International Journal of Pharmacological Research
ISSN: 2277-3312 (Online)
Journal DOI: https://doi.org/10.7439/ijpr **Research Article**

To evaluate the efficacy of addition of dexmedetomidine to bupivacaine versus bupivacaine administered as a nerve block for post operative analgesia in patients undergoing lefort I osteotomy

P. Pravahitha* and M. R. Mutushekar

Department of Oral and Maxillofacial Surgery, Saveetha Dental College, Saveetha University, Chennai, India

QR Code

***Correspondence Info:**
Dr. P. Pravahitha
Department of Oral and Maxillofacial Surgery,
Saveetha Dental College, Saveetha University, Chennai, India

***Article History:**
Received: 03/08/2018
Revised: 04/10/2018
Accepted: 17/10/2018
DOI: https://doi.org/10.7439/ijpr.v8i10.4686

Abstract

Background and objective: The effect of dexmedetomidine on the duration of sensory blockade has not been studied in humans. We evaluated the effect of adding dexmedetomidine to bupivacaine on the duration of postoperative analgesia in children who underwent Lefort I osteotomy.

Methods: Ten patients who were scheduled for Lefort I osteotomy using a combination of general anaesthesia and greater palatine nerve block was allocated randomly into one of two equal groups. In both groups, two infraorbital and two posterior superior alveolar nerves was performed bilaterally using 2 ml of solution on each side. The Bupivacaine-dexmedtomidine group received bupivacaine 0.25%, with 1mg/kg dexmedetomidine whereas the Bupivacaine group received bupivacaine 0.25%. Heart rate, systolic blood pressure, pain score, the time to the first request for analgesia, and the degree of sedation were recorded.

Results: There was no difference in haemodynamic variables between the two groups. The pain score was significantly higher in the B group as compared with the Bupivacaine-Dexmedetomidine group. The time to the first request for analgesia was significantly longer in patients in the Bupivacaine-Dexmedetomidine group (mean 22 h, range 20.6 – 23.7 h) as compared with those who received bupivacaine alone (14.2 h, 13 – 15 h). Sedation scores in the postoperative period did not differ between the study groups.

Conclusion: Nerve block with a combination of dexmedetomidine and bupivacaine increased the duration of analgesia after Lefort I osteotomy by 50% with no clinically relevant side effects.

Keywords: Dexmedetomidine, Bupivacaine, Lefort I osteotomy, Regional anaesthesia.

1. Introduction

It has been advocated that regional anaesthesia can provide analgesia in patients without the risk of respiratory depression.[2] However regional blocks are problematic because they provide only a partly effective block with a limited duration of analgesia after a single dose. This problem can be overcome by the addition of various adjuvants to local anaesthetics with the aim of potentiating and prolonging the analgesic effect.[3]

Clonidine is an a2-adrenoceptor agonist that has been used as an adjuvant to regional anaesthesia in several studies.[4] Although some clinical reports have found that clonidine can prolong the duration of analgesia in peripheral nerve blocks,[5-7] others have shown no beneficial effect.[8-10] Dexmedetomidine (DEX) is a potent a_2- adrenoceptor agonist and is approximately eight timesmore selective for the a2-adrenoceptor than clonidine.[11] Several studies have found Dexmedetomidine to be well tolerated and effective in various neuraxial and regional anaesthetics in humans, including during the delivery of intrathecal,[12] caudal,[13] This is the first prospective randomized study to compare the analgesic efficacy of a bupivacaine – Dexmedetomidine mixture with that of bupivacaine alone after perineural

injection in humans[14-15]. We hypothesized that the addition of 1 mg/ kg Dexmedetomidine to 0.25% bupivacaine would prolong the duration of analgesia of nerve block in a series of patients who were undergoing Lefort I osteotomy.

2. Methods

After the approval of the study by Ethical committee of Saveetha Dental College, we recruited 10 patients who had American Society of Anesthesiologists (ASA) physical status I or II and who were scheduled for Lefort I osteotomy .Written informed consent was obtained from the patients. Exclusion criteria included a history of allergic reaction to local anaesthetics, coagulopathy, or major systemic illness. General anaesthesia was induced by the inhalation of 6% isoflurane in 100% oxygen via face mask with spontaneous ventilation. Anaesthesia was maintained with isoflurane adjusted between 3 and 4% in an oxygen/air mixture. Lactated Ringer's solution was infused at a rate of 10– 15 ml kg 1 h 1. All patients received dexamethasone (1 mg kg 1 i.v.) before the start of surgery. No additional analgesia or sedative agents were given.

After the induction of anaesthesia, patients were allocated randomly into one of two equal groups. The randomization was achieved by the opening of a sealed envelope by the attending physician. In both groups, the infraorbital and posterior superior alveolar was performed bilaterally using 2ml of solution on each side. The Bupivacaine group received bupivacaine 0.25%, whereas the Bupivacaine-Dexmedetomidine group received bupivacaine 0.25% with 1 mg/kg Dexmedetomidine. After the surgical procedure 4 blocks were administered 2 blocks on either side using 1ml of the solution. Attending physician was not blinded to the study drug.

