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Original Research Article

Efficacy of Addition of Dexmedetomidine to Levobupivacaine in Patients Posted Electively for Upper Limb Orthopedic and Soft Tissue Surgery

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Conflict of interest: Nil

Abstract:

Aim: To assess the effect of levobupivacaine 0.5% alone and with dexmedetomidine 100 µg as an adjuvant to levobupivacaine 0.5% on the onset and duration of sensory and motor block, the duration of perioperative analgesia, complications and sedation score.

Methodology: This analytical comparative study was carried out Department of Anesthesiology for one year on 50 patients in hospital The participants were divided randomly into two groups of 25 each using sealed envelope technique. The first group (LD group) was administered 1 ml (100µg) dexmedetomidine with 39 ml of 0.5% Levobupivacaine. The second group was given 1 ml of 0.9% normal saline and 39 ml of 0.5% Levobupivacaine as anesthetic agent. Saturation of oxygen (SpO2), heart rate, diastolic blood pressure, systolic blood pressure, were noted at 0, 5, 10, 15, 30, 60, 90, and 120 minutes. Side effects like heart rate less than fifty per min (bradycardia) and blood pressure less than 20% with respect to resting conditions (hypotension) were treated with appropriate measures. Then we noted the period of motor and sensory blocks once the surgery is started.

Results: In the LD group males and females were 64% and 36% respectively. In LS group, it was 56% and 44% respectively. All the study participants in LD group did not require post-operative analgesia while all in LS group were given Postoperative analgesia. 28% in LD group were slightly drowsy compared to 100% in LS group. The mean duration of onset of sensory and motor block was nearly 4 min earlier in LD group compared to LS group.(5.42 vs 9.21 min of sensory and 8.40 vs 12.33 min of motor). The mean duration of sensory block (533 vs 921.75 min) and motor block (553.73 vs 943.18 min) were approximately 400 minutes lesser respectively between both the groups. The duration post-operative analgesia was 579 and 980.74 min in both the groups respectively. All the results were statistically significant. 24% of study population in LD group had bradycardia compared to 0% in LS group. No other adverse effects was recorded in the study subjects.

Conclusion: Based on the findings of this study, perineural infiltration of dexmedetomidine as an adjunct to 0.5% levobupivacaine increases the sensory and motor block duration. It also prolongs the duration of analgesia and also provides a good intraoperative sedation as well and helps to reduce the postoperative analgesic requirement.

Keywords: Dexmedetomidine, Levobupivacaine, Perineural, Brachial Plexus.

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Introduction

Peripheral nerve blocks are widely used in upper limb surgery because they improve postoperative pain control and reduce the possibility of delirium or cognitive dysfunction [1]. For surgeries on the upper limb, brachial block (BB) is more advantageous than general anesthesia (GA) as it provides ideal conditions for the surgery and satisfactory analgesia extending to the postoperative period. Ultrasound-guided BBs offer the advantages of proper nerve localization, optimal needle placement, and a higher rate of success of the block [2, 3]. The effectiveness of Brachial plexus block had been proved as the best for a long period for the surgeries in upper limb [4]. It is found to be one of the efficient methods for emergency and routine upper limb surgeries. It provides very good intraoperative anesthesia as well as postoperative analgesia without any systemic side effects. The complications like side effects of anesthetic agents, stress of tracheal intubation and laryngoscopy are avoided in this type of block and therefore commonly used in

regional nerve block of upper extremity. Post operatively, patients are free from edema, pain, cerebral depression, nausea, vomiting and vasospasm.

Levobupivacaine has the duration of action ranging from three to eight hours and hence it is the most commonly used local anesthetic drug [5]. This anesthetic drug has established itself as cheaper and safer for many years [6]. But patchy or incomplete analgesia and delayed onset are few of the practical constraints. On the other hand, because the length of the sensory block following a single injection of LAs is often insufficient to obviate the need for postoperative opioids, several adjuvants have been used to extend the duration of nerve blocks [7].

