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Original Research Article

Brachial plexus block- A comparison between clonidine and dexmedetomidine as an adjuvant to local anaesthetic agent ropivacaine in supraclavicular approach

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Abstract: Local anaesthetics are used widely in regional and peripheral nerve blocks inspite of many disadvantages like short duration of action, associated allergic reaction and systemic toxicity. To overcome the above drawbacks different measures tried. The search for ideal additive continues and led us to try the novel α2 adrenergic agonist dexmedetomidine and clonidine as an adjuvant to local anaesthetics in supraclavicular brachial plexus block. Ninety patients aged 18 to 60 years, scheduled for elective Orthopaedic/Plastic surgery operations distal to elbow in the upper limb, under supraclavicular brachial plexus block, were included in this study. The study was designed as a prospective, randomized, double-blind, placebo-controlled trial. Group RC - 20 ml of 0.5% Ropivacaine and Clonidin (1 mcg/kg) diluted to 30 ml with normal saline, Group RD - 20 ml of 0.5% Ropivacaine and Dexmedetomidine (1 mcg/kg) diluted to 30 ml with normal saline, Group R - 20 ml of 0.5% Ropivacaine diluted to 30 ml with normal saline. . All observations (level of sedation, time required to achieve surgical block in the operation theatre, hemodynamic variables and the time to rescue analgesic in the post anaesthesia care unit) were also recorded in a blinded manner. Continuous data are presented as mean ± SD one way ANOVA test were used for parametric data analysis. Results of this study demonstrate that adding 1µg/kg Dexmedetomidine to 0.5% Ropivacaine hastens the onset of sensorimotor block and prolongs the duration of postoperative analgesia more than 1 g/kg clonidine to 0.5% Ropivacaine in brachial plexus block . Hemodynamics remained stable throughout the study period with both the drugs.
Keywords: Dexmedetomidine, Ropivacaine, Local anaesthetics, nerve block

INTRODUCTION

Local anaesthetics are used in various type of regional and peripheral nerve blocks. The disadvantages are its short duration of action, associated allergic reaction and systemic toxicity[1]. To overcome the above drawbacks different measures tried are addition of enzymes, buffers, carbonated solutions, opioids, vasoconstricting agents, alkalinization and warming of local anaesthetic solutions and potentiation of block by pain and muscular exercise[2]. The search for ideal additive continues and led us to try the novel α2 adrenergic agonist dexmedetomidine and clonidine as an adjuvant to local anaesthetics in supraclavicular brachial plexus block.

α2 receptors are located presynaptically in sympathetic nerve endings and in nor-adrenergic neurons in the CNS. Dexmedetomidine is a potent α2 agonist and its α2/α1 selectivity is approximately 8 times more towards α2, than clonidine[3,4].

MATERIALS AND METHODS

Ninety patients aged 18 to 60 years, scheduled for elective Orthopaedic/Plastic surgery operations distal to elbow in the upper limb, under supraclavicular brachial plexus block, were included in this study. All the patients were of ASA grade I or II. Patients receiving chronic analgesic therapy, severe cardiopulmonary disease, thyroid disorders, diabetes mellitus, central or peripheral neuropathies, pregnant woman, bleeding disorders , history of allergy to local anaesthetics, or contraindications to regional anaesthesia were excluded from the study.

The study was designed as a prospective, randomized, double-blind, placebo-controlled trial. Participants were randomly allocated to three equal groups of 30 each .

- Group RC - 20 ml of 0.5% Ropivacaine and Clonidin (1 mcg/kg) diluted to 30 ml with normal saline
- Group RD - 20 ml of 0.5% Ropivacaine and Dexmedetomidine (1 mcg/kg) diluted to 30 ml with normal saline
- Group R - 20 ml of 0.5% Ropivacaine diluted to 30 ml with normal saline

All the patients received brachial plexus block through the supraclavicular approach and neural localization was achieved by using a nerve locator connected to a 22G, 50mm long stimulating needle. Following negative aspiration,30ml of a solution as mentioned above was injected.