The success of the block was measured by assessment of the haemodynamic stability, as indicated by the absence of an increase in heart rate and/or systolic arterial pressure of more than 20% compared with baseline values obtained just before the first surgical incision. If the block had failed, fentanyl (1 mg kg 1 i.v.) was administered. Clinically relevant bradycardias or hypotension (defined as a 30% decrease in heart rate and systolic blood pressure, respectively, as compared with the base- line values) were treated with atropine or ephedrine as appropriate

2.1 Patient monitoring:

Haemodynamic variables (heart rate and systolic blood pressure) were recorded at the baseline (after the induction of anaesthesia and before placement of the block) and every 30min until the end of surgery [16]. Postoperative pain was assessed using the VAS by quantifying pain behaviours with scores that range from 0 (no pain) to 10 (the maximum possible pain).[17] The pain score was assessed at the time of extubation at the end of surgery and subsequently every 1 h for 3h postoperatively. When the postoperative pain score exceeded four, rescue analgesia was given with a 20 mg kg 1 ketorolac. The time to the first demand for analgesia and the total number of patients who required postoperative pain medication during the 24-h period were recorded.

The degree of sedation was evaluated by using Ramsay sedation scale based on eye opening: alert with spontaneous eye opening; drowsy with eyes only opening in response to glabellar tap sedated with eyes opening in response to physical stimulation [18] Sedation was assessed hourly for the first 3 h postoperatively. Complications such as nausea, vomiting, and haematoma formation at the site of injection were recorded. All the assessments of the variables studied were recorded by nurse observers who were unaware of the allocation of treatment group.

2.2 Statistical analysis

The means and SDs used to calculate the sample size were obtained from a previous pilot study. An a priori t-test power analysis indicated that 5 patients would be needed in each of the two groups to detect a 30% increase in the duration of analgesia with the addition of Dexmedetomidine with 90% power. Categorical variables are assessed using the x2 or Fisher exact test, wherever appropriate. Haemodynamic data are presented as the mean (SD) and were analysed by two- way analysis of variance with repeated measures and post- hoc Dunnett's tests.

The pain and sedation scores were analysed with the Mann – Whitney U-test. The duration of postoperativepain relief was also compared with a log-rank test using the Kaplan–Meier survival analysis. A P value lower than 0.05 was considered to be statistically significant. SPSS v15.0 for Windows software (SPSS, Inc, Chicago, Illinois, USA) was used for statistical analyses.

3. Results

Ten patients were enrolled in and all completed the study. Demographic data were comparable between the study groups. In both groups, heart rate and systolic blood pressure decreased significantly relative to the baseline values; however, no differences in the haemodynamic variables were observed between the two groups.

The Kaplan–Meier survival curves for the two groups showed that the time to the first request for analgesia was longer in children who received the bupivacaine – Dexmedetomidine mixture [mean 22 (21 – 24) h, 95% confidence interval (CI)] as compared with those who received bupivacaine alone [14.2 (13 – 15) h, 95% CI, $P < 0.001$ by log-rank test for equality in survivor function. The pain scores of the patients at 8, 12, 16, 20,

and 24 h were significantly higher in the Bupivacaine group as compared with the Bupivacaine-dexmedetomidine group.

All patients in the B group required postoperative pain medication during the first 24h compared with 2 patients (66.6%) in the BD group (P1⁄40.04). The sedation score in the postoperative period did not differ between the studies groups, one of the patient in the Bupivacaine group vomited compared with two in the Bupivacaine-Dexmedetomidine group.

4. Discussion

The main result of the study described herein was that the addition of Dexmedetomidine to bupivacaine extended the duration of analgesia afternerve blocks in patientsundergoing Lefort I osteotomy.

Recently, Brummett *et al* showed that the sensory blockade in rats was enhanced significantly when Dexmedtomidine was added to bupivacaine.

The mechanism of action of a2-adrenoceptor agonists in peripheral nerve blocks is not understood fully. Proposedmechanisms include central analgesia, vasoconstriction, and anti-inflammatory effects.[19] However, none of these mechanisms can explain fully the synergistic effect of a2-adrenoceptor agonists when added to a local anaesthetic in peripheral nerve blocks. The direct action of a2-adrenoceptors on the peripheral nerve may be mediated through an increase in hyperpolarization of the afterpotential that follows a single compound action potential.[20] It is well known that in peripheral myelinated and nonmyelinated fibres, membrane hyperpolarization develops during and after stimulation and mainly results from the activation of the sodium–potassium pump after the transient influx of sodium ions.[21]

Dalle *et al* [22] found that clonidine increases the hyperpolarization that develops during low-frequency stimulation by inhibiting the hyperpolarization-activated cation current. The Ih current is activated during the hyperpolarization phase of an action potential and acts to reset a nerve for sub- sequent action potentials. Thus, clonidine enhances the level of hyperpolarization by blocking the Ih current and thus inhibits subsequent action potentials. Dexmedetomidine is a selective a2-adrenoceptor agonist and it may enhance the sensory blockade in a manner similar to clonidine.

