

Comparison between Dexmedetomidine and Ketorolac as an Adjuvant to Local Anaesthetic for IVRA to Prolong Post-Operative Analgesia

Videet Shah^{1*}, Karthikeyen RK², Pramod Patil³, Dhanashree Mahajan⁴

¹Junior Resident, Department of Anesthesia, SMBT Institute of Medical Sciences and Research Centre, Nashik, India

²Junior Resident, Department of Anesthesia, SMBT Institute of Medical Sciences and Research Centre, Nashik, India

³Professor, Department of Anesthesia, SMBT Institute of Medical Sciences and Research Centre, Nashik, India

⁴Junior Resident, Department of Anesthesia, SMBT Institute of Medical Sciences and Research Centre, Nashik, India

Received: 23-01-2023 / Revised: 27-02-2023 / Accepted: 10-03-2023

Corresponding author: Dr. Videet Shah

Conflict of interest: Nil

Abstract

Introduction: Intravenous regional anesthesia (IVRA) is a technique for inducing anaesthesia in a part of the limb by injecting a local anaesthetic intravenously into an extremity that is isolated from the remainder of the circulatory system with a tourniquet. Dexmedetomidine is an α_2 -adrenoreceptor (AR) agonist and ketorolac works by preventing the production of inflammatory mediators.

Aims and Objectives: To compare the efficacy between Dexmedetomidine and Ketorolac as adjuvants to local anaesthetic for IVRA to prolong post-operative analgesia.

Materials and Methods: A randomized observer-blind prospective study was conducted on patients who are undergoing intravenous regional anesthesia for upper limb surgery. They were divided into two groups group D Lignocaine 0.5% solution, 0.6ml/kg (maximum- 40ml) + Dexmedetomidine 30mcg and group K Lignocaine 0.5%, 0.6ml/kg (maximum- 40ml) + Ketorolac 15mg, 30 patients in each group. Post-operative patients were observed in recovery for two hours before being transferred to the appropriate ward. Timing of drug injection, beginning of sensory and motor block, pain from tourniquet, and initial demand for painkillers were all reported.

Results: The mean time for the requirement of first rescue analgesia (140.67 vs 131.23 mins; p=0.26) and VAS score at the demand (6.47 vs 6.17; p=0.47) were comparable in cases of group A and group B respectively. Mean systolic blood pressure was comparable between the two groups at baseline and throughout surgery till 2 hours follow-up period (p>0.05). Mean diastolic blood pressure was comparable between the two groups at baseline and throughout surgery till 2 hours follow-up period (p>0.05).

Conclusion: The study has concluded that lignocaine and dexmedetomidine are both almost beneficial but the duration of the post-operative analgesia between the two groups was statistically significant.

Keywords: Ketorolac, Intravenous Regional Anesthesia (IVRA), Dexmedetomidine, Adjuvants.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative

(<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

To avoid the effects of general anaesthesia and upper airway instrumentation, intravenous regional anaesthesia (IVRA) is a technique for inducing anaesthesia in a part of the limb by injecting a local anaesthetic intravenously into an extremity that is isolated from the remainder of the circulatory system with a tourniquet [1,2]. It causes skeletal muscle relaxation and anaesthesia to start working quickly. Due to its quick start of the action, topical anaesthetic activity, and intermediate length of activity, lidocaine 0.5% is probably the local anaesthetic that is used for this method the most frequently [3,4]. The discomfort of the tourniquet is a limiting factor for prolonged procedures. Tourniquet pain has been theorized to result from either nerve fibre activation directly beneath the tourniquet or from ischemia of the peripheral neurons or nociceptors distant to it. Moreover, tourniquet discomfort is caused by the release of mediators of inflammation as a result of mechanical damage and tissue ischemia beneath or distal to the tourniquet [5,6].

The more often used regional anaesthetic method for procedures on the upper limb is the brachial plexus block via the supraclavicular route. But it needs technical know-how, solid anatomical understanding, and accurate surface landmark recognition [7]. It is vulnerable to problems such as pneumothorax, accidental intravascular injection, patchy or insufficient analgesia, block failure, delayed onset of analgesia, and infrequent nerve damage. For short-term procedures on the upper limbs, intravenous regional anaesthesia (IVRA), which has a high success rate [1], can be a feasible substitute for brachial plexus block. When compared to peripheral nerve blocks, IVRA's biggest flaw is its inability to give postoperative analgesia [8,9].

