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RESEARCH ARTICLE

A COMPARATIVE STUDY OF CLONIDINE (1ug/kg) AND DEXMEDETOMIDINE (1ug/kg) AS AN ADJUVANT TO 0.25% BUPIVACAINE IN BRACHIAL PLEXUS BLOCK (SUPRACLAVICULAR APPROACH) IN PATIENTS POSTED FOR ORTHOPEDIC SURGERIES OF UPPER LIMB

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ABSTRACT

Dexmedetomidine has evolved as a panacea for various applications/ procedures in the perioperative or critical care settings with multiple promising delivery routes. It is fast emerging as a valuable adjunct to regional anaesthesia and analgesia, where future studies are required to build the evidence for its use in central neuraxial blocks, peripheral nerve blocks or even for local site infiltration. Although Dexmedetomidine has α1/α2 selectivity eight times higher than clonidine, an equipotent dosage of both the drugs in supraclavicular brachial plexus block has not been found in literature. We in this study compare clonidine (1ug/kg) and dexmedetomidine (1ug/kg) as an adjuvant to 0.25% bupivacaine in brachial plexus block and found dexmedetomidine as a safe, superior and far better adjuvant.

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INTRODUCTION

Regional anaesthesia (brachial plexus block) is the preferred method of providing anaesthesia for surgeries of upper limb. The Supraclavicular approach is an easy technique to perform, landmarks are quiet predictable and a small volume of solution can be administered at a point where three trunks are in close proximity, resulting in a rapid onset of a reliable sensory and motor blockade (Thompson *et al*., 1988). A wide variety of drugs like opioids, epinephrine, magnesium sulphate, potassium chloride, ketamine, neostigmine etc have been used as an adjuvant to local anaesthetic drugs with an aim to prolong the duration of sensory and motor block and decrease the dose of local anaesthesia. Alpha – 2 agonists like clonidine and dexmedetomidine are the latest drugs which are being increasingly used as an adjuvant to regional anaesthesia (Daniel *et al*., 2009 and Kenan *et al*., 2012).

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We in this study compare clonidine (1ug/kg) and dexmedetomidine (1ug/kg) as an adjuvant to 0.25% bupivacaine (35ml) in brachial plexus block in orthopedic surgeries of upper limb.

MATERIALS AND METHODS

After seeking ethical committe clearance, study titled "A comparative study of clonidine (1ug/kg) and dexmedetomidine (1ug/kg) as an adjuvant to 0.25% bupivacaine in brachial plexus block (supraclavicular approach) in patients posted for orthopedic surgeries of upper limb" was carried out on 80 patients of either sex. The study design comprised of two groups of 40 patients each of ASA I/II of age groups 18-60yrs posted for upper limb surgeries under brachial plexus block (supraclavicular approach).

Total volume of drug solution being 35cc in all groups.

Group C :- 0.25% bupivacaine + 1µg/kg Clonidine.
Group D :- 0.25% bupivacaine + 1µg/kg Dexmedetomidine.

Exclusion criteria included

Infection at the site of injection, bleeding disorder or patient on anticoagulant therapy, operation on shoulder joint, failed blocks and patients who were supplemented intraoperatively with opioids, analgesics or converted into General Anaesthesia. Patients who were uncooperative or could not tolerate any degree of respiratory compromise due to underlying diseases. Patients with abnormal psychological profile & drug allergy (local anaesthetics). Patients with history of opioid addiction, peripheral neuropathy & neurological deficit, convulsions, hepatic dysfunction, renal diseases, phrenic nerve palsy, pneumothorax, ischemic heart disease, increased intracranial pressure, intraocular pressure and cerebrovascular accident. Sensory block was assessed by pin prick method in all dermatomal areas corresponding to radial, ulnar, median and musculocutaneous nerves, every minute till complete sensory block and post-operatively until resolution of block. Onset time for sensory block was defined as the time interval between the end of local anaesthetic administration and sensory block score 1 for all nerves. Duration of sensory block was defined as the time interval between the sensory block score 1 and complete resolution of anaesthesia on all the nerves (score 0). Motor block was assessed on modified Bromage scale for upper extremity on a three point scale every minute till complete motor block and postoperatively until resolution of block. Onset time for motor block was defined as the time interval between total local anaesthetic administration and motor block grade 1. Duration of motor block was defined as the time interval from motor block grade 1 to complete recovery of motor function of hand and forearm (grade 0). Sedation was assessed on Ramsay sedation score at every minute upto 15 minutes there after every 15 minutes till 180 minutes. Operative quality was be assessed on a numeric scale. Post-operative analgesia was assessed on VAS (visual analogue score) from 0 to 10. It was explained preoperatively to all the patients that, one end of the line depicts '0' which represents no pain at all, while the other end depicts '10' which represents worst pain he/she has ever felt. Rescue analgesia was given in the form of inj. diclofenac sodium (1.5mg/kg) intramuscularly at Numeric Rating Scale of 5. Post-operative analgesia was the time interval between sensory block grade 1 and the Numerical Rating scale 5 i.e. when rescue analgesia was given. At the end of the procedure all the patients were shifted to the recovery room and monitored.