Alpha 2 adrenergic agonists not only decrease the requirements of intraoperative anesthetic agents, but also they have cardiovascular stabilizing properties, sympatholytic analgesic and sedative property. In order to reduce the time of onset of nerve block, to prolong the duration of block and to improve the quality of blockade, these can be given in peripheral nerve blocks, intrathecal, epidural either alone or with local anesthetic agents [5, 8]. An α2 receptor agonist, dexmedetomidine (DMT), is eight times more sensitive than clonidine [9, 10].

DMT, an alpha-2-adrenergic receptor agonist, has emerged as the most popular adjuvant based on evidence that addition of DMT to local anesthetics prolongs the duration of analgesia and sensory and motor blocks, besides reducing the time of onset of sensory and motor blocks. Further, it is also reported to provide stable hemodynamics, sedative, analgesic, and sympatholytic effects without causing any respiratory depression [11]. The analgesic effect of DMT is mediated through stimulation of the α^2C and α^2A receptors in the dorsal horn, thereby directly suppressing the pain transmission by reducing the release of pronociceptive transmitters, substance P, glutamate, and hyperpolarization of interneurons [12, 13].

The effectiveness of dexmedetomidine in developing the time of a brachial plexus block during upper limb surgery has been investigated in several studies. It was hypothesized that it has a synergistic effect with LAs and extends the duration of their activity [14-16]. Researches have also found that dexmedetomidine, when used in many animals and humans had improved the onset and duration of motor / sensory blockade. When used as an adjuvant to local anesthetic agents in peripheral nerve blocks, it has increased the duration of analgesia [17-20]. The present study was designed to assess the effect of levobupivacaine 0.5% alone and with dexmedetomidine 100 µg as an adjuvant to levobupivacaine 0.5% on the onset and duration of sensory and motor block, the duration of perioperative analgesia, complications and sedation score.

Methodology

This comparative study was carried out Department of Anesthesiology on 50 patients in Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India for one year. A pre-anesthetic checkup including complete history, general and systemic examination and fitness was assessed for all patients. Complete hemogram like RBC, WBC counts, platelets and other tests like blood urea, random blood sugar, bleeding time, clotting time, serum creatinine and ECG is mandatory if the subject is more than 45 years. Patients were informed to be on nil per oral after 8 pm on the previous day of surgery.

Inclusion criteria: Patients posted electively for upper limb orthopedic and soft tissue lesion, between the age of 18 and 60 years of any gender, weighing above 60 kilograms with ASA Grade I and II and those who fulfilled the selection criteria and those who gave consent to participate in the study were included in the study.

Exclusion criteria: Patients with chronic kidney disease, hypertension, pregnant women, uncontrolled diabetes mellitus, cerebrovascular accident, COPD, coronary artery disease on anticoagulants, those with history of bleeding disorders, and those who were allergic to amide local anesthetics /alpha 2 agonist were excluded from the study.

The participants were divided randomly into two groups of 25 each using sealed envelope technique. The first group (LD group) was administered 1 ml (100µg) dexmedetomidine with 39 ml of 0.5% Levobupivacaine. The second group was given 1 ml of 0.9% normal saline and 39 ml of 0.5% Levobupivacaine as anesthetic agent. Once the study participant entered the operation theatre, the chief consultant had used the pre assigned 30 envelope for each group in the pre shuffled order. Neither the investigator nor the patient knew which group they were assigned (double blinding).

The vital signs like respiratory rate, heart rate, systolic and diastolic blood pressure, pulse rate, and oxygen saturation were monitored and noted immediately on entering the OT. Ringer lactate was started in the already secured intravenous line. Brachial plexus block was applied through the supraclavicular approach. Nerve locator was used for neural localization and it was achieved by connecting to a 22 G, 50-mm-long stimulating needle. The location end point was a distal motor response with an output lower than 0.5 milliamperes in the median nerve region. Local

anaesthetic solution in the labelled coded syringe was injected following negative aspiration.