We found that 1 mg/kg Dexmedetomidine prolonged the duration of postoperative analgesia by nearly 50%.[5] In the current study, the mean pain score remained low in the Bupivacaine-Dexmedtomidine group during the first 24 h after surgery with no relevant intraoperative cardiovascular effects or systemic sedative effects.

Another limitation of the current study was that we could not elucidate the mechanism by which Dexmedetomidine enhances local anaesthetics in peripheral nerve blocks.

5. Conclusion

In conclusion, the addition of DEX to bupivacaine in nerve blocks in children undergoing Lefort I osteotomy resulted in a 50% increase in the duration of postoperative analgesia with no adverse side effects

References

[1]. Strong EB, Buckmiller LM. Management of the cleft palate. *Facial Plast Surg Clin North Am* 2001; 9:15–25.

[2]. Hatch DJ. Analgesia in the neonate. *Br Med J (Clin Res Ed)* 1987; 294:920.

[3]. Hager H, Marhofer P, Sitzwohl C, *et al*. Caudal clonidine prolongs analgesia from caudal S(þ)-ketamine in children. *Anesth Analg* 2002; 94:1169-1172.

[4]. Eisenach JC, De Kock M, Klimscha W. alpha (2)-Adrenergic agonists for regional anesthesia: a clinical review of clonidine (1984–1995). *Anesthesiology* 1996; 85:655–674.

[5]. Casati A, Magistris L, Fanelli G, *et al*. Small-dose clonidine prolongs postoperative analgesia after sciatic-femoral nerve block with 0.75% ropivacaine for foot surgery. *Anesth Analg* 2000; 91:388–392.

[6]. El Saied AH, Steyn MP, Ansermino JM. Clonidine prolongs the effect of ropivacaine for axillary brachial plexus blockade. *Can J Anaesth* 2000; 47:962 – 967.

[7]. Eledjam JJ, Deschodt J, Viel EJ, *et al*. Brachial plexus block with bupivacaine: effects of added alpha-adrenergic agonists – comparison between clonidine and epinephrine. *Can J Anaesth* 1991; 38:870–875.

[8]. Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anesthetic does not prolong postoperative analgesia after brachial plexus block but does induce hemodynamic changes. *Anesth Analg* 2001; 92:199–204.

[9]. Duma A, Urbanek B, Sitzwohl C, *et al*. Clonidine as an adjuvant to local anaesthetic axillary brachial plexus block: a randomized, controlled study. *Br J Anaesth* 2005; 94:112–116.

[10]. Gaumann D, Forster A, Griessen M, *et al*. Comparison between clonidine and epinephrine admixture to lidocaine in brachial plexus block. *Anesth Analg* 1992; 75:69-74.

[11]. Jaakola ML, Ali-Melkkila T, Kanto J, *et al*. Dexmedetomidine reduces intraocular pressure, intubation responses and anaesthetic requirements in

patients undergoing ophthalmic surgery. *Br J Anaesth* 1992; 68:570-575.

[12]. Kanazi GE, Aouad MT, Jabbour-Khoury SI, *et al*. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. *Acta Anaesthesiol Scand* 2006; 50: 222 – 227.

[13]. Saadawy I, Boker A, Elshahawy MA, *et al*. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. *Acta Anaesthesiol Scand* 2009; 53: 251–256.

[14]. Memis D, Turan A, Karamanlioglu B, *et al*. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. *Anesth Analg* 2004; 98: 835 – 840.

[15]. Brummett CM, Norat MA, Palmisano JM, Lydic R. Perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat. *Anesthesiology* 2008; 109: 502–511.

[16]. Malamed SF, Trieger N. Intraoral maxillary nerve block: an anatomical and clinical study. *Anesth Prog* 1983; 30: 44–48.

[17]. Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatr Nurs* 1997; 23: 293–297.

[18]. Doyle E, Harper I, Morton NS. Patient-controlled analgesia with low dose background infusions after lower abdominal surgery in children. *Br J Anaesth* 1993; 71: 818–822.

[19]. Iskandar H, Benard A, Ruel-Raymond J, *et al*. The analgesic effect of interscalene block using clonidine as an analgesic for shoulder arthroscopy. *Anesth Analg* 2003; 96: 260–262.

[20]. Gaumann DM, Brunet PC, Jirounek P. Hyperpolarizing afterpotentials in C fibers and local anesthetic effects of clonidine and lidocaine. *Pharmacology* 1994; 48: 21–29.

[21]. Gordon TR, Kocsis JD, Waxman SG. Electrogenic pump (Naþ/K(þ)- ATPase) activity in rat optic nerve. *Neuroscience* 1990; 37:829–837.

[22]. Dalle C, Schneider M, Clergue F, *et al*. Inhibition of the I(h) current in isolated peripheral nerve: a novel mode of peripheral antinociception? *Muscle Nerve* 2001; 24: 254–261.

[23]. Dalle C, Schneider M, Clergue F, *et al*. Inhibition of the I(h) current in isolated peripheral nerve: a novel mode of peripheral antinociception? *Muscle Nerve* 2001; 24:254–261.