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COMPARISON OF DEXMEDETOMIDINE AND BUTORPHANOL AS AN ADJUVANT TO BUPIVACAINE-LIGNOCAINE COMBINATION IN ULTRASONOGRAPHY GUIDED BRACHIAL PLEXUS BLOCK

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ABSTRACT

Background: Ultrasonography guided supraclavicular brachial plexus block is now an established method of anaesthesia for upper limb surgery. Various drugs have been used to prolong its intraoperative and postoperative analgesia. In this prospective, randomised double-blind controlled study, Butorphanol and Dexmedetomidine were compared as an adjuvant to local anaesthesia.

Materials and Methods: 60 ASA Grade I patients with age between18-60 years posted for repair of fracture of long bones of forearm were randomly divided in two groups. Group B patient received 14ml 0.5% Bupivacaine + 14ml 2% lignocaine + 2 mg Butorphanol while Group D received 1mcg/kg Dexmedetomidine with the local anaesthetics. Block characteristics, haemodynamic stability, duration of analgesia and adverse effects were observed and compared.

Results: Onset time of sensory (7.87 ± 2.69 mins Vs 13.87 ± 2.96 mins for grade 2) and motor block was significantly less in Butorphanol than Dexmedetomidine group. While mean duration of sensory blockade was significantly more ($p < 0.01$) in group D [543 (± 69.46) mins] than in group B [359 (± 54.68) minutes]. There was fall in mean heart rate, Systolic and mean BP which comparable and within physiological range in both the groups. Also, duration of postoperative analgesia was longer in group D (428.33 ± 77.02 mins) than group B (621.00 ± 83.72 minutes).

Conclusion: Butorphanol has early onset of action while Dexmedetomidine provides longer nerve blockade and analgesia.

KEYWORDS : Dexmedetomidine, Butorphanol, Supraclavicular block, Analgesia.

INTRODUCTION:

There has always been a search for adjuvants to the local anaesthetics that prolong the duration of peripheral nerve block with minimum adverse effects. Several drugs have been used as adjuvant with local anaesthetics to achieve quick, dense and prolonged block. Commonly used drugs are opioids like Morphine, Fentanyl[1,] Butorphanol[2] Buprenorphine[3] and alpha 2 agonists like Clonidine[4] and Dexmedetomidine[5.]

α-2 adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, perioperative sympatholytic and cardiovascular stabilizing effects with reduced anaesthetic requirements[6]. Dexmedetomidine has also shown to prolong the duration of block and post-operative analgesia when added to local anaesthetic in various regional blocks.[5,7]

Butorphanol is a synthetic opioid analgesic like morphine having partial agonist and antagonist activity at the μ opioid receptor, as well as competitive antagonist activity and partial agonist activity at the κ opioid receptor. It has been used alone & in combination with a local anaesthetic for axillary brachial plexus blockade.[2,3]

In this prospective, randomised study, we have compared Butorphanol and Dexmedetomidine as an adjuvant to bupivacaine and lignocaine in supraclavicular brachial plexus block with respect to the onset and duration of sensory and motor block as well as duration of analgesia.

METHODS:

After obtaining approval from the Institutional Ethics Committee, 60 ASA Grade I patients with age between18-60 years with fracture of long bones of forearm were selected. All the patients were to undergo surgeries under supraclavicular brachial plexus block. Patients with traumatic forearm nerve injury were not included. Also, patients with history of neuromuscular or cardiovascular diseases, bleeding disorders, seizures or allergy to local anaesthetic agents were excluded from the study. All patients underwent pre-anaesthetic check-up which included detail history, examination and necessary investigations. Procedure was explained and a written, informed consent was obtained from each patient. Patients were randomly allocated to one of the two groups **group B** (n= 30) or **group D** (n= 30) using randomization table.

In operation theatre, monitors were attached to the patient in supine position and all the baseline parameters such as heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SPO_2), electrocardiography were noted. An i.v. infusion was started. With patient in supine position, using all aseptic precautions, ultrasound guided supraclavicular brachial plexus block[8] was performed. Local anaesthetic solutions used for nerve blocks were as following:

Group B – 14ml 0.5% Bupivacaine + 14ml 2% lignocaine + 2 mg Butorphanol (made up to 2ml with normal saline). Final volume of the injectate was 30ml.

