A PROSPECTIVE STUDY ON THE ADVERSE EFFECTS OF DEXMEDETOMIDINE AS AN ADJUVANT TO 0.5% BUPIVACAINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

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INTRODUCTION

Pain is an unpleasant sensory and emotional experience associated with actual and potential tissue damage. It is the duty of every anaesthetist to provide adequate pain relief. Regional anaesthesia of the trunk and the extremities is an alternative to general anaesthesia in many situations. It avoids the unwanted effects of the anaesthetic drugs used during general anaesthesia and the stress of laryngoscopy & tracheal intubation and CNS is also spared, so that the patient is conscious, fully awake during the surgical procedure without recognising pain.
Peripheral nerve blocks provide longer and more localised pain relief than systemic opioids and non-steroidal anti- inflammatory drugs. Early postoperative mobilisation and rehabilitation with minimally associated pain and discomfort is the most desirable feature in modern orthopaedic surgery.

For surgeries upon upper extremities, brachial plexus block provides better tourniquet tolerance and post operative analgesia. It is a sole technique in emergency situation with inadequate starvation time and where general anaesthesia is contraindicated.

Local anaesthetics alone provide good operative conditions but have shorter duration of postoperative analgesia. This problem can be overcome by using long acting local anaesthetics like Bupivacaine. Bupivacaine is one of the most frequently used local anaesthetic as it has a longer duration of action varying from 3 to 8 hours. However, it has limiting factors like delayed onset, patchy or incomplete analgesia. To minimize these drawbacks adjuvants like Clonidine, Dexamethasone, Dexmedetomidine, Ketamine, Magnesium Sulphate etc., have been added to improve the quality and duration of action and postoperative analgesia.

Lately, dexmedetomidine, a highly selective α2 adrenergic agonist, has been used as an adjuvant to local anaesthetics. Various clinical trials performed in both animals and humans have shown dexmedetomidine to be safe when used as an adjuvant to local anaesthetic in subarachnoid, caudal, epidural, and Peripheral Nerve Blocks. However, there remains limited knowledge on the analgesic efficacy and clinical haemodynamic utility of adding dexmedetomidine to local anaesthetics during peripheral nerve block in humans.

The primary outcome of this study measures the hemodynamic changes associated with Dexmedetomidine as an adjuvant in Brachial Plexus Blocks. Secondary outcome includes the adverse effects and the degree of sedation associated with the same.

MATERIALS AND METHODS

This is a prospective, randomized, case control study. It was done after the approval of our hospital ethical committee. Written informed consent was taken from 60 patients undergoing elective upper limb surgery including arm, forearm, and hand fractures; with American Society of Anesthesiologist (ASA) I, II and III; of both sexes; and age range from 18–60 years. Patients unwilling to give consent, with a history of neuromuscular, pulmonary, neurological, cardiovascular, renal, or hepatic diseases were excluded from the study. Also, patients with bleeding disorders, any known allergy to the studied drugs, and failure of the block were excluded.

All patients included were allocated randomly (using computer-generated number lists and opaque sealed envelopes) into two groups of 30 each. Patients were randomly allocated into the following groups: group B received 30 ml bupivacaine 0.5% and group D received 30 ml bupivacaine 0.5% containing 40 μg dexmedetomidine.

The anaesthesia machine, emergency oxygen source (E type cylinders), pipeline O_2 supply, LMA Proseal, working laryngoscopes, appropriate size endotracheal tubes and connectors were kept ready for emergency resuscitation. Apart from this, working suction apparatus with suction catheter, Oropharyngeal airways and drugs including Thiopentone, Propofol, Midazolam, Fentanyl, Succinylcholine, Vecuronium, Hydrocortisone, Atropine, Ephedrine, Adrenaline, glycopyrrolate, sodium bicarbonate and Intralipid 20% emulsion were also kept ready. For the block, Senstim MNS – 01 Peripheral nerve stimulator and Senstim Stimuplex needles (50mm) were used.