In IVRA, several substances have been used as adjuvants to local anesthetics to increase tourniquet tolerance and postoperative analgesia, and decrease the amount of local anesthetic used. These substances include opioids like fentanyl and morphine, clonidine, and ketorolac, muscle relaxants like cisatracurium and ketamine, and bicarbonate alkalization [10,11].

Due to its calming and analgesic properties, dexmedetomidine is an α_2 -adrenoreceptor (AR) agonist that has been the focus of numerous anesthetic studies. Compared to clonidine, it is about 8 times more specific for the α_2 -AR [12,13]. It causes analgesia in individuals and can reduce the need for anesthesia by up to 90%. As a result, it is regarded as a complete receptor agonist (with more potent neurological and fewer cardiovascular effects). Its extremely lipophilic nature enables fast binding to the α_2 -AR of the spinal cord and α_2A -AR of peripheral neurons as well as absorption into the cerebrospinal fluid [14-16]. In IVRA, dexmedetomidine has been used successfully. The only NSAID with approval for intravenous usage, ketorolac works by preventing the production of inflammatory mediators [17].

Materials and methods

Study design

A randomized observer-blind prospective study was conducted on patients who came to the anesthesiology department of a tertiary care hospital who are undergoing intravenous regional anaesthesia for upper limb surgery. A total of 60 patients were included in the study and divided into two groups group D Lignocaine 0.5% solution, 0.6ml/kg (maximum- 40ml) + Dexmedetomidine 30mcg and group K Lignocaine 0.5%, 0.6ml/kg (maximum-40ml) + Ketorolac 15mg, 30 patients in

each group. The study was conducted for two years.

A co-resident used the Sealed Envelope approach to randomly assign patients in the preoperative room to either group "D" (lignocaine with dexmedetomidine) or "K" (lignocaine with ketorolac) to keep the observer in the dark.

Pulse oximetry, NIBP, and ECG were constantly monitored in the operating room during the surgery by the Indian Society of Anaesthesiologists' (ISA) minimal monitoring standards.

A non-surgical extremity was given intravenous (IV) access for the delivery of medication and fluids. Pre-medication for the patients included intravenous administration of Midazolam 1 mg, Ondansetron 4 mg (iv), and antibiotics.

The elastic tourniquet was then withdrawn once the proximal pneumatic tourniquet was inflated to a pressure that was at least 50 to 100 mm Hg higher than the patient's systolic pressure (maximum 250 mm Hg).

The absence of a radial pulse and the loss of a pulse oximetry trace in the ipsilateral index finger served as evidence that the upper limb was circulatory isolated. The early signs of lignocaine toxicity, such as circumoral numbness, a metallic taste, dizziness, tongue paraesthesia, tinnitus, and blurred vision, were explained to the patients.

The intravenous medicine (local anaesthetic solution) was administered over two to three minutes, as per the group's instructions, while indicators of local anesthetic toxicity were being watched for. With the help of the "Modified Bromage scale for upper limb," motor function was evaluated.

We inflated the distal cuff with the same pressure after achieving total sensory blackout, then deflated the proximal cuff. After that, we carried out the procedure while keeping an eye out for any adverse effects of the local anesthetic.

Post-operative patients were observed in recovery for two hours before being transferred to the appropriate ward. Timing of drug injection, and initial demand for painkillers were all reported.

Inclusion criteria

1. Below elbow surgery with predicted surgical time less than 90 min.
2. Age 18 – 60 years.
3. Both Genders.
4. Weight 50-80kg.
5. ASA Grade I, II (Elective and Emergency cases)

Exclusion criteria

1. Cellulitis / Infected extremities
2. Neurovascular injuries to the affected limb
3. Sickle Cell disease.
4. Arteriovenous Fistula
5. Compound Fractures
6. H/O Local Anaesthetic hypersensitivity.
7. The patient requires general anesthesia

Statistical analysis

A pre-made study proforma contained all the data that was recorded. The frequency and percentage forms of qualitative data were used. By using the Chi-Square test, associations between qualitative variables were evaluated. Mean and SD was used to represent quantitative data. When comparing quantitative data from the two groups, an unpaired t-test was used if the data passed the "Normality test" and a Mann-Whitney test if it failed. The level of significance was set at a p-value of 0.05 or lower. If it was thought necessary, results were illustrated graphically. For the majority of the analysis, SPSS Version 21.0 and Microsoft Excel 2010 were utilized, respectively.

Ethical approval

The patients were given a thorough explanation of the study by the authors. The patients' permissions have been obtained.

The concerned hospital's ethical committee has approved the study's methodology.

Results

The present study included 60 cases undergoing intravenous regional anaesthesia for upper limb surgery in a tertiary care centre. Cases were divided into 2 equal groups of 30 each using computer-generated random numbers:

- Group 'A' (30 patients): Lignocaine 0.5% solution, 0.6ml/kg (maximum- 40ml) + Dexmedetomidine 30 mcg.
- Group 'B' (30 patients): Lignocaine 0.5%, 0.6ml/kg (maximum- 40ml) + Ketorolac 15mg.

The mean age of the cases was 34.3 years with no difference between study groups ($p=0.95$). The mean weight of the cases was 64.02 Kg with no difference between study groups ($p=0.24$). Out of the total 60 cases, 48.3% were in ASA grade I while 51.7% were in ASA grade II with no difference between study groups ($p=1.0$). The mean duration of analgesia i.e. from deflation of tourniquet and time of 1st analgesia demand was significantly comparable between groups A and B respectively (74.13 vs 66.63; $p=0.047$). The mean time for the requirement of first rescue analgesia (129.67 vs 141.23 mins; $p=0.26$) and VAS score at the demand (6.47 vs 6.17; $p=0.47$) were comparable in cases of group A and group B respectively (Table 1).

Table 1: Characteristics of patients included in the study

Characteristics	Group A (lignocaine + Dexmedetomidine) N=30	Group B (lignocaine + ketorolac) N=30	P value
Age (years) (mean \pm SD)	34.10 \pm 11.20	34.60 \pm 11.53	0.95
Weight (kg) (mean \pm SD)	65.77 \pm 12.62	62.27 \pm 10.05	0.24
ASA grade (%)			
I	15 (50%)	14 (46.7%)	1.0
II	15 (50%)	16 (53.3%)	
Duration of post-operative analgesia (mins) (mean \pm SD)	74.13 \pm 41.35	66.63 \pm 30.98	0.047
Postoperative pain parameters (mean \pm SD)			
Time to first analgesia (mins)	129.67 \pm 35.74	141.23 \pm 28.58	0.26
VAS score at first demand of analgesia	6.47 \pm 1.48	6.17 \pm 1.70	0.47

The mean pulse rate was comparable between the two groups at baseline and throughout surgery till 2 hours follow-up period ($p>0.05$). The mean respiratory rate was comparable between the two groups at baseline and throughout surgery till 2 hours follow-up period ($p>0.05$). Mean systolic

blood pressure was comparable between the two groups at baseline and throughout surgery till 2 hours follow-up period ($p>0.05$). Mean diastolic blood pressure was comparable between the two groups at baseline and throughout surgery till 2 hours follow-up period ($p>0.05$) (table 2).

Table 2: Mean comparison of study groups as per pulse rate, respiratory rate, SBP, and DBP.

Mean comparison	Group A (lignocaine + Dexmedetomidine) N=30	Group B (lignocaine + ketorolac) N=30	P value
Pulse rate (mean \pm SD)			
10 min	82.53 \pm 12.79	80.63 \pm 10.59	0.53
30 min	81.23 \pm 12.11	80.27 \pm 11.40	0.75
90 min	78.90 \pm 11.96	78.37 \pm 10.21	0.85
120 min	77.43 \pm 11.25	76.27 \pm 9.90	0.67
Respiratory rate (mean \pm SD)			
10 min	17.13 \pm 1.55	17.03 \pm 1.45	0.79
30 min	17.20 \pm 1.54	17.10 \pm 1.24	0.78
90 min	17.30 \pm 1.47	17.33 \pm 1.52	0.78
120 min	17.33 \pm 1.52	17.10 \pm 1.35	0.53
SBP (mean \pm SD)			
10 min	133.09 \pm 10.37	134.75 \pm 9.82	0.53
30 min	133.89 \pm 10.92	134.37 \pm 9.25	0.85
90 min	131.68 \pm 10.28	133.79 \pm 10.27	0.43
120 min	131.77 \pm 10.92	132.36 \pm 11.05	0.84
DBP (mean \pm SD)			
10 min	88.50 \pm 6.27	89.61 \pm 5.91	0.55
30 min	89.04 \pm 6.65	89.36 \pm 5.53	0.87
90 min	87.55 \pm 6.22	88.97 \pm 6.21	0.46
120 min	87.62 \pm 6.65	88.01 \pm 6.73	0.82

Discussion

As a comparison to employing an upper arm tourniquet, using a forearm tourniquet during intravenous regional anesthesia (IVRA) may be a possibly safer procedure. For IVRA, ketorolac is a helpful adjuvant to lidocaine [18]. For outpatient hand surgery, research was done to evaluate the effectiveness of IVRA lidocaine and ketorolac administered with either a forearm or upper arm tourniquet. 40 mL of a solution containing 200 mg of lidocaine and 20 mg of ketorolac (0.5 mg/mL) were used to establish upper arm IVRA. 20 mL of a solution containing 100 mg of lidocaine and 10 mg of ketorolac (0.5 mg/mL) were used to establish the forearm IVRA. According to the study, perioperative analgesia for patients having ambulatory hand surgery is safe and effective when given as forearm IVRA with lidocaine and ketorolac. When compared to upper arm IVRA, this method prolongs the sensory

block for a longer period and uses just half the amount of lidocaine and ketorolac [24].

A straightforward, safe, and successful approach with a high success rate for procedures on the upper limbs is intravenous regional anesthesia [19]. The length of postoperative analgesia is a significant drawback of this method. Several adjuvants have been employed to get around this problem [20,21]. Dexmedetomidine 0.5 g/kg-1 as an adjuvant for lignocaine intravenous regional anesthesia was investigated in a study. As an adjuvant to lignocaine for IVRA, dexmedetomidine 0.5 kg-1 shortens the initiation of motor and sensory blocks, enhances the quality of anesthesia, and prolongs postoperative analgesia, according to the study's findings [25].

For distal arm and forearm procedures, an infraclavicular brachial plexus block is the best method. To enhance the effectiveness

of nerve blocks, local anesthetic adjuvant drugs are employed. Adjuvants of two different kinds, dexmedetomidine, and ketorolac, have been applied in several studies [22,23]. The goal of the study was to determine how the local anesthetic adjuvants dexmedetomidine and ketorolac affected the start and duration of infraclavicular brachial plexus block when performed with ultrasound guidance. Due to the presence of lidocaine adjuvants in both protocols for infraclavicular brachial plexus block, the study demonstrated that dexmedetomidine had superior effects on motor and sensory block duration and motor block initiation in comparison to ketorolac. Yet, it took ketorolac longer than dexmedetomidine to respond to an analgesic request. This study is consistent with our study [26].

For upper limb surgery, brachial plexus nerve blocks offer improved analgesia and lower the need for opioids. There are very few trials on ketorolac, but dexamethasone has been a successful adjuvant to local anesthetics in brachial plexus block [24]. The purpose of the study is to examine the duration of analgesia and block features when axillary plexus blocks are performed using dexamethasone or ketorolac as an adjuvant to bupivacaine. In comparison to our study, their study also finds that Dexamethasone and ketorolac dramatically extended analgesia and the duration of the motor and sensory block when used as an adjuvant to bupivacaine in axillary plexus blocks. Dexamethasone exacerbated these effects more than ketorolac did [27].

The effects of administering dexmedetomidine to lidocaine for IVRA on 30 patients were examined by Memis et al. in two groups, group L and group LD. IVRA was accomplished using either 0.5 g/kg of dexmedetomidine plus 3 mg/kg of 2% lidocaine diluted with saline to a final concentration of 40 ml in the dexmedetomidine group or 3 mg/kg of 2% lidocaine diluted with saline to a total dose of 40 ml in the lidocaine group. They

reported that there was a substantial delay in the recovery of motor and sensory blocks in the dexmedetomidine group as well as a reduction at the beginning of the motor and sensory blocks in the dexmedetomidine group, which is consistent with our results [28,29].

Conclusion

The study has concluded that ketorolac and dexmedetomidine are both equally beneficial although the duration of the post-operative analgesia between the two groups was statistically significant.

The goal of the current study was to compare the onset of tourniquet pain after intravenous regional anesthesia using ketorolac versus dexmedetomidine as a lignocaine addition. The results of the trial demonstrated that effective post-operative analgesia can be achieved by IVRA with lignocaine in combination with either ketorolac or dexmedetomidine.

References

1. Stoelting RK. Local anesthetics. In Pharmacology and physiology in anesthetic practice. 3rd ed. Lippincott-Raven. 1999; 158-181.
2. Choyce A, Peng P. A systematic review of adjuncts for intravenous regional anesthesia for surgical procedures. *Can J Anaesth.* 2002; 49:32-45.
3. Esmoğlu A, Akin A, Mizrak A, Turk Y, Boyacı A. Addition of cisatracurium to lidocaine for intravenous regional anesthesia. *J Clin Anesth.* 2006; 18: 194-197.
4. Reuben SS, Steinberg RB, Maciolek H, Manikantan P. An evaluation of the analgesic efficacy of intravenous regional anesthesia with lidocaine and ketorolac using a forearm versus upper arm tourniquet. *Anesth Analg.* 2002; 95:457-460.
5. Tverskoy M, Oren M, Vaskovich M, Dashkovsky I, Kissin I. Ketamine enhances local anesthetic and analgesic effects of bupivacaine by peripheral mechanism: a study in postoperative