Group D – 14ml 0.5% Bupivacaine + 14ml 2% lignocaine + 1mcg/kg Dexmedetomidine (made up to 2 ml with normal saline). Final volume of the injectate was 30ml.

Preparation of study drugs and assessment of vital and made by anaesthesiologists blinded to the study. Onset of sensory block was assessed by pin prick method. Motor block was graded according to the 3-point modified Bromage score[9]. The duration of analgesia was assessed by using an 11-point (0-10) verbal numeric rating scale (VNRS).[10] Data was recorded in printed proforma. Qualitative data is presented with the help of Frequency and Percentage table and association among study group has been assessed with the help of Chi-Square test. Quantitative data is presented with the help of mean and standard deviation. Comparison among study group has been done with the help of Unpaired T test if data passed normality test, or Mann-Whitney Test if data failed normality test. P value less than 0.05 is taken as significant level.

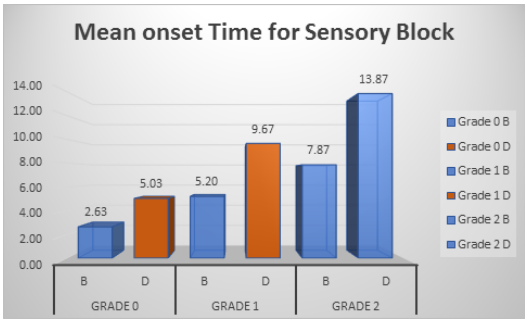
Results:

TABLE 1. DEMOGRAPHIC DATA

Variables	Group B (Mean + S. D.)	Group D (Mean + S. D.)	P value
N	30	30	
Age (yrs)	33.17+13.16	36.07 + 14.95	0.428
weight (kg)	55.53+9.12	58.03 + 6.99	0.238
Gender			
Female	5	5	0.532
	16.70%	16.70%	
Male	25	25	
	83.30%	83.30%	
Duration of Surgery (mins)	127.17+44.66	144+ 38.69	0.124

Comparison of block characteristics:

Mean time of onset for grade 1 sensory block for group B (5.20 ± 2.14 mins) was significantly less than group D (9.67 ± 2.40), (p value <0.01). (Fig. 1) Also, mean time of onset of grade 2 sensory block was also less for group B (7.87 ± 2.69 mins) than group D (13.87 ± 2.96 mins).



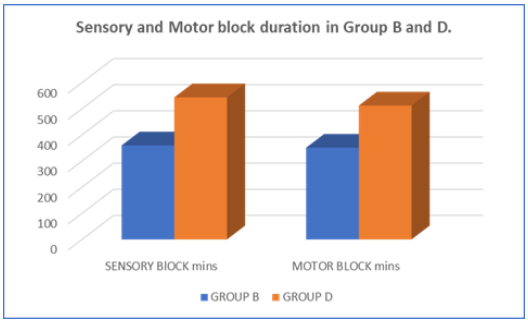
[Fig. 1] comparison of onset of sensory blockade in group B and D

Time required for onset (5.37 ± 1.47 vs 8.37 ± 1.97 mins) and complete establishment of grade 3 motor block (10.20 ± 2.58 Vs 18.33 ± 2.94 mins) was also significantly higher in group B than group D. (Table.2)

Table2. Comparison of motor block onset (in minutes) between group B and D

Motor Block	Group	N	Mean	SD	p- value
Grade 1	B	30	5.37	1.47	<0.01
	D	30	8.37	1.97	
Grade 2	B	30	7.53	2.10	<0.01
	D	30	13.37	2.33	
Grade 3	B	30	10.20	2.58	<0.01
	D	30	18.13	2.94	

Comparison of sensory and motor block duration between Group B and Group D: As seen in fig. 2 The mean duration of sensory blockade was significantly more (p < 0.01) in Dexmedetomidine group [543 (± 69.46) mins] than in Butorphanol group [359 (± 54.68) minutes].



[Fig.2] Sensory & Motor block duration in Group B and Group D.

Similarly, the mean duration of motor blockade in Group D [512.33 (± 78.29) minutes] was also significantly higher than in Group B [351.00 (± 60.48) minutes]. (p < 0.01)

Haemodynamic Parameters:

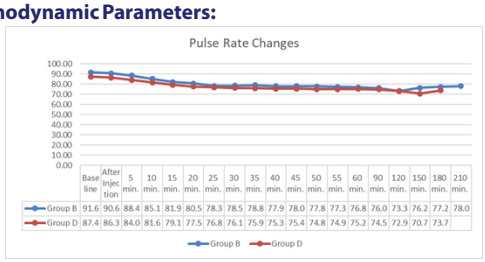


Fig. 3: Changes in heart rate

There was fall in mean heart rate compared to baseline from 5 min to 210 minutes in group B. The lowest heart rate was 73.35 ± 7.49 bpm at 120th min after giving block. group D also, there was fall in mean heart rate as compared to baseline from 5 min to 210 minutes. The lowest heart rate was 70.73 ± 7.00 bpm at 60th min after giving block However, this fall in heart rate was comparable and within physiological range in both the groups and none of the patients developed bradycardia.

Table 3: 10. Comparison of SBP between group B and group

SBP (mm hg)	Group	N	Mean	SD	p- value
Baseline	B	30	127.33	9.15	0.68
	D	30	128.23	7.52	
After Injection	B	30	126.93	9.82	0.79
	D	30	127.57	8.40	
5 min.	B	30	125.03	8.58	0.65
	D	30	124.00	8.72	
10 min.	B	30	120.47	7.44	0.32
	D	30	123.27	13.26	
15 min.	B	30	117.80	9.13	0.54
	D	30	119.17	8.14	
20 min.	B	30	115.90	9.31	0.40
	D	30	117.90	9.02	
25 min.	B	30	114.20	10.16	0.70
	D	30	112.57	21.02	
30 min.	B	30	113.10	10.79	0.40
	D	30	115.33	9.70	
35 min.	B	30	112.30	10.80	0.72
	D	30	113.27	9.73	
40 min.	B	30	110.83	10.93	0.16
	D	30	114.47	8.92	
45 min.	B	30	110.73	9.52	0.14
	D	30	114.33	9.20	
50 min.	B	29	112.35	10.45	0.75
	D	30	113.20	9.89	
55 min.	B	29	110.00	11.57	0.06
	D	30	115.57	10.37	
60 min.	B	29	110.24	11.44	0.05
	D	30	115.63	9.65	
90 min.	B	27	110.78	11.27	0.19
	D	30	114.50	9.72	
120 min.	B	21	112.76	13.02	0.85
	D	28	113.39	10.49	
150 min.	B	13	115.31	10.06	0.71
	D	18	113.89	10.91	
180 min.	B	9	112.00	6.40	0.76
	D	12	113.33	11.38	
210 min.	B	4	114.00	7.30	0.93
	D	7	113.43	11.53	
240 min.	B	1	116.00	.	NA
	D	0	.	.	

There was fall in mean SBP compared to baseline from 5 min to 240 minutes in group B. The lowest SBP was110.00 ± 11.57 mm of Hg at 55th min after giving block. However, this fall in SBP was within physiological range. None of the patients developed hypotension (SBP< 90 mm of Hg). In group D also, there was fall in mean SBP compared to baseline from 5 min to 210 minutes. The lowest SBP was 112.57 ±21.02 mm of Hg at 25th min after giving block. However, this fall in SBP was within physiological range and none of the patients developed hypotension (SBP< 90 mm of Hg). There was no statistically significant difference in mean systolic blood pressure of the two groups at all the respective intervals. (p >0.05).

As shown in Fig no. 4 there was fall in MAP from 5 mins to 240 mins in both the groups as compared to baseline MAP. In group B, the lowest MAP was 64.89 ± 24.45 mm of Hg at 210th min after the block. In group D, the lowest MAP was 78.76 ± 20.23 mm of Hg at 210th min after the block. However, the fall in MAP was within physiological range and the difference in MAP between the two groups was statistically not significant at all the respective intervals (p > 0.05).

Changes in mean arterial pressure:

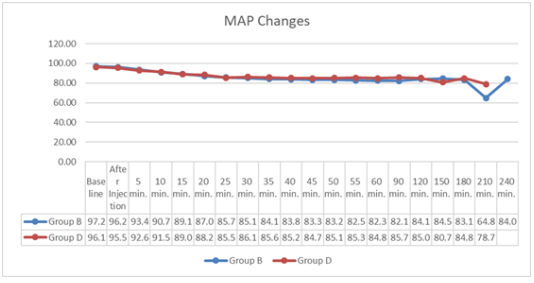


Fig 4: comparison of mean arterial blood pressure (MAP)

Diastolic (DBP) followed tends similar to SBP and mean arterial BP (MAP).

Duration of Analgesia:

Postoperative analgesia was calculated using VNRS scale.

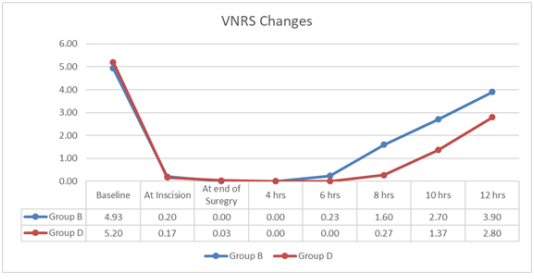
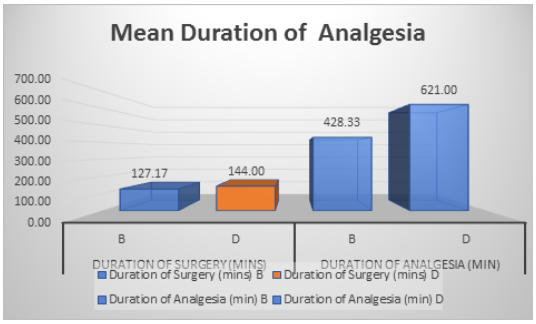


FIG 5: CHANGES IN VNRS PAIN SCALE

The difference in mean value of basal VNRS was statistically not significant in both groups (4.93 ± 4.93 and 5.20 ± 1.45 in group B and D respectively) (p > 0.05). At incision, at the end of surgery, at 4th hour and at 6th hour also the difference was not statistically significant (p > 0.05). At 8, 10 and 12 hour the mean values of VNRS in group B were 1.60 ± 1.13, 2.70 ± 0.79 and 3.90 ± 0.92 respectively, while in group D the values were 0.27 ± 0.69, 1.37 ± 1.19 and 2.80 ± 0.96 respectively. The difference was statistically significant at the respective intervals between the two groups. (p < 0.05)



The mean duration of analgesia in group B was significantly higher (428.33 ± 77.02 minutes), than in group D (621.00 ± 83.72 minutes). (p value < 0.01).

Discussion:

Butorphanol is a mixed agonist-antagonist with low intrinsic activity at receptors of the 11-opioid type (morphine-like). It is also an agonist at k-opioid receptors. While, Dexmedetomidine belongs to the imidazole subclass of α2 receptor agonists, similar to Clonidine, Dexmedetomidine is a more selective α2 agonist with a 1600 times greater selectivity for the α2 receptor compared with the α1 receptor.

In our study Butorphanol has earlier onset of sensory block compared to Dexmedetomidine. In 2017, Kapse et al[11] found similar results in their study on comparison of bupivacaine with fentanyl and butorphanol. They found that the mean time of onset of sensory block was earlier in group B (2.29 +/- 0.62 min) as compared to group F (7.53 +/- 2.24 min). The mean time of onset of motor block was less in group B (4.13 +/- 0.78 min) than in group F (9.98 +/- 2.94 min).

Dexmedetomidine in our study had longer the duration of sensory blockade (543.60 ± 69.46 minutes) compared to Butorphanol (359.67 ± 54.68 minutes).

Biswas S et al.[12] studied the role of Dexmedetomidine as an adjuvant to levobupivacaine in supraclavicular brachial plexus block. They observed that sensory block duration was longer in Dexmedetomidine group (898 ± 32.33 min vs 234.8 ± 47.9 min) compared to levobupivacaine alone. Kaygusuz K et al[4] studied effects of adding Dexmedetomidine to levobupivacaine in axillary brachial plexus block. They observed that sensory block onset time was shorter in Dexmedetomidine group (7.75 min vs 10.75 min, P < 0.05) and duration of sensory block was longer (924.15 min vs 664.62 min, P < 0.05) in Dexmedetomidine group compared to levobupivacaine alone.

The mean duration of motor blockade was 351.00 (± 60.48) minutes in group B and 512.33 (± 78.29) minutes in group D. This difference was statistically significant (p < 0.01). Similar results were observed by Swami et al.[5] in their study using Dexmedetomidine (472.24±90.06 min) and Clonidine (292.67±59.13 min). However, in our study duration of motor block for Dexmedetomidine group was even longer (512.33 ± 78.29 minutes). The haemodynamic profile of both the groups was comparable in our study. Although heart rate SBP and MAP showed a gradual smooth decline in values over time, all parameters were well within physiological limits.

Kaygusuz K et al. (2012)[4] found that after adding Dexmedetomidine to levobupivacaine in axillary brachial plexus block, intraoperative MAP and HR values, except at 5 minutes and postoperatively at 10 and 30 minutes, were significantly lower in Dexmedetomidine group.

Agarwal S et al. (2014)[13] studied the effect of addition of Dexmedetomidine in bupivacaine in supraclavicular brachial plexus block. They observed that heart rate levels in Dexmedetomidine group were significantly lower (P < 0.001) compared to bupivacaine alone except for the initial recordings at 0, 5, 10, and 15 min. SBP and DBP levels in Dexmedetomidine group at 15, 30, 45, 60, 90 and 120 min were significantly lower than bupivacaine alone (P < 0.001).

In the present study, duration of post-operative analgesia was taken till the time patient asked for rescue analgesia (VNRS >3). The mean duration of analgesia was 428.33 ± 77.02 minutes in group B, while it was 621.00 ± 83.72 minutes in group D. The difference between the two groups was statistically significant. (p value < 0.05). Thus, Dexmedetomidine significantly lowered the VNRS pain score and increased the duration of analgesia compared to Butorphanol.

Ammar AS et al.[14] observed lower VNRS pain scores and prolonged analgesia in Dexmedetomidine group as compared to bupivacaine

alone (403 vs 233 min, P=0.00 2) in their study. However mean duration of analgesia in their study (403 vs 233 min, P=0.00 2) was shorter than our study (621.00 ± 83.72 minutes).

The mechanism of action of opioids prolonging analgesia differs from that of local anaesthetics. Local anaesthetics act by blocking the sodium channels at nodes of Ranvier whereas opioids increase potassium current and decrease calcium current in the cell bodies of sensory neurons. This inhibits the neuronal firing and transmitter release as well as the calcium-dependent release of excitatory pro-inflammatory compounds (e.g., substance P) which contributes to their analgesic and anti-inflammatory actions.[15] Hence, the combination of local anaesthetics and opioid has a synergistic effect. Also, as this analgesic activity occurs without activation of opioid receptors in CNS, centrally mediated side effects such as respiratory depression, mental clouding and altered consciousness are not seen.[1]

Dexmedetomidine belongs to the imidazole subclass of α2 receptor agonists, similar to Clonidine, Dexmedetomidine is a more selective α2 agonist with a 1600 times greater selectivity for the α2 receptor compared with the α1 receptor. In many studies, perineural injection of alpha 2 agonists is reported to influence post op analgesia.[16] Centrally, α-2 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 α-2 adrenoceptors in the locus coeruleus[17]. Peripheral action of dexmedetomidine was caused by activation of hyperpolarization activated cation current which prevents the nerve from returning from hyperpolarized state to resting membrane potential for subsequent firing. High concentrations of dexmedetomidine inhibit compound action potentials in sciatic nerves without α-2 adrenoreceptors activation.) This effect is dose and concentration dependent and peripheral i.e. not caused by centrally mediated or systemic analgesia.[18,19]

Lastly, side effect like bradycardia, hypotension, nausea, vomiting etc. were not seen in both the groups in our study which marks the safety profile of both the drugs by this route.

Conclusion:

In this prospective double-blind study comparing Butorphanol and Dexmedetomidine in bupivacaine based supraclavicular block, we found that onset of sensory and motor block is significantly earlier in Butorphanol when compared to Dexmedetomidine. However, duration of sensory block, motor block and postoperative analgesia is longer with Dexmedetomidine compared to Butorphanol. Hemodynamic profiles of both the drugs are smooth and comparable with no significant adverse effects. Hence, they can be safely used for prolongation of supraclavicular block.

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