Original Research Article

Study of effect of dexmedetomidine with levobupivacaine on the onset and duration of analgesia and anaesthesia in brachial plexus block

Prajnyananda Das[1*], Satyajit K Sahoo[2], Basanta K Pradhan[3]

[1]Assistant Professor, Department of Anaesthesiology, Acharya Harihara Post Graduate Institute of Cancer, Cuttack, Odisha, India

[2]Assistant Professor, Department of Anaesthesiology and Critical Care, SJMC, Puri, Odisha, India

[3]Professor and Head, Department of Anaesthesiology and Critical Care, MKCGMCH, Berhampur, Odisha, India

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Abstract

Objective: To Compare the efficacy Of Dexmedetomidine as an Adjuvant to Levobupivacaine in Axillary Brachial Plexus Block in Upper Limb Surgeries. **Materials and methods**: Hundred patients aged 18 to 60 years, scheduled for elective orthopedic operations in the upper limb, under axillary approach of brachial plexus block were randomized to two equal groups of 50 each into Group LBD receiving 25 ml of 0.5% levobupivacaine and Dexmedetomidine(1 mcg/kg) , while group LB received 25 ml of 0.5% levobupivacaine .The primary objective was to compare duration of sensory (post operative analgesia) block with or without addition of Dexmedetomidine to levobupivacaine . The secondary objective was to compare the onset and duration of sensory and motor block and hemodynamic parameters following the block between the groups intraoperatively at regular intervals. **Results**: There is significant prolonged duration of sensory and motor blockade in group LBD compared to group LB (P<0.001). Mean duration of sensory blockade (Group LBD, 14.91±1.19 hrs and Group LB, 10.73±.888 hrs). There is significant early onset of sensory and motor block in group LBD compared to group LB (P<0.001) [Onset of sensory block (group LBD, 7.8±1.58min; group LB, 11.04±1.55 min). Onset of motor block (group LBD, 14.2 ± 2.12min; group LB, 16.14 ± 2.119 min)]. **Conclusion**: Dexmedetomidine 1µg/kg when added to 25mL of Levobupivacaine 0.5% for axillary brachial plexus block speeds the onset of sensory and motor blocks (P < 0.05). The combination produces improved analgesia, resulting in a prolonged effect and reduced requirements for rescue analgesics

Key words: Analgesia, Brachial Plexus, Dexmedetomidine, Levobupivacaine

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Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage[1]. It is always a subjective experience. Pain has been a major concern of human kind and ubiquitous efforts have been made to understand and to control it. Peripheral nerve blocks provide longer and more localized pain relief than neuraxial techniques while also avoiding the side effects of systemic medication associated with GA. Regional anaesthesia of the extremities and of the trunk is a useful alternative to general anaesthesia in many situations[2].

Regional anaesthesia acts by interruption of the pain impulse by physiological blockade at a certain point along their pathway of transmission in peripheral nerves. Trephination was practiced by Incas, and their tradition holds that the 'Shaman' performing the procedure chewed cocoa leaves and spat into the wound producing local anaesthetic effect[3].

In 1884 Koller demonstrated ocular surface anaesthesia with cocaine which has led to use of regional anaesthetics for prevention of pain associated with surgery.

The techniques of peripheral neural blockade were developed early in the history of anaesthesia. The first brachial plexus block was performed by William Stewart Halsted[4] in 1885, less than a year after Koller demonstrated the anaesthetic properties of Cocaine. Halsted freed the cords and nerves of the brachial plexus – after blocking the roots in the neck with 0.1% cocaine solution[4].

*Correspondence

Dr. Prajnyananda Das

Assistant Professor, Department of Anaesthesiology, Acharya Harihara Post Graduate Institute of Cancer, Cuttack, Odisha, India.

E-mail: drprajnyadas@rediffmail.com

Brachial plexus block has evolved into a valuable and easy procedure for upper limb surgeries. The Peripheral neural blockade is now a well accepted component of comprehensive anaesthetic care. Its role has expanded from the operating suite into post operative and chronic pain management. The recent emergence of pain management as a formal subspeciality, the advantage of regional over general anaesthesia in case of emergency surgeries and the increasing importance of outpatient (ambulatory) surgery in anaesthetic practices have further bolstered interest in peripheral nerve blocks.In 1957 Ekenstam[5] synthesized Bupivacaine, an amide local anaesthetic and was first clinically used in 1963. The well-known benefits of ropivacaine, and levobupivacaine are reduced cardiac toxicity and more specific effects on sensory rather than motor nerve fibres.

