



## COMPARISON OF DEXAMETHASONE AND MIDAZOLAM IN IMPROVING THE EFFICACY OF 0.5% BUPIVACAINE IN ULTRASOUND GUIDED SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK.

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**ABSTRACT... Objectives:** The objective of this study was to compare the additive effect of dexamethasone versus midazolam as an adjuvant to bupivacaine for the mean duration of onset of sensory block and duration of analgesia with ultrasound guided supraclavicular block. **Study Design:** Randomized control trial. **Setting:** Research was jointly conducted at Arif Memorial Hospital affiliated with Rashid Latif Medical College and KEMU/Mayo Hospital Lahore under the auspices of Department of Anesthesiology. **Period:** 01/02/2017 to 30/06/2017. **Material & Methods:** Involved 264 patients of either sex, aged between 20-60 years undergoing upper limb surgery under ultrasound guided supraclavicular brachial plexus block. After obtaining informed consent, patients were randomly allocated into two treatment groups. Along with 0.5% bupivacaine, patients in Group-I received dexamethasone while those in Group-II received midazolam. Outcome variables were mean time to onset of sensory block and mean duration of analgesia which were noted and compared among the groups. **Results:** The mean age of the patients was  $38.90 \pm 11.92$  years. There were 201 (76.1%) male and 63 (23.9%) female patients in the study group. Majority (79.2%) of the patients belonged to ASA Class-I followed by ASA Class-II (20.8%). Mean time to onset of sensory block was significantly shorter with dexamethasone ( $10.02 \pm 1.26$  vs.  $11.07 \pm 1.38$  minutes;  $p < 0.001$ ) as compared to midazolam and this difference was significant across all age, gender and ASA groups. Mean duration of analgesia was also significantly longer with dexamethasone ( $19.11 \pm 1.32$  vs.  $13.07 \pm 1.43$  hours;  $p < 0.001$ ) as compared to midazolam and this difference was also significant across all age, gender and ASA groups. **Conclusion:** Addition of dexamethasone to bupivacaine in ultrasound guided supraclavicular brachial plexus block resulted in early onset of sensory block ( $10.02 \pm 1.26$  vs.  $11.07 \pm 1.38$  minutes;  $p < 0.001$ ) and longer duration of analgesia ( $19.11 \pm 1.32$  vs.  $13.07 \pm 1.43$  hours;  $p < 0.001$ ) as compared to midazolam in patients undergoing upper limb surgery irrespective of patient's age, gender and ASA status.

**Key words:** Bupivacaine, Dexamethasone, Midazolam and Bupivacaine, Supraclavicular Brachial Plexus Block, Ultrasound Guidance.

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## INTRODUCTION

Focus of anesthesia has shifted in favor of regional blocks as compared to general anesthesia because of demerits like airway instrumentation, multidrug exposure and risks of aspiration if inadequate nil per oral status. It provides limited drug exposure, prolonged analgesia and early mobilization.<sup>1</sup> Various techniques and methods of regional anesthesia have been employed for upper limb surgery. Intravenous regional anesthesia (Bier's Block) has been among the most favored techniques available for short duration surgery.<sup>2</sup> For shoulder surgery, interscalene block has

been practiced extensively.<sup>3,4</sup> Ultrasound guided supraclavicular block is associated with high success rates of surgical anesthesia and low rate of complications.

In most regional anesthetic techniques bupivacaine is utilized as the drug of choice. It has the advantage of prolonged analgesia and reduced postoperative opioid requirement.<sup>5,6</sup> Bupivacaine leads to adequate sensory and motor block in the affected limb. Many adjuncts to bupivacaine like adrenaline, magnesium sulphate, alpha-2 agonists (i.e., clonidine,

dexmedetomidine), midazolam, 5% dextrose and bicarbonate have been used to improve its efficacy, duration and onset of sensory blockade.<sup>7</sup>

Midazolam is known to produce antinociception and potentiate the effects of LAs by its action on ionotropic  $\gamma$ -amino butyric acid-A receptors, stimulating influx of chloride ions and resulting in inhibition of nerve impulse conduction because of membrane hyperpolarization.<sup>8,9</sup> More recently corticosteroids have been studied as adjuncts in regional blocks.<sup>10</sup> The addition of dexamethasone to regional anesthesia with local anesthetics has added a newer aspect to medical uses of corticosteroids. Steroids have very strong anti-inflammatory and immunosuppressive effects.

Numerous randomized controlled trials and meta-analyses have examined the advantages and disadvantages of various individual adjuvants but very little comparative data is available. El-Baradei et al. studied 60 patients and found that addition of dexamethasone and midazolam provided a rapid onset of action in supraclavicular blocks ( $p < 0.05$ ).<sup>11</sup> Dexamethasone alone increased rapidity of onset to  $10.4 \pm 4.2$  min as compared to  $11.5 \pm 1.6$  min in midazolam and prolonged duration of analgesia to  $19.4 \pm 2.2$  hrs in comparison to  $13.2 \pm 2.6$  hrs in midazolam. In a local study, Laiq et al. found that bupivacaine alone had onset of  $22 \pm 3.5$  min and duration of  $6.20 \pm 1.8$  hrs but when used with midazolam, the onset was decreased to  $14 \pm 3.1$  min and duration increased to  $9.30 \pm 4.50$  hrs.<sup>12</sup>

This advantage of regional anesthesia and adjuvants has been validated by multiple international studies but local literature is sparse. Secondly very little data is available on the comparative effect of adding dexamethasone or midazolam to bupivacaine in local or regional population. The current study has been designed to look for unique demographic and racial features of population of Pakistan and to test the improvement in efficacy of bupivacaine when an adjuvant such as dexamethasone or midazolam is used in ultrasound guided supraclavicular brachial plexus block for upper limb surgery.

## MATERIAL & METHODS

This study is a randomized control trial, conducted at the Department of Anesthesiology Arif Memorial Hospital affiliated with Rashid Latif Medical College and KEMU/Mayo Hospital Lahore from 01/02/2017 to 30/06/2017. Approval was acquired from the ethical review board. Patients were enrolled through consecutive, non probability 1:1 sampling. Informed consent was obtained. Sample size of 264 cases (132 in each group) was calculated with 80% power of test and 95% confidence level while taking expected mean  $\pm$  sd of mean duration of onset of sensory block in both groups; i.e.  $10.4 \pm 4.2$  minutes in dexamethasone group vs.  $4.5 \pm 1.6$  minutes in midazolam group when used as adjuvant in ultrasound guided supraclavicular block.<sup>9</sup> Patients undergoing elective surgery of the upper limb e.g. for fracture of radius, ulna and hand were enrolled. Patients of either sex, in the age range of 20-60 years were included. All of them belonged to American Society of Anