfeld had a third group which used saline as placebo but our study had only two groups; hence the data cannot be directly compared, but Rosenfeld's patients also received medication when a specific pain score was attained.

Desmet a similar study showed statistically significant improvement in pain scores up until 48 h in the dexamethasone groups, whereas we have found an improvement only until 16 h [15]. As noted by Abdallah the significance of Desmet pain score analysis is difficult to determine as they used a four-point verbal rating scale with a strategy that considers up to 75% of pain scores equivalent [16]. We used an 11-point visual analogue scale

with pain scores reported at more frequent intervals. It has been shown that visual analogue scales are more sensitive and potentially superior to four-point verbal categorical rating scale when assessing acute pain [17].

Abdallah performed a three arm study with similar treatment groups as of Rosenfeld, utilizing supraclavicular blocks in upper extremity surgeries with 8 mg dexamethasone. Their difference existed in choice of local anaesthetics as Abdallah and collegues used 0.5% bupivacaine, whereas Rosenfeld used 0.5% ropivacaine which is similar to that of our study. All three studies Rosenfeld, Abdallah and Desmet were consistent with their conclusion, demonstrating improved effectiveness of both perineural and intravenous dexamethasone vs placebo. Our study differs from the above three studies in a manner, that we used two arm study comparing perineural and intravenous dexamethasone alone. Their primary outcome was duration of analgesia, defined as the time until first report of postoperative pain at the surgical site. Abdallah's supraclavicular blocks with 0.5% bupivacaine lasted 25 h in both dexamethasone groups, whereas ours with 0.5% ropivacaine lasted 15.5 h and 18 h in the perineural and intravenous dexamethasone groups, respectively. They also demonstrated a significant improvement in patient satisfaction.

Kawanishi published results of similar three-arm design with interscalene block using a 0.75% ropivacaine and 4 mg dexamethasone in arthroscopic shoulder surgeries [18]. Their primary outcome was time until first request for breakthrough analgesia. They concluded that perineural dexamethasone provided longer lasting blockade than either systemic dexamethasone or placebo; however, as noted by Abdallah, with only 39 patients in total, their study lacked statistical power to definitively differentiate between groups.

Baeriswyl concluded that there is moderate evidence that perineural dexamethasone combined with bupivacaine but not with ropivacaine slightly prolongs the duration of analgesia when compared with systemic dexamethasone, without an impact on the other secondary pain-related outcomes [19]. The administration of dexamethasone in this setting should be balanced properly with recognition of the off-label indication of perineural administration and with consideration for the possibility of crystallization when combined with ropivacaine. This study is in our favour supporting the use of intravenous dexamethasone as an adjunct to local anaesthetics but not perineural dexamethasone. However there is not enough studies supporting the use of intravenous dexamethasone over perineural dexamethasone as an adjunct to local anaesthetics for brachial plexus blockade.

The use of a single intravenous dose of corticosteroids to reduce postoperative pain was reviewed by Waldron [20]. They found a small but significant reduction in postoperative pain, opioid consumption, rescue analgesia and a longer time to first rescue analgesic dose. No increase in risk for infection or delayed wound healing was noted, although there was slight hyperglycemia on the first postoperative day. There are patient populations where avoidance of intravenous dexamethasone should be considered, including those at high risk for peri-operative hyperglycemia, increased infection risk or patients whose wounds might heal poorly.

There is a debate whether perineural corticosteroids may be harmful; there is, however some consensus. Reports of neurotoxicity seem to be related to the vehicle polyethylene glycol and the preservative benzyl alcohol in some preparations, as well as the presence of insoluble steroid particulate matter in the injectate [21]. Dexamethasone is non-particulate and is available in a preservative-free formulation; this was used in our study.

This study has several advantages and few limitations. Our study calculated the sample size from Rosenfeld who used three arm study compared to two arm study as ours which has very few studies of this kind. We chose 8 mg as the dose for perineural injection and used the same dose intravenously [22]. Desmet further examined intravenous dexamethasone infused immediately before interscalene block. Both 2.5 mg and 10 mg doses prolonged the time until the first request for rescue analgesic compared with 1.25 mg dexamethasone and saline. An 8 mg dexamethasone dose was not studied. We opted for 8 mg dexamethasone, as Rosenfeld used 8 mg dose and found no side effects and attained the expected results of prolonging the block duration. Although we did explore patient satisfaction, it was not measured using a validated specialized satisfaction assessment tool. These are, however, unlikely to have a significant impact on our findings.

Conclusion

We have demonstrated that 8 mg of intravenous dexamethasone with ropivacaine 0.5% supraclavicular block in forearm surgeries extended the duration of analgesia and reduced pain scores. Both routes of administration also reduced opioid consumption and request for antiemetics, with perineural dexamethasone showing superiority over intravenous dexamethasone in reducing opioid consumption. We suggest that intravenous dexamethasone be preferred, as its use is licensed and the possibility of neurotoxicty is avoided.

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