Bupivacaine, a racemic mixture of R and S enantiomers, has been used as the preferred local anesthetic agent. Bupivacaine is a long-duration local anaesthetic that has remained popular within regional and obstetric anaesthesia over three decades. Bupivacaine shows good motor/sensory separation and does not require the addition of epinephrine to prolong its effect or reduce its systemic accumulation. It is not associated with tachyphylaxis – unlike lidocaine, which requires ever increasing and more frequent doses to maintain analgesia.Levobupivacaine[6,7] is the isolated S(-) stereoisomer of the racemic mixture. It is a long acting amino-amide local anesthetic. It has longer duration of action 8 to 14 hours. Levobupivacaine has less potential for cardiovascular and central nervous system toxicity than Bupivacaine, for this reason it has recently been introduced. Literary evidence has shown, the incidence of adverse cardiac and neurological events was significantly higher with Bupivacaine as compared to levobupivacaine when used in regional anesthesia. Similarly, the potential for CNS toxicity is lower with levobupivacaine as compared to Bupivacaine[8].The use of clonidine,

a partial $\propto_2$ adrenoreceptor agonist, in peripheral nerve blocks, has been reported to be safe and beneficial (prolongs the duration of anesthesia and analgesia)[9,10]. Dexmedetomidine is also a $\propto_2$ receptor agonist, and its $\propto_2/\propto_1$ selectivity is 8 times more than clonidine. It has been reported to improve the quality of intrathecal and epidural anaesthesia[11,12].

In this study, we investigated the effect of adding dexmedetomidine to levobupivacaine for axillary brachial plexus blocks. The primary endpoints are the onset time and duration of motor and sensory blocks.

Material & methods

After obtaining Institutional Ethical Committee approval and written informed consent from all the patients a randomized clinical study was conducted over period of 1 year. Hundred patients scheduled for elective orthopedic operations in the upper limb, of age group 18 to 55 years, under axillary approach of brachial plexus block, were included in this study. The procedures were of moderate duration and included implant removal, both bone plating and fixation of fractures below the elbow joint.

Inclusion criteria

1. ASA class I and II patients
2. Age between 18 to 60 years, of both sexes undergoing elective orthopaedic surgeries of upper limb under axillary block.

Exclusion criteria

1. Allergic to study medications.
2. Pregnant and lactating women.
3. Patients receiving chronic analgesic therapy
4. cardiopulmonary disease
5. Endocrinopathies
6. Neuropathies
7. history of allergy to local anesthetics, or other contraindications to regional anesthesia

Randomization and Blinding

The study was designed as a prospective, randomized, double-blind trial using a computer-generated random number list. Participants were divided to two equal groups of 50 each. Group LBD patients received 25 ml of 0.5% levobupivacaine and Dexmedetomidine (1 mcg/kg), while group LB received 25 ml of 0.5% levobupivacaine through axillary approach for brachial plexus block. The performing anesthesiologist was blinded for serially numbered sealed envelopes for the anesthetic mixture to be administered. The person loading the drugs did not take part in any further interventions of the study procedure All variables were recorded in a blinded manner like hemodynamic variables, oxygen saturation, time required to achieve surgical block in the operating room and the time to rescue analgesic in the post anesthesia care unit.

Interventions

Standard monitoring was set up, including noninvasive blood pressure, heart rate, and pulse oximetry after patient was allowed in the operating room .18-gauge running IV line was started with lactated Ringer's solution. Midazolam 0.05 mg/kg IV bolus was used for sedation before the block was achieved, to decrease apprehension and anxiety during the entire procedure. The standard arm tourniquet inflated to 100 mmHg higher than systolic blood pressure. Hemodynamic variables block placement and every 5 min thereafter till the end of surgery were recorded. By using B BRAWN Stimuplex® HNS 12 nerve stimulator, 22G short-beveled, insulated 5 cm long stimulating needle nerve block was performed. Stimulation frequency set at 2 Hz, intensity of stimulating current was initially set to 1 mA and gradually decreased to < 0.4 mA after the stimulation of the intended nerve. Negative aspiration was done at regular intervals while injecting the drug solution to avoid any intravascular placement. The limb to be operated was evaluated at 2, 5, 10 min of completion of anaesthetic solution by one of the authors who were blinded for the drug administered. Pinprick for sensory and forearm movement against resistance along with flexing of arm for motor evaluation was done by the block performing anaesthesiologist. Pin prick comparison were done with the other normal unblocked hand. The time required from injection of local anaesthetic to pinprick sensory loss along the ulnar and radial nerve distributions and inability of rotation of thumb of the blocked limb is defined as time to time surgical block. Even after 30 min of injection if surgical anaesthesia was not achieved it was declared as failed block and converted to general anaesthesia with or without endotracheal intubation and surgery completed.

All patients were observed in PACU and received rescue analgesic tramadol 100 mg IM as soon as they complained of any pain. Patients got clear instruction to elicit a rescue analgesic as they detected discomfort caused by pain on the operated hand. The time from the start of anaesthetic injection in the operated hand until the primary request for surgical rescue analgesic was recorded in every patient.

Assessments

1. Duration of analgesia - time interval from placement of the block till first injection of rescue analgesic.
2. Onset and duration of sensory and motor blockade
3. Any adverse drug reactions.
4. Noninvasive blood pressure, heart rate and hemoglobin oxygen saturation monitoring.

Clinically relevant bradycardia (heart rate < 45 bpm) spells were treated with atropine (0.6 mg IV) and their occurance was recorded.

All patients were followed up and assessed for any neurological complications before discharge and again during their regular postoperative visit as scheduled.

All patients were considered for adverse event analysis. However, subjects with failed blocks were excluded from effectiveness assessment and further study procedure.

Statistical Analysis

Data are summarized as mean ± standard deviation or as percentages. Comparison of categorical variables between the two groups was by Chi-square test. Numerical variables were normally distributed and were compared by Student's unpaired 't'-test. All analyses were two-tailed and $P < 0.05$ was considered statistically significant.

Results

Table 1: Demographic Profile

	Group LBD (n=50)	Group LB (n=50)
Mean age in years ± SD	33.24 ± 10.88	33.22± 10.52
MALE: FEMALE	32:18	33:17
Mean wt in kg ± SD	64.24 ± 8.544	64.22 ± 7.437

Mean onset of blocks

Table 2: Mean onset of sensory block (min)

Study group	Onset time(min) (Mean ± SD)	t* value	P value	Significant
LBD	7.8 ± 1.58	10.26	P< 0.001	H S
LB	11.04 ± 1.55			

* Student's unpaired t test HS – Highly significant

Table 3: Mean Time for onset of motor block (min)

Study group	Onset time (min) (Mean ± SD)	t*	P value	Significant
LBD	14.2± 2.12	4.617	P< 0.001	HS
LB	16.14 ± 2.119			

* Student's unpaired t test HS – Highly significant

Mean durations of block

Table 4: Mean duration of sensory block (hour)

Study group	Duration block (hrs) (Mean ± SD)	t* value	P value	Significant
LBD	14.91 ± 1.19	19.87	P< 0.001	HS
LB	10.73 ± 0.888			

* Student's unpaired t test HS – Highly significant

Table 5: Mean duration of motor block (hour)

Study group	Duration of block (hrs)	t*	P value	Significant
LBD	11.67 ±0.909	14.677	P<0.001	HS
LB	8.824 ±1.024			

* Student's unpaired t test, HS – Highly Significant

Duration of analgesia

Table No.6: Duration of analgesia (in hours)

Groups	Mean duration of analgesia (mean ± SD)
Group LBD	16.66 ± 1.23
Group LB	12.07 ± 0.894
t* value	21.35
p value	<0.001

*Student's unpaired t test

Table No.7: Number of rescue analgesics in post-op 24 hours

No. of RA in 24 hours post-op	No. of patients (%)	
	GROUP LBD(n=50)	GROUP LB(n=50)
1	43 (86%)	0 (0%)
2	7 (14%)	48 (96%)
3	0(0%)	2(4%)