Pin prick method was used to assess the sensory block. Sensory onset was considered when there was dull sensation to pin prick along the distribution of any two of the following nerves like musculocutaneous nerve, radial nerve, median nerve, ulnar nerve. When there was complete loss of sensation to pin prick, we can consider it as complete sensory block. Modified Bromage scale. Motor and sensory blocks were assessed for 30 minutes for every 3 minutes until after injection, and then every 30 minute until they have resolved. [15]

Saturation of oxygen (SpO2), heart rate, diastolic blood pressure, systolic blood pressure, were noted at 0, 5, 10, 15, 30, 60, 90, and 120 minutes. Side effects like heart rate less than fifty per min (bradycardia) and blood pressure less than 20% with respect to resting conditions (hypotension) were treated with appropriate measures. Then we noted the period of motor and sensory blocks once the surgery is started. When the subject's visual analogue score >5, a rescue analgesia like intramuscular diclofenac sodium 75mg (1.5 mg/kg) was administered. Ramsay Sedation Scale (RSS) was used to assess the sedation before the block and 15 min then after. All the data noted was entered in Microsoft excel sheet and was double checked. SPSS 16 software was used to analyze the collected data. P< 0.05 was considered as statistically significant.

Results

In the LD group males and females were 64% and 36% respectively. In LS group, it was 56% and 44% respectively. There was no statistical significance between the two groups. All the study participants in LD group did not require post-operative analgesia while all in LS group were given Postoperative analgesia. 28% in LD group were slightly drowsy compared to 100% in LS group. Both the results were statistically significant.

Table 1: Association between various parameters between groups

Parameters		LD group	LS group	P-value
Gender	Males	16 (64%)	14 (56%)	0.05
	Females	9 (36%)	11 (44%)	
Post-operative analgesia requirement	Not needed	25 (100%)	0 (0%)	<0.001
	Needed	0 (0%)	25 (100%)	
Sedation score	Sleeping but arousable	18 (72%)	0 (0%)	0.001
	Slightly drowsy	7 (28%)	30 (100%)	

The average age of study participants were 32.5±12.52 vs 30.7±11.23 in LD and LS group respectively. The mean weight of study participants in study and control group was 64.8±3.20 vs 63.6±4.42 respectively. Both the results were not statistically significant. The mean duration of onset of sensory and motor block was nearly 4 min earlier in LD group compared to LS group.(5.42 vs 9.21 min of sensory and 8.40 vs 12.33 min of motor). The mean duration of sensory block (533 vs 921.75 min) and motor block (553.73 vs 943.18 min) were approximately 400 minutes lesser respectively between both the groups. The duration post-operative analgesia was 579 and 980.74 min in both the groups respectively. All the results were statistically significant.

Table 2: Comparison of mean values of various parameters between both groups

Mean Parameters	LD group	LS group	P-value
Age (in years)	32.5±12.52	30.7±11.23	0.62
Weight (Kg)	64.8±3.20	63.6±4.42	0.22
Onset of sensory block (min)	5.42±1.05	9.21±0.92	<0.001
Onset of motor block (min)	8.40±1.99	12.33±1.10	<0.001
Duration of sensory block (min)	533±53.10	921.75±37.34	<0.001
Duration of motor block (min)	553.73±49.12	943.18±34.66	<0.001
Duration of post op analgesia (min)	579±53.87	980.74±46.86	<0.001

The diastolic blood pressure, systolic blood pressure, heart rate were comparatively maintained lesser than baseline for LD group from fifth min after induction of drug till two hours. 24% of study population in LD group had bradycardia compared to 0% in LS group. No other adverse effects was recorded in the study subjects.

Table 3: Comparison of heart rates between both groups at different time intervals

Time (min)	LS group		LD group		P-value
	Mean	SD	Mean	SD	
0	85.63	8.27	84.28	8.17	0.894
5	83.37	7.93	79.29	7.56	0.030
10	81.37	7.38	76.88	8.53	0.009
15	79.38	7.92	72.37	7.66	<0.001
30	76.83	7.48	69.28	9.87	<0.001
60	75.28	6.83	67.02	6.24	<0.001
90	79.72	7.48	71.29	5.86	<0.001
120	82.92	8.28	73.44	7.37	<0.001

Discussion

Alpha 2 adrenergic agonists not only decrease the requirements of intraoperative anesthetic agents, but also, they have cardiovascular stabilizing properties, sympatholytic analgesic and sedative property. In order to reduce the time of onset of nerve block, to prolong the duration of block and to improve the quality of blockade, these can be given in peripheral nerve blocks, intrathecal, and epidural either alone or with local anesthetic agents [5, 8].