The surgical procedure was performed by using a standard arm tourniquet inflated to 100 mmHg higher than systolic blood pressure. Hemodynamic variables were measured 10 min before block placement, every 5 min till the end of surgery and thereafter every 60 minutes till complete recovery. All observations (level of sedation, time required to achieve surgical block in the operation theatre, hemodynamic variables and the time to rescue analgesic in the post anaesthesia care unit) were also recorded in a blinded manner.

Assessment :

Sensory block was assessed by the pinprick method. Assessment of sensory block was done at each min after completion of drug injection in the dermatomal areas corresponding to median nerve, radial nerve, ulnar nerve & musculocutaneous nerve till complete nerve blockade. Sensory onset was considered when there was a dull sensation to pin prick along the distribution of any of the above-mentioned nerves. Complete sensory block was considered when there was loss of sensation to pinprick.

Sensory block was graded as-

Grade-0: Sharp pin felt.
Grade-1: Analgesia, dull sensation felt.
Grade 2: Anaesthesia, no sensation felt.

Assessment of motor block was carried out by the same observer at each minute till complete motor blockade after drug injection. Motor blockade was determined according to a modified Bromage scale for upper extremities on a 3-point scale.

Grade 0: Normal motor function with full flexion and extension of elbow, wrist and finger.
Grade 1: Decreased motor strength with ability to move the fingers only.
Grade 2: Complete motor block with inability to move the fingers.

The block was considered incomplete any of the segments supplied by median, radial, ulnar and musculocutaneous nerve did not have analgesia even after 30min of drug injection. In this case, general anaesthesia was given intra-operatively.

Patients were monitored for haemodynamic variables such as heart rate, blood pressure every 5min after the block intra-operatively and every 60min post-operatively clinically recorded. Clinically relevant bradycardia (heart rate <45bpm) spells were treated with atropine (0.6mg IV).

At the end of the procedure, quality of the operative condition were assessed according to the following numeric scale:
Grade 4: (Excellent) No complaint from patient
Grade 3: (Good) Minor complaint from patient with no need for the supplemental analgesics.
Grade 2: Moderate) Complaint that required supplemental analgesics.
Grade 1 :(Unsuccessful)Patient given General anaesthesia.

Assessment of the blood loss was done and fluid was administered as per the loss. Duration of surgery was noted.

Patients were assessed for duration of analgesia as per a numeric rating scale of 0 to 10.The numeric rating scale was recorded post-operatively every 60min till the score of 5.The rescue analgesia was given in the form of inj. Tramadol 100mg intramuscularly at the Numeric Rating Scale of 5 and the time of administration was noted. All patients were observed for any side-effect like nausea, vomiting, dryness of mouth and complications like pneumothorax, haematoma, local anaesthetic toxicity and post-block neuropathy in the intra-operative and post-operative periods.

The duration sensory block was defined as the time interval between the end of local anaesthetic administration and the complete resolution of anaesthesia on all nerves. The duration motor block was defined as the time interval between the end of local anaesthetic administration and the recovery of complete motor function of the hand and forearm.

Statistical Analysis:

The statistical software namely SPSS(Statistical Package for Social Sciences) software version 21, were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables etc.

Statistical Methods

Continuous data are presented as mean ± SD one way ANOVA test were used for parametric data analysis.

OBSERVATION

Table-1. Age, sex and weight distribution of Study groups

Parameters	R	RC	RD	P-value	Significance
No of pts	30	30	30		
Age in yrs (Mean± SD)	33.43±10.86	34.27±9.32	33.23±10.30	>0.05	NS
Weight(kg) (Mean± SD)	57.27±6.05	56.47±6.12	57.17±6.37	>0.05	NS
Gender(M/F)	18:12	20:10	17:13	>0.05	NS

All the groups are comparable according to their number of patients, age,weight and gender.

Table-2 .Time for onset of sensory block (min)

Study group	Onset time in min (Mean ±SD)	P value	Significant
R	6.70±1.11	<0.0 01	HS
RC	4.47±.93	<0.01	HS
RD	3.40±1.00		

The time for onset of sensory block in group RC and group RD were significantly faster than group R. Onset of sensory block was also faster in group RD when compared to group RC & highly significant (P< 0.01).