*Chi square test

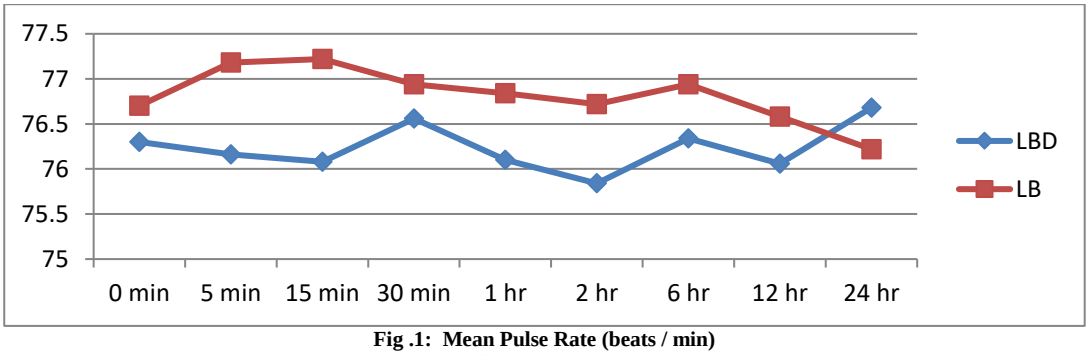

Fig .1: Mean Pulse Rate (beats / min)

In group LBD, the mean systolic blood pressure ranged from 117.04±10.13 to 117.76±10.61 mm of Hg. In group LB, the mean systolic blood pressure ranged from 116.8±10.53 to 118.2±11.07 mm of Hg. The statistical analysis by unpaired student's "t" test showed that there was no significant difference in systolic blood pressure between the two group (P>0.05).In group B, the mean diastolic blood pressure ranged from 76±6.9 to 77±7.1 mm of Hg. In group BD, the mean diagnostic blood pressure ranged from 77±6.6 to 77±6.9 mm of Hg. The statastical analysis by student's unpaired "t" test showed that there was no significant difference in diastolic blood pressure between the two groups (P>0.05)The statistical analysis by students unpaired "t" test showed that there was no significant difference in O2 saturation between the two groups (P>0.05).

Complications

Incidence of complications like were nil in either group. Post block hemodynamic parameters were also within normal in both the groups requiring no intervention.

Discussion

Brachial plexus block provides postoperative analgesia of short duration, even when a long-acting local anaesthetic like Levobupivacaine if used alone. Various adjuvant drugs like Opioids, Midazolam, Neostigmine and Hyaluronidase have been evaluated in conjunction with local anaesthetics to prolong the period of analgesia, but they were found to be either not effective or incidence of adverse effects are unacceptably high. Dexmedetomidine is known to produce anti nociception and to enhance the effect of local anaesthetic when administered intrathecally and epidurally. Dexmedetomidine produces this effect by its action on Alpha 2 adrenergic receptors found in peripheral nerves. Hence an attempt had been made to assess the efficacy of Dexmedetomidine as an adjuvant to levobupivacaine (0.5%) in brachial plexus block (axillary approach) in terms onset time, duration of analgesia and anaesthesia. Hemodynamic variables and rescue analgesic requirements in first 24 hours were also studied.

A total of 100 patients within the age group of 18-55 were in included in the study, 50 in each group. Out of which the mean age of group LB (receiving only Levobupivacaine) was 33.22 ± 10.52 years and

the mean age of group LBD (receiving Dexmedetomidine with Levobupivacaine) was 33.24± 10.88 years. Hence both groups were comparable for age. Male and female distribution in both the groups were also comparable with male predominance in both the groups.

In our study we noticed significantly early onset of sensory and motor block in group LBD (receiving Dexmedetomidine with Levobupivacaine) compared to group LB (P<0.001) [Onset of sensory block (group LBD, 7.8±1.58min; group LB, 11.04±1.55 min). Onset of motor block (group LBD, 14.2±2.12min; group LB, 16.14±2.119 min)]. This could be due to a local direct action of Dexmedetomidine and its synergistic action with that of local anaesthetics.

In our study, we also noticed significantly prolonged duration of sensory and motor blockade in group LBD compared to group LB (P<0.001) [Mean duration of sensory blockade (Group LBD, 14.91±1.19 hrs and Group LB, 10.73±.888 hrs). Mean total duration of motor blockade (Group LBD, 11.67 ± .909 hrs and Group LB, 8.824±1.024 hrs)].

Our results showed that sensory block tended to last longer as compared to motor block which agrees with the observation by de Jong et al[13]. These authors explained that large fibres require a higher concentration of local anaesthetic than small fibres. The minimal effective concentration of local anaesthetic for large (motor) fibres is greater than for small (sensory) fibres. Thus, motor function return before pain perception and duration of motor block is shorter than the sensory block.

Various studies in which Dexmedetomidine was used in peripheral nerve block found that Dexmedetomidine with Levobupivacaine improves analgesic characteristics compared to

Levobupivacaine alone.Esmaoglu A et al, 2010[14] found that Dexmedetomidine added to levobupivacaine for axillary brachial plexus block shortens the onset time and prolongs the duration of the block and the duration of postoperative analgesia. However, dexmedetomidine also may lead to bradycardia.Kenan Kaygusuz, MD et al 2012 found that adding dexmedetomidine to levobupivacaine for an axillary brachial plexus block shortens sensory block onset time, increases the sensory and motor block duration and time to first analgesic use, and decreases total analgesic use with no side effects.

The duration of pain relief (postoperative analgesia) was also markedly prolonged in group LBD (16.66±1.23 hr) compared to group LB (12.07±0.694 hr) (P<0.001). The mean number of supplemental analgesic boluses required were also significantly lower in Group LBD(1.50±0.68) in comparison with group LB (2.80±0.41) (P<0.001).Similar observation was made in the above mentioned study by Esmaoglu A et al, 2010& Kenan Kaygusuz, MD et al 2012. The prolonged analgesia in Group LBD could be due to the action of Dexmedetomidine by inhibiting action potential of A & C fibers in peripheral nerves as demonstrated by Gaumann et al[15].

Conclusion

From our study, we conclude that, the addition of Dexmedetomidine (1µg / kg) as an adjuvant to Levobupivacaine (0.5%) has following effects:

i) Faster onset of sensory block.
ii) Faster onset of motor block.
iii) Longer duration of sensory block.
iv) Longer duration of motor block.
v) Less number of rescue analgesics in post-op 24 hours.
vi)No significant difference in haemodynamic variables i.e., pulse rate, systolic BP, diastolic BP and O2 saturation.

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References

1. Stephen E.Abram. Chronic pain management. In: Barash PG, Cullen BF, Stoelting RK. Clinical anaesthesia, 5th ed. Lippincott Williams and Wilkins, Philadelphia. 2006:1449.
2. Michael FM. Peripheral nerve blockade. In: Barash PG, Cullen BF, Stoelting RK. Clinical anaesthesia, 5th ed. Lippincott Williams and Wilkins, Philadelphia. 2006:718
3. Singer C. Underwood EA. A short history of medicine. 2nd ed. Clarendon Press, Oxford. 1962:349.
4. Lee's synopsis of anaesthesia. 13th Edition. Page no. 427
5. David LB and Raymond BF. The history of neural blockade and pain management. In: Cousins MJ and Phillip OB. Neural blockade in clinical anesthesia and management of pain. 3rd ed. Lippincott-Raven, Philadelphia. 1998:10.
6. Updates on Local anaesthetics. A focous on levobupivacaine. Crinalurlacu and Donal J Buggy. TherClin Risk Manag.2008 April;4(2):381-392.published online 2008 april.
7. Bardsley H, Baker H; A comparison of the cardiovascular effects of levobupivacaine and racemic bupivacaine following intravenous administration to healthy volunteers. British journal of clinical pharmacology 1998;245-249
8. Sukhminder J. S Bajwa, Jasleen kaur. Clinical profile of levobupivacaine in regional anaesthesia, clinical pharmacology 2013;29;4;530-539
9. Singelyn FJ, Gouverneur JM, Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesth Analg 1996;83:1046–50
10. Singelyn FJ, Dangoisse M, Bartholomee S, Gouverneur JM. Adding clonidine to mepivacaine prolongs the duration of anesthesia and analgesia after brachial plexus block. Reg Anesth 1992;17:148–50
11. Kanazi GE, Aouad MT, Jabbour-KHoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, Bulbul M, Baraka AS. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesth Scand 2006;50:222–7
12. Congedo E, Sgreccia M, De Cosmo G. New drugs for epidural analgesia. Curr Drug Targets 2009;10:696–706.
13. De Jong RH, Wagman IH. Physiological mechanism of peripheral nerve block by local anaesthetics. Anesthesiology, 1963; 24: 684-727.
14. Esmaoglu A et al, Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. Anesth Analg. 2010 Dec;111(6):1548-51.
15. Gaumann DM, Brunet PC, Jirounek P. Clonidine enhances the effects of lidocaine on C-fiber action potential. Anesth Analg. 1992;74:719–25.

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