Dexmedetomidine 100 μg when used as an adjuvant to levobupivacaine 0.5% reduces the onset of sensory and motor blockade, prolongs the analgesic effect of motor and sensory block. The mechanism of action of α2 agonists causing sedation and analgesia is not completely known, but it seems to have multifactorial. Centrally, α2 agonists inhibits the substance P release at dorsal root neuron in the pain pathway and activates α2 adrenoceptors in the locus coeruleus and thereby causing analgesia and sedation. Peripherally, α2 agonists decrease the release of noradrenaline, produce analgesia and produces α2 receptor independent restraints on nerve action potentials.

Activation of cation current by hyperpolarization causes the peripheral action of dexmedetomidine. For subsequent firing the nerve will not return from hyperpolarized state to resting membrane state [21-24]. Studies done by various other authors have also showed that addition of dexmedetomidine reduces the onset time of motor and sensory block and prolongs the duration of postoperative analgesia [25-30]. Addition of dexmedetomidine improves the hemodynamic stability of the patients. Similar findings were obtained in the several other researchers conducted worldwide [31, 32].

Balakrishnan et al. [33] conducted a study on 120 patients divided into four groups and administered plain levobupivacaine and 30-μg, 60-μg and 100-μg dexmedetomidine along with levobupivacaine. They found that the 100-μg dexmedetomidine group had a statistically significant increase in sensory and motor blockade durations, a decrease in onset time, and a prolongation of analgesia duration compared with the other three groups. Reddy et al. [34] also evaluated two doses of dexmedetomidine, 50 μg and 100 μg, added to 0.5% levobupivacaine, on 120 patients undergoing upper limb surgeries under supraclavicular brachial plexus block. They reported that adding 100-μg dexmedetomidine to 0.5% levobupivacaine lengthened the duration of sensory and motor blocks and accelerated their onset. Rescue analgesia in the form of diclofenac sodium injection was required in 20 patients (33.33%) in the 50-μg group and nine patients (15%) in the 100-μg group.

Furthermore, a recent meta-analysis that included 18 randomized controlled trials (n= 1,014) conformed to the current findings on adding dexmedetomidine (50–100 μg) to LAs in brachial plexus block. They have found that in patients who received 100-μg dexmedetomidine, the mean sensory block duration increased by 257 min, the mean motor block duration increased by 242 min, and the mean time to the first demand for analgesia increased by 266 min [35]. A comparable meta-analysis by Hussain et al. [36] on 18 studies (n = 1,092) found that the addition of dexmedetomidine to LAs increased the duration of sensory (261.41 min) and motor (200.9 min) blocks, reduced the onset of sensory (3.19 min) and motor (2.92 min) blocks, increased the duration of analgesia (289.31 min), and significantly reduced postoperative analgesic requirement 24 h after the block compared with the control; however, three studies have found no significant difference between the dexmedetomidine and control groups.

Several clinical trials have established the fact that the administration of DMT as an adjuvant to local anesthetics in neuraxial and peripheral nerve blocks prolonged the duration of sensory and motor blocks [37]. These improved block characteristics are believed to be mediated through activation of alpha-2A adrenoceptors (α^2-AR).They reduce the release of peripheral norepinephrine by stimulation of prejunctional inhibitory α^2-AR and inhibit central neural transmission in the dorsal horn by presynaptic and postsynaptic mechanisms. They also have direct sympatholytic effects on spinal preganglionic sympathetic neurons. Centrally, α^2 agonists produce analgesia and sedation by inhibiting the release of substance *P* in the

nociceptive pathway at the level of the dorsal root neuron and by activatingα^2-AR in the locus coeruleus [38, 39].

Conclusion

Based on the findings of this study, perineural infiltration of dexmedetomidine as an adjunct to 0.5% levobupivacaine increases the sensory and motor block duration. It also prolongs the duration of analgesia and also provides a good intraoperative sedation as well and helps to reduce the postoperative analgesic requirement.

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