Table-3. Time for onset motor block (min)

Study group	Onset time (Mean ± SD)	P value	Significant
R	12.43±1.67	P<0.001	HS
RC	6.63±.99	P>0.05	NS
RD	6.03±1.40		

The time for onset of motor block was significantly faster in group RC and RD when compared to group R (P<0.001).Onset of motor block was faster in Dexmedetomidine group than Clonidine group but not statistically significant.

Table-4. Duration of sensory block (min)

Study group	Duration block (Mean ±SD)	P value	Significance
R	426.50±30.77	P<0.001	HS
RC	703.83±16.33		
RD	745.00±19.25		

The time for duration sensory block were significantly longer in group RC and RD when compared to group R (P<0.001).In group RD duration of sensory block was significantly longer than the group RC(P<0.001)

Table-5. Duration of motor block (min)

Study group	Duration of block (Mean ±SD)	P value	Significant
R	396.47±23.61	P<0.001	HS
RC	660.33±18.04		
RD	707.50±25.85		

The time for duration motor block were significantly longer in group RC and RD when compared to group R (P<0.001). In group RD duration of motor block were significantly longer than the group RC(P<0.001)

Table-6. Duration of Analgesia(min)

Study group	Duration of analgesia (Mean ±SD	P value	Significant
R	452.63±12.29	< 0.001	HS
RC	744.07±13.54		
RD	778.13±21.77		

The time for duration analgesia were significantly longer in group RC and RD when compared to group R (P<0.001). In group RD duration of analgesia was significantly longer than the group RC (P<0.001)

Table-7. Number of rescue analgesics in post-op 24 hours

No. of Rescue analgesia used	Ropivacaine	Ropivacaine + Clonidine (%)	Ropivacaine+ Dexmedetomidine (%)
1	0(0%)	13(43.3%)	23(76.7%)
2	23(76.7%)	9(30%)	7(23.3%)
3	7(23.3%)	8(26.7%)	0(0%)

Table-8. Quality of block

Quality of block	Mean +/ -SD		
	Ropivacaine N(%)	Ropivacaine + Clonidine N(%)	Ropivacaine + Dexmedetomidine N(%)
I	0	0	0
II	17(57.7)	8(26.7)	2(6.7)
III	10(33.3)	10(33.3)	4(13.3)
IV	3(10)	12(40)	24(80)

In group RD, 80% of the patients achieved Grade-IV quality of block as opposed to 40% in group RC. There were a total of 27 patients in Group R, 18 patients in Group RC and 6 patients in Group RD with Grade II and Grade III block who required sedation or sedation with analgesia. The Grade IV quality of block was significantly high in group RD in comparison to the group RC and group R.

Table-9.Haemodynamic variables :

Pulse Rate (beats / min)

Time of Assessment	Mean +/ -SD			P Value	Significance
	Ropivacaine	Ropivacaine + Clonidine	Ropivacaine + Dexmedetomidine		
0 min	78.87±7.14	79.33±9.02	78.70±6.86	P>0.05	NS
5 min	76.67±6.69	75.67±7.54	76.70±5.87	P>0.05	NS
15 min	73.83±6.74	73.37±7.04	73.90±6.53	P>0.05	NS
30 min	69.47±6.36	69.57±7.52	68.60±5.31	P>0.05	NS
60 min	69.17±6.25	68.80±7.38	68.17±5.46	P>0.05	NS
2 hr	75.47±6.67	74.77±7.59	74.87±5.43	P>0.05	NS
6 hr	76.17±5.84	76.77±7.61	76.77±5.78	P>0.05	NS
12 hr	77.63±6.51	78.07±7.68	78.57±6.38	P>0.05	NS
24 hr	77.73±6.96	77.70±8.01	78.93±6.48	P>0.05	NS

Systolic blood pressure (mm of Hg)