Patients were kept nil per oral overnight and premedicated with Inj. Pantoprazole 40mg & Inj. Ondensetron 4mg. Once shifted to the operation theatre, baseline heart rate, blood pressure, and oxygen saturation were recorded. An intravenous line with an 18-gauge (G) intravenous (iv) cannula was secured in the unaffected limb and Ringer's Lactate infusion was started. Patient was kept in supine position on the operation table with arms by

the side and head turned to the contralateral side. With all aseptic precautions subclavian artery pulsations were felt and a skin wheel was raised with local anaesthetic cephalo-posterior to the pulsations. A 22 gauge, 50mm stimulating needle (Senstim) was introduced through the point located parallel to head and neck in a caudal and slight medial and posterior direction. The location end point was a distal motor response of muscle twitch of the fingers with an output lower than 0.8 mA (milliamperes). After observing elicited outcome and encountering the negative aspiration of blood, the needle was kept in the same position, 30ml of 0.5% Bupivacaine containing 40mcg dexmedetomidine was injected slowly by ruling out the intravascular injection intermittently.

Heart rate (HR), mean arterial blood pressure (MAP), respiratory rate, and oxygen saturation were recorded at the following times:

- T_0 = basal readings before performing the block
- $T_1 – T_3$ = readings obtained every 5 min after local injection for 15 min
- $T_4 – T_{10}$ = readings obtained every 15 min for 2 hr after injection of LA.

Untoward adverse effects, such as incidence of bradycardia, hypotension, respiratory depression and degree of sedation were also documented.

Bradycardia was considered if the HR went below 50 bpm and was proposed to be managed with atropine 0.3–0.6 mg.

Hypotension was defined as a decrease in MAP of more than 20% of baseline value and was proposed to be treated with crystalloid infusion and 6 mg bolus of Ephedrine iv.

The patient was considered hypoxic if the oxygen saturation dropped below 90% and was managed with supplemental oxygen through nasal cannula or face mask.

This was further classified as respiratory depression if the above-mentioned rescue techniques failed to maintain oxygen saturation, in which case, a Laryngeal Mask Airway (LMA Proseal) was introduced into the patient's oropharynx with adequate sedation to secure airway till the end of the procedure.

Nausea and vomiting if occurred were recorded and treated with Ondensetron 8 mg intravenously. Sedation was evaluated every 30 min (T_0 = sedation level by the end of injection of LA) for 3 h, then every 1 h for the next 6 h by the anaesthetist in the Post-Anaesthetic ICU. The Modified Ramsay Sedation Scale was used:

1. Anxious, agitated, restless.
2. Cooperative, oriented, tranquil.
3. Responds to commands only.
4. Brisk response to light glabellar tap or loud noise.
5. Sluggish response to light glabellar tap or loud noise.
6. No response.

Statistical analysis was done using the Statistical Package for Social Science (SPSS15.0 Evaluation version). To calculate the sample size, a power analysis of α=0.05 and α=0.90, showed that 30 patients per study group were needed. Data are expressed as either mean and standard deviation or numbers and percentages. Continuous covariates were compared using analysis of variance (ANOVA). The comparison was studied using the Chi-square test or Fisher's exact test as appropriate, with the P value reported at the 95% confidence interval. $P < 0.05$ was considered statistically significant.

RESULTS

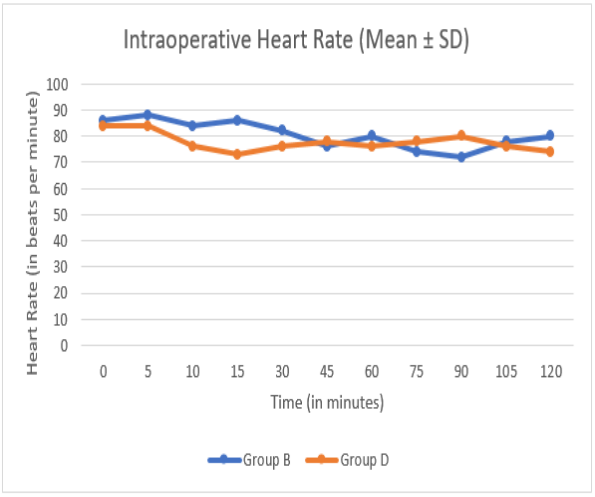
The demographic data were comparable in both the groups. Among the adverse effects, hypotension was seen in 4 patients and bradycardia in 5 patients of Group D. The mean Ramsay sedation score was 2.32 ± 0.618 in Group D and 2.00 in Group B. Desaturation was noted in 2 patients in group D. Side effects such as nausea, vomiting or pruritis were not observed in either of the groups. Two failure cases were found in Group B and one failure case were found in Group D. These cases were subsequently converted to general anaesthesia. Therefore, statistical analysis was applied on 28 patients in Group B and 29 patients in Group D.