Observations and Tables

Table 1. Distribution of cases in study groups

Groups	No. of Cases	Percentage
C	40	50
D	40	50
Total	80	100

In both groups C and D, there were 40 patients each.

Table 2. Sex wise distribution in study groups

SEX	Group C	Group D
Male	25	25
Female	15	15
Total	40	40

In both groups C and D, there were 25 male patients and 15 male patients each.

Table 3. Comparison of age (years) in study groups

	Group C	Group D	p value
Age (Years) (Mean ± SD)	39.9 ± 13.63	38.72 ± 11.12	Not significant

In both groups C and D, age groups of the patients were comparable.

Table 4. Comparison of height (cm) in study groups

	Group C	Group D	p value
Height (cms) (Mean ± SD)	162.55 ± 76 cm	163.37 ± 5.56 Cm	Not significant

In both groups C and D, height of the patients were comparable.

Table 5. Comparison of weight (kg) in study groups

	Group C	Group D	p value
Weight (kg) (Mean ± SD)	69.92 ± 5.28 (kg)	69.47 ± 3.88 (kg)	Not Significant

In both groups C and D, weight of the patients were comparable.

Table 6. Comparison of sensory onset response between group c and group d

Onset (min)	Group C	Group D	F value	P value
Grade I	7.90 ± 1.35	6.70 ± 1.40	3.901	0.000

The onset of sensory block was earlier in Group D: Dexmedetomidine (6.7 ± 1.40 min) as compared to Group C: Clonidine (7.9 ± 1.35 min) which was statistically highly significant.

Table 7. Comparison of motor onset response between group c and group d

Onset (min)	Group C	Group D	F value	p Value
Grade I	13.05 ± 1.56	12.10 ± 1.97	0.624	0.020

The onset of motor block was earlier in Group D: Dexmedetomidine (12.10 ± 1.97 mins) as compared to Group C: Clonidine (13.05 ± 1.56 mins) and independent samples t test showed significant difference statistically.

Table 8. Comparison of duration of sensory block between group c and group d

Duration (minutes)	Group C	Group D	F value	p Value
Grade 0	267.38 ± 20.908	611.25 ± 32.890	10.021	0.000

The duration of sensory block was higher in Group D: Dexmedetomidine (611.25 ± 32.890 min) as compared to

Group C: Clonidine (267.38 ± 20.908 min) and independent samples t test showed high significant difference statistically.

Table 9. Comparison of duration of motor block between group c and group d

Duration (minutes)	Group C	Group D	F Value	p value
Grade 0	228.75 ± 18.21	566.6 ± 37.28	17.756	0.000

The duration of motor block was higher in Group D: Dexmedetomidine (566.6 ± 37.28 min) as compared to Group C: Clonidine (228.75 ± 18.21 min) and independent samples t test showed high significant difference statistically.

Table 10. Comparison of duration of postoperative analgesia between group c and group d

Duration (minutes)	Group C	Group D	F value	p Value (2-tailed)
Grade 0	294.38 ± 29.74	637.50 ± 30.19	0.156	0.000

The duration of Post – operative analgesia was longer in Group D: Dexmedetomidine (637.50 ± 30.192 min) as compared to Group C: Clonidine (294.38 ± 29.747 min). Independent samples t test showed high significant difference statistically.