Time of Assessment	Mean± SD			P-Value	Significance
	Ropivacaine	Ropivacaine +Clonidine	Ropivacaine + Dexmedetomidine		
0 min	124.87±9.44	124.13±9.03	123.60±9.17	P>0.05	NS
5 min	124.13±9.05	124.33±8.53	123.07±9.29	P>0.05	NS
15 min	123.67±8.13	124.53±7.66	122.27±8.01	P>0.05	NS
30 min	122.07±8.09	123.93±8.50	121.53±7.92	P>0.05	NS
60 min	114.80±9.67	113.87±8.56	112.00±8.56	P>0.05	NS
2 hr	114.87±10.98	113.87±9.29	111.73±8.59	P>0.05	NS
6 hr	124.93±8.78	124.67±7.45	123.47±8.30	P>0.05	NS
12 hr	125.50±9.56	125.47±8.69	124.53±9.21	P>0.05	NS
24 hr	125.33±10.14	125.60±9.59	124.20±9.90	P>0.05	NS

Diastolic blood pressure (mm of Hg)

Time of Assessment	Mean+/-SD			P value	Sigificance
	Ropivacaine	Ropivacaine + Clonidine	Ropivacaine + Dexmedetomidine		
0 min	74.80±4.83	74.93±4.44	74.47±4.05	P>0.05	NS
5 min	74.80±4.35	74.40±4.18	74.27±4.03	P>0.05	NS
15 min	74.07±4.62	74.00±3.82	73.60±3.76	P>0.05	NS
30 min	72.87±5.37	73.13±5.05	72.73±4.44	P>0.05	NS
60 min	68.37±4.68	68.60±4.07	66.93±3.31	P>0.05	NS
2 hr	68.60±4.00	68.20±3.57	66.73±2.80	P>0.05	NS
6 hr	74.27±4.22	74.07±3.69	73.87±3.78	P>0.05	NS
12 hr	74.73±4.50	74.60±3.97	74.47±3.70	P>0.05	NS
24 hr	75.47±3.63	75.40±3.71	75.13±3.55	P>0.05	NS

There was no significant variation in the hemodynamic variables.

Table-10.SIDE EFFECTS

Side effects	Ropivacaine	Ropivacaine + Clonidine	Ropivacaine + Dexmedetomidine	Sigificance
Nausea	1	1	0	NS
Vomiting	1	1	1	NS
Dryness of mouth	0	1	0	NS

During our study we monitored for any side effect, we found out in Group R one patient complained for nausea and one patients for vomiting, in Group RC one patient complained for nausea, one patient for vomiting and one patient for dryness of mouth and in Group RD only one patient complained for vomiting.

DISCUSSION

Results of this prospective, randomized, double-blinded study demonstrate that adding 1µg/kg Dexmedetomidine to 0.5% Ropivacaine hastens the onset of sensorimotor block and prolongs the duration of postoperative analgesia more than 1 g/kg clonidine to 0.5% Ropivacaine in brachial plexus block . Hemodynamics remained stable throughout the study period with both the drugs. The mechanism by which α2 adrenergic receptor agonists produce analgesia and sedation is not fully understood but is likely to be multifactorial. Peripherally, α2agonists produce analgesia by reducing release of norepinephrine and causing α2 receptor-independent inhibitory effects on nerve fiber action potentials. Centrally, α2 agonists produce analgesia and sedation by inhibiting substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activating α2 adrenoceptors in the locus coeruleus

The role of clonidine as an adjuvant to local anaesthetics in upper limb peripheral nerve blocks has been extensively studied. Dose range of 30-300 µg has been used in various studies with up to 150µg doses being associated with minimal side effects. But some authors have shown that clonidine even at such doses can cause significant hemodynamics compromise which challenges its use in peripheral nerve blocks in outpatients. Besides, there is no study suggestive of any appropriate dose of clonidine according to weight/kg.

However all studies carried out so far to peripheral action of α2 agonists were animal studies[3,4]. Very few human trials have been conducted. Several studies have found dexmedetomidine to be safe and effective in various neuraxial and regional anesthesia techniques including intrathecal and I.V. regional anesthesia). A dexmedetomidine - lidocaine mixture has been used to provide Bier"s block and was shown to improve the quality of anesthesia and tourniquet pain and reduce postoperative analgesic requirement. Keeping these facts in mind we decided to compare the effects of addition of dexmedetomidine and clonidine with Ropivacaine in peripheral nerve block.

In our study we found that onset of sensory block was a little faster with group RD (3.40±1.00 min) as compared to group RC (4.47±.93), and was statistically significant. Both the group RC and Group RD significantly faster sensory onset than the plain Ropivacaine group (6.70±1.11 min). The onset of motor block was a little longer in Group RC (6.63±.99 min) than Group RD (6.03±1.40) but not significant statistically. However both Group RC and Group RD significantly shorter onset of motor block than Group R (12.43±1.67). Esmaoglu et al. in 2010 added dexmedetomidine to levobupivacaine for axillary brachial plexus block and showed that it shorten the onset time of both sensory and motor block, prolongs the duration of block and the duration of post-operative analgesia. This may be because peripheral α_2 agonist produces analgesia by reducing the release of

norepinephrine, leading to α_2 receptor-independent inhibitory effects on nerve fiber action potentials

The duration sensory block were significantly longer in group RC and RD when compared to group R (P<0.001). In group RD duration of sensory block were significantly longer than the group RC(P<0.001). The time for duration motor block were significantly longer in group RC and RD when compared to group R (P<0.001). In group RD the duration of motor block were significantly longer than the group RC (P<0.001).

The mean duration of analgesia in Group RD (778.13±21.77min) were longer than in Group RC (744.07±13.54min) and it was statistically significant. Both the Group RD and Group RC were longer duration of analgesia than Group R (452.63±12.29min) which was statistically significant.All the above findings relating to onset and duration of sensory and motor block and duration of analgesia ware similar to the study conducted by Swami SS *et al* [3].

Memis *et al*. [5] in their study showed that addition of dexmedetomidine to lignocaine for intravenous anaesthesia improves both the quality of anaesthesia as well as intraoperative and post operative analgesia. A study by *Brumett et al [6]* showed that dexmedetomidine enhances duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any damage to nerve. Hutschala *et al[7]*. and El Saied *et al.[8]* observed longer duration of analgesia and motor block with the use of clonidine as an adjuvant as compared to placebo. An increase in the duration of postoperative analgesia was also observed by Eledjam *et al.[9]*, Iohom *et al.[10]*, and Iskandar *et al.[11]*, Singelyn *et al.[12]* observed a linear increase in the duration of analgesia from 0.1µg /kg to 0.5µg /kg clonidine but not with 1 and 1.5µg /kg, indicating no further increase in analgesia with increasing dose.

The quality of block in 80% of the patients in Group RD were grade IV (i.e excellent block without any supplementary sedation or analgesia) while 40% in Group RC achieved grade IV quality, which was similar to the study conducted by Swami S.S *et al*. [3]. This improved quality of block might be the result of various mechanisms of nerve conduction block such as hyperpolarisation, decreased CAP and inhibition of voltage gate of sodium pump as per the study conducted by Popping DM *et al.* [13] and Kosugi T *et al.* [14].

In our study group RD, 76.7% patients required only 1 rescue analgesia dosage and 23.3% of patients required 2 rescue analgesic dosage in post operative 24hrs, in group RC 43.3% of the patients required 1, 30% patients required 2 rescue analgesia and 26.7% patients required 3 rescue analgesia dosage and in group R 76.7% patients required 2 analgesia dosage and 23.3% patients required 3 analgesia dosage. The number of rescue analgesia used were significantly less in group RC and RD when compared to group R . The prolonged analgesia in Group RD could be due to the action of Dexmedetomidine by inhibiting action potential of A & C fibers in peripheral nerves.

With these doses we had stable haemodynamics in patients and comparable within groups with respect to PR, SBP, DBP, SPO2.

So to conclude dexmedetomidine 1µg/kg when added to 30ml mixture of Ropivacaine 0.5% + NS for supraclvicular brachial plexus block speeds the onset of sensory and motor blocks, prolongs the duration of sensory and motor block. The combination produces improved analgesia resulting in a prolonged effect and reduces the requirement of rescue analgesia as compared to Clonidine. The above findings suggest that the Dexmedetomidine combination with Ropivacaine (as adjuvant) much superior to the Clonidine combination with ropivacaine and Plain Ropivacaine group.

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