- patients. *Neurosci Lett* 1996; 215:5-8.
6. Kol IO, Ozturk H, Kaygusuz K, Gursoy S, Comert B, Mimaroglu C. Addition of dexmedetomidine or lornoxicam to prilocaine in intravenous regional anaesthesia for hand or forearm surgery: a randomized controlled study. *Clin Drug Investig.* 2009; 29:121-129.
 7. Lavin PA, Henderson CL, Vaghadia H. Non-alkalinized and alkalinized 2-chloroprocaine vs lidocaine for intravenous regional anesthesia during outpatient hand surgery. *Can J Anaesth.* 1999; 46:939-945.
 8. Reuben SS, Syeinberg RB, Kreitzer JM, Duprat KM. Intravenous regional anesthesia using lidocaine and ketorolac. *Anesth Analg.* 1995; 81:110-113.
 9. Bigat Z, Boztug N, Hadimioglu N, Cete N, Coskunfirat N, Ertok E. Does dexamethasone improve the quality of intravenous regional anesthesia and analgesia? A randomized, controlled clinical study, *Anesth Analg.* 2006; 102:605-609.
 10. Carollo DS, Nossaman BD, Ramadhyani U. Dexmedetomidine: a review of clinical applications. *Curr Opin Anaesthesiol.* 2008; 21:457-461.
 11. Santini G, Patrignani P, Sciulli MG, Seta F, Tacconelli S, Panara MR, et al. The human pharmacology of monocyte cyclooxygenase 2 inhibition by cortisol and synthetic glucocorticoids. *Clin Pharmacol Ther.* 2001; 70:475-483.
 12. Kaygusuz K, Kol IO, Duger C, Gursoy S, Ozturk H, Kayacan U, et al. Effects of adding dexmedetomidine to levobupivacaine in axillary brachial plexus block. *Curr Ther Res Clin Exp.* 2012; 73:103-111.
 13. Steinberg RB, Reuben SS, Gardner G. The dose-response relationship of ketorolac as a component of intravenous regional anesthesia with lidocaine. *Anesth Analg.* 1998; 86:791-793.
 14. Goel SN, Daftary SR, Pantavaidya SH. Intravenous regional anesthesia using tramadol hydrochloride and ketorolac. *Indian J Anesth.* 2002; 46:369-372.
 15. Brown EM, McGriff JT, Malinowski RW. Intravenous regional anaesthesia (Bier block): Review of 20 years' experience. *Can J Anaesth.* 1989;36(3 Pt 1):307-10.
 16. Choyce A, Peng P. A systematic review of adjuncts for intravenous regional anesthesia for surgical procedures. *Can J Anaesth.* 2002;49:32-45.
 17. Gentili M, Bernard JM, Bonnet F. Adding clonidine to lidocaine for intravenous regional anesthesia prevents tourniquet pain. *Anesth Analg.* 1999;88:1327-30.
 18. Memis D, Turan A, Karamanlioglu B, Pamukcu Z, Kurt I. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. *Anesth Analg.* 2004;98:835-40.
 19. Johnson CN. Intravenous regional anesthesia: New approaches to an old technique. *CRNA.* 2000;11:57-61.
 20. Sardesai SP, Patil KN, Sarkar A. Comparison of clonidine and dexmedetomidine as adjuncts to intravenous regional anaesthesia. *Indian J Anaesth.* 2015;59:733-8.
 21. Gupta A, Mahobia M, Narang N, Mahendra R. A comparative study of two different doses of dexmedetomidine as adjunct to lignocaine in intravenous regional anaesthesia of upper limb surgeries. *Int J Sci Study.* 2014;2:53-62.
 22. Esmaoglu A, Mizrak A, Akin A, Turk Y, Boyaci A. Addition of dexmedetomidine to lidocaine for intravenous regional anaesthesia. *Eur J Anaesthesiol.* 2005;22:447-51.
 23. Kol IO, Ozturk H, Kaygusuz K, Gursoy S, Comert B, Mimaroglu C. Addition of dexmedetomidine or lornoxicam to prilocaine in intravenous regional anaesthesia for hand or forearm surgery: A randomized controlled study. *Clin Drug Investig.* 2009;29:121-9.
 24. Reuben SS, Steinberg RB, Maciolek H, Manikantan P. An evaluation of the

- analgesic efficacy of intravenous regional anesthesia with lidocaine and ketorolac using a forearm versus upper arm tourniquet. *Anesth Analg*. 2002 Aug;95(2):457-60. Retraction in: Shafer SL. *Anesth Analg*. 2009 Apr;108(4):1350.
25. Subramanya V., Kapinigowda S. T., Math A. T., & Chennaiah V. B. Dexmedetomidine as an Adjuvant for Intravenous Regional Anesthesia in Upper Limb Surgeries. *Anesthesia, Essays and Researches*. 2017; 11(3): 661-664.
26. Mirkheshti, A., Saadatniaki, A., Salimi, A., Rasi, A. M., Memary, E., & Yahyaei, H. (2014). Effects of Dexmedetomidine Versus Ketorolac as Local Anesthetic Adjuvants on the Onset and Duration of Infraclavicular Brachial Plexus Block. *Anesthesiology and Pain Medicine*, 2014;4(3).
27. Paramaswamy R., Mahipathy S. R. R. V., Durairaj A. R., & Sundaramurthy N. Comparison of Dexamethasone and Ketorolac as an Adjuvant To Bupivacaine in Axillary Brachial Plexus Blocks for Isolated Hand and Forearm Injuries: A Randomised Double-Blind Prospective Study. *Journal of Clinical and Diagnostic Research*. 2018.
28. Memis D, Turan A, Karamanhoglu B, Pamukçu Z, Kurt I. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. *Anesth Analg* 2004; 98:835-840.
29. M.O. O., T.P. O., & I.A. S.O. Malacological Survey of Intermediate Hosts of Public Health Importance in Akure South and Owo Local Government Areas of Ondo State, Nigeria. *Journal of Medical Research and Health Sciences*. 2023; 6(2): 2414–2423.