Table 11. Comparison of sedation scores in group candd group d

	0 (min)	30	60	90	120	150	180
C – Grade 1	15	-	-	-	-	-	-
C – Grade 2	25	38	23	23	40	40	40
C – Grade 3	-	2	17	17	-	-	-
C - Grade 4	-	-	-	-	-	-	-
D – Grade 1	16	-	-	-	-	-	-
D – Grade 2	24	13	-	-	-	1	2
D - Grade 3	-	23	15	12	28	39	38
D - Grade 4	-	4	25	28	12	-	-
Asymp. Sig. (2-sided)	0.818	0.000	0.000	0.000	0.000	0.000	0.000

Sedation scores in Group C and Group D were compared applying "Chi-Square test" test and showed statistically significant difference at 30, 60, 90, 120, 150 and 180 minutes, which was clinically not significant as no intervention was required.

Table 12. Comparison of operative quality between group c and group d

	Grade 1	Grade 2	Grade 3	Grade 4	Total
Group C	-	-	18	22	40
Group D	-	-	9	31	40

Operative quality was compared by applying Chi-Square test with Asymp. Sig. (2-sided) 0.000, which was statistically highly significant.

DISCUSSION

Gupta *et al*. (2013) in 2013 studied effect of concentration of local anaesthetic solution on the ED_{50} of bupivacaine for supraclavicular brachial plexus block. They studied three different concentration 0.25%, 0.375%, or 0.5% of bupivacaine. They suggested the mass of bupivacaine rather than the concentration is the major determinant of the ED_{50} for achieving supraclavicular brachial plexus block. They demonstrated that the ED_{50} dose of bupivacaine for supraclavicular block is not dependent on the concentration. Lowering the concentration or the strength of the local anaesthetic leads to an increase in the volume required for successful block. The rationale for using the concentration of Bupivacaine 0.25% and volume of 35 cc was avoid to toxic levels of bupivacaine and to compare adjuvants Clonidine and dexmedetomidine. Singelyn *et al*. in 1996 did a comparative study of minimum dose of Clonidine when added to Mepivacaine prolonged the duration of anaesthesia and analgesia after axillary Brachial Plexus Block. They concluded that the dose of clonidine required to prolong significantly the duration of both anaesthesia and analgesia after axillary brachial plexus blockade is 0.5 µg/kg. No added benefits were reported with doses exceeding 1.5µg/kg body weight. The enhancing effect of small dose of Clonidine on mepivacaine may be because of C- fiber action potential. Although Dexmedetomidine has α1/α2 selectivity eight times higher than clonidine, an equipotent dosage of both the drugs in supraclavicular brachial plexus block was not available when we started the study. Dose selection was based on previous studies where 1µg/kg body weight Dexmedetomidine and 1µg/kg body weight Clonidine were used in Bier's Block with Lignocaine by Abosideira *et al* in 2008.

Similar dosing was also used by Swami *et al*. in 2012 in comparison between Clonidine and Dexmedetomidine. From the Table 1- 5, we observe that in both groups C and D, there were 40 patients each. Of them 25 male patients and 15 male patients were present in each group. Age groups, height and weight of the patients in either group were comparable. From the table 6, we observe that the onset of sensory block was earlier in Group D: Dexmedetomidine (6.7 ± 1.40 min) as compared to Group C: Clonidine (7.9 ± 1.35 min) which was statistically highly significant. In our study onset of sensory blockade in Group C i.e. Clonidine was 7.9 ± 1.35 min. Hutschala *et al*. (2004) reported sensory block of nerves at 1µg Clonidine as 17±11,17±11, 19±7,16±7 min for median cubital radial and musculocutaneous nerve distribution respectively. Duma *et al*. (2005) reported the median onset time (min-max) to be 10 (5–60) min. Chakraborty *et al*. (2010) reported onset of sensory block with 25 ml of 0.25% Bupivacaine and 30 µg clonidine as adjuvant to be 6.2 ±0.78 min. Kulkarni *et al* [11] reported the onset with 75 µg Clonidine as adjuvant to 25 ml of 0.25% Bupivacaine to be 3.4± 0.67 min. Our result i.e 7.9 ± 1.35 min lies between the values observed by Duma*et al*[9] 10 (5–60) and Chakraborty *et al*. (2010) 6.2 ±0.78 min respectively.

The onset of sensory blockade in Group D i.e. Dexmedetomidine was 6.7± 1.40 min. Gandhi *et al*. (2012) reported onset of complete sensory blockade to be 21.4 ± 2.51 min with 0.25% Bupivacaine and 30 µg Dexmedetomidine. Agarwal *et al*[13] reported it to be 13.20±1.848 min with 30 ml of 0.325% bupivacaine + 1 ml (100 µg) Dexmedetomidine. From the table 7, we observe that the onset of motor block was earlier in Group D: Dexmedetomidine (12.10 ± 1.97 mins) as compared to Group C: Clonidine (13.05 ± 1.56 mins) and independent samples t test showed significant difference statistically. In our study onset of motor blockade in Group C was 13.05 ± 1.56 min. Duma *et al*. (2005) reported the median onset time (min-max) to be 30 (5–60) min. Chakraborty *et al*.[10] reported onset of sensory block with 25 ml of 0.25% Bupivacaine and 30 µg clonidine as adjuvant to be 10.6 ±1.36 min. Our observation of 13.05 ± 1.56 was comparable to that of Chakraborty *et al*. (2010) with 10.6 ±1.36 min. The onset of motor blockade in Group D was 12.10± 1.97 min. Gandhi *et al*.[12] reported onset of complete motor blockade to be 11.2 ± 2.1 min with 0.25% Bupivacaine and 30 µg Dexmedetomidine. Agarwal *et al*. (2014) reported it to be 16.3±1.7 min with 30 ml of 0.325% bupivacaine + 1 ml (100 µg) Dexmedetomidine. Our observation of 12.10± 1.97 min is comparable to that of Gandhi *et al*. (2012) From the table 8, we observe that the duration of sensory block was higher in Group D: Dexmedetomidine (611.25 ± 32.890 min) as compared to Group C: Clonidine (267.38 ± 20.908 min) and independent samples t test showed high significant difference statistically. In our study duration of sensory block in Group C was 267.38 ± 20.908 min. Swami *et al*. (2012) reported it to be 227±48.36 min. Duma *et al*. (2005) reported the median duration time (min-max) to be1040 (520–2380) min. Chakraborty *et al*. (2010) reported duration of sensory block with 25 ml of 0.25% Bupivacaine and 30 µg clonidine as adjuvant to be 279.1 ± 28.98 min. Our observation of 267.38 ± 20.908 min was comparable to that of Chakraborty *et al*. (2010) with 279.1 ± 28.98 min. The duration of sensory block in Group D was 611.25 ± 32.890 min. Swami *et al*. (2012) reported it to be 413.97 ± 87.31 min. Gandhi *et al*. (2012) reported it to be732.4 ± 48.9 min with 0.25% Bupivacaine and 30 µg Dexmedetomidine. Agarwal *et al*. (2014) reported it to be755.6 ± 126.8 min with 30 ml of 0.325% bupivacaine + 1 ml (100 µg) Dexmedetomidine.

From the table 9, we observe that the duration of motor block was higher in Group D: Dexmedetomidine (566.6 ± 37.28 min) as compared to Group C: Clonidine (228.75 ± 18.21 min) and independent samples t test showed high significant difference statistically. In our study duration of motor block in Group C was 228.75±18.213min. Swami *et al*. (2012) reported it to be 292.67 ± 59.13 min. Chakraborty *et al*. (2010) reported duration of motor block with 25 ml of 0.25% Bupivacaine and 30 µg clonidine as adjuvant to be 330.4 ± 31.68 min. The duration of motor block in Group D was 566.62 ± 37.286 min. Swami *et al*. (2012) reported it to be 472.24 ± 90.06 min. Gandhi *et al* (2012) reported the duration of motor blockade was to be 660.2 ± 60.4 min with 0.25% Bupivacaine and 30 µg Dexmedetomidine. Agarwal *et al*. (2014) reported it to be702.0±111.6 min with 30 ml of 0.325% bupivacaine + 1 ml (100 µg) Dexmedetomidine. Our observation of 566.62 ± 37.286min lies in between to that of Swami *et al*. and Gandhi *et al*. (2012) From the Table 10, we observe that the duration of post – operative analgesia was longer in Group D: Dexmedetomidine (637.50 ± 30.192 min) as compared to Group C: Clonidine (294.38 ± 29.747 min). Independent samples t test showed high significant difference statistically. In our study duration of postoperative analgesia in Group C was 294.38 ± 29.747 min. Swami *et al*. (2012) reported it to be 289.67 ± 62.50 min. Chakraborty *et al* (2010) reported duration of postoperative analgesia with 25 ml of 0.25% Bupivacaine and 30 µg clonidine as adjuvant to be 415.4 ± 38.18 min. Our observation of 294.38 ± 29.747 min was comparable to that of Swami *et al*. (2012) with 289.67 ± 62.50 min. The duration of postoperative analgesia in Group D was 637.50 ± 30.192 min. Swami *et al*. (2012) reported it to be 456.21 ± 97.99 min. Gandhi *et al* (2012) reported the duration of postoperative analgesia was to be 732.4 ± 95.1 min with 0.25% Bupivacaine and 30 µg Dexmedetomidine. Agarwal *et al* (2014) reported it to be 776.4±130.8 min with 30 ml of 0.325% bupivacaine + 1 ml (100 µg) Dexmedetomidine. Our observation of 637.50 ± 30.192min is comparable to that of Gandhi *et al* (2012) From the table 11, the sedation scores in Group C and Group D were compared applying "Chi-Square test" test and showed statistically significant difference at 30, 60, 90, 120, 150 and 180 minutes, which was clinically not significant as no intervention was required. In our study, sedation score was compared using Ramsay sedation scale. In Group C 37.5% patients were anxious at the start of the procedure. At 30 minutes 95% patients were cooperative, orientated and tranquil, while 5% patients were sedated but responding to commands. The percentage of patients sedated but responding to commands increased to 42.5% at 60 minutes and continued till 90 minutes. Thereafter almost all the patients were in cooperative, orientated and tranquil grade. In Group D 40% patients were anxious at the start of the procedure. While at 30 minutes 32.5% were cooperative, orientated and tranquil, 57.5% were sedated but responding to commands and 10% were sedated and gave brisk response to stimulus. Percentage of patients in grade 4 increased to 62.5% and 70% at 60 and 90 minutes respectively. After which most of the patients were in grade 3.

No active intervention was required any point of time intraoperatively or postoperatively for any grade of sedation. Sedation in study groups can be explained on the basis that some amount of systemic absorption of the drugs could be present. (Shivinder Singh and Amitabh Aggarwal, 2010) As α2 agonist produce sedation by central action, they produce inhibition of substance P release in the nociceptive pathway at the level of dorsal root neuron and by activation of α2 adrenoreceptor in locus coeruleus. We did not find any literature available for comparison of sedation of these two drugs in supraclavicular brachial plexus block. From the table 12, we observe that the operative quality was compared by applying Chi-Square test with Asymp. Sig. (2-sided) 0.000, which was statistically highly significant. In Group C 45% patients had grade 3 operative quality and 55% had grade 4 operative quality i.e. (excellent) no complaint from patient. While in Group D 22.5% patients had grade 3 operative quality and 77.5% patients had grade 4 operative quality. Swami *et al*. (2012) also had compared operative quality using same methodology and reported that 80% patients in

dexmedetomidine group and 40% patients in clonidine group had grade 4 operative quality, which is comparable to our study.

Conclusion

Dexmedetomidine had shorter onset of both sensory as well as motor block when compared to Clonidine. Dexmedetomidine had significantly longer duration of both sensory and motor block compared to Clonidine. Dexmedetomidine had significantly longer duration of post-operative analgesia compared to Clonidine. Operative quality was significantly better in Dexmedetomidine group as compared to Clonidine group. We conclude that Dexmedetomidine is superior adjuvant to Clonidine. It should be preferred if the duration of surgery is longer and in cases where extended post-operative analgesia is required.

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