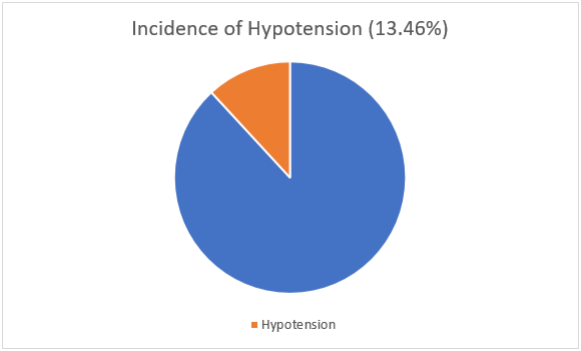
Demographic data: Age and sex distribution in both groups

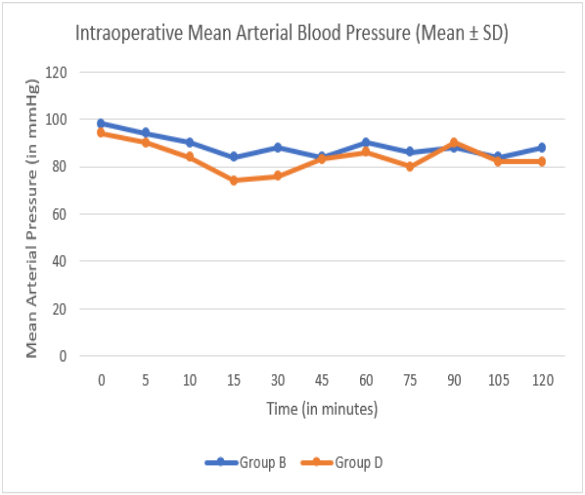
	Group B (n = 28)	**Group D (n = 29)**	**Statistical Analysis**
Age (years)	32.94 ± 14.8	33.26 ± 15.03	Not Significant
Sex (male : female)	16:12	18:11	Not Significant

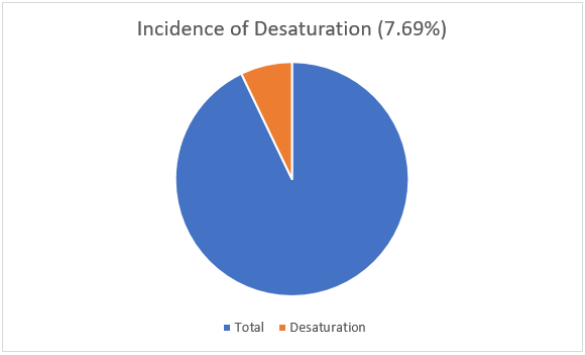
Incidence of Adverse events

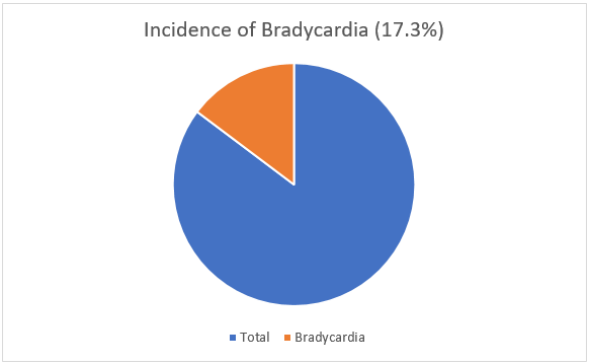
	Group B	Group D	P value
Nausea	0	0	-
Vomiting	0	0	-
Pruritis	0	0	-
Respiratory Depression	0	2	> 0.05
Bradycardia	0	5	> 0.05
Hypotension	0	4	> 0.05

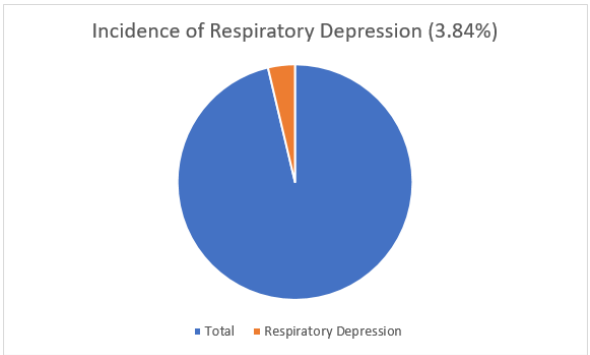












Mean Ramsay Sedation Score

	Group B (n = 28)	Group D (n = 29)	Statistical Analysis
Mean Ramsay Sedation Score	2.00	2.32 ± 0.618	Not Significant

DISCUSSION

Dexmedetomidine, the pharmacologically active d-isomer of medetomidine is a highly specific and selective α2 adrenoceptor agonist with α2:α1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine, thus decreasing the unwanted side effects of α1 receptors. Studies have shown that presynaptic activation of α2 adrenoceptor in central nervous system inhibits the release of norepinephrine, terminating the propagation of pain signals, and their postsynaptic activation inhibits sympathetic activity, thereby decreasing HR and BP. Hence it is known to increase the risk of bradycardia, hypotension, also sedation, and respiratory depression.

Transient hypertensive response with doses 1-4 μg/kg is attributed to initial stimulation of α- 2B subtype receptors in vascular smooth muscles. Bradycardia is a reflex response to this transient response and it persists subsequently due to central sympathetic inhibition. Baroreceptor reflex and HR response to a pressor agent is well preserved with the use of dexmedetomidine, thus hypotension and bradycardia are easily treatable conferring hemodynamic stability. High selectivity for α-2A receptors mediates analgesia, sedation, and anxiolysis. The research done so far shows encouraging results for its use in intravenous sedation (ICU and operative patients), spinal, epidural, caudal anesthesia, and Bier's block.

Yoshitomi *et al*., demonstrated that dexmedetomidine as well as clonidine enhanced the local anesthetic action of lignocaine via peripheral α-2A adrenoceptors. Studies have shown that clonidine and dexmedetomidine when added to bupivacaine prolongs the duration of anesthesia and analgesia in brachial plexus block, but was associated with bradycardia, hypotension, and respiratory depression as side effects.

In the results published by Pal Singh et al, hypotension was seen in 22 patients and bradycardia in 26 patients of Group II. SBP was never <20% from the baseline value, so no treatment was given. Fall in pulse rate was more than 20% from baseline in one patient of study group who responded well to atropine. The decrease in blood pressure is due to the inhibition of central sympathetic outflow. The presynaptic alpha-2 receptors are also stimulated by dexmedetomidine, thereby decreasing norepinephrine release and causing a fall in blood pressure and HR. In this study, intraoperative complications in both the groups were not statistically significant. There was not a single episode of respiratory depression in any of the groups.

Esmaoglu *et al*., reported prolongation of axillary brachial plexus block when dexmedetomidine was added to levobupivacaine. They observed bradycardia in seven out of 30 patients in study group while we observed it in only one out of 25 patients.

In our study, hypotension was seen in 4 patients and bradycardia in 5 patients of Group D, which was statistically not significant. SBP was never <20% from the baseline value, so no treatment was given. Fall in pulse rate was more than 20% from baseline in one patient of Group D who responded well to atropine. The decrease in blood pressure is due to the inhibition of central sympathetic outflow. The presynaptic alpha-2 receptors are also stimulated by dexmedetomidine, thereby decreasing norepinephrine release and causing a fall in blood pressure and HR. There were two episodes of respiratory depression in patients of group D, which were intervened with a Supraglottic Airway Device, LMA Proseal to maintain airway patency. However, this incidence was also not statistically significant. Therefore, it can be opined through review of previous literature that the incidence of adverse events was documented at a higher dose of dexmedetomidine, and at doses of 40 μg, these adverse events are insignificant. Hence, we can conclude from our study that there are no significant adverse events when Dexmedetomidine was supplemented as an adjuvant to supraclavicular brachial plexus block at a dose of 40 μg.

CONCLUSION

In view of the literature justifying Dexmedetomidine as an efficient adjuvant to peripheral regional anaesthesia with documented prolongation of sensory blockade, motor blockade, and duration of analgesia, its use has become more pronounced in the recent decade. With our study, we conclude that a dose of 40 μg Dexmedetomidine poses minimal haemodynamic compromise and a significantly lower incidence of untoward adverse events when used as an adjuvant in peripheral nerve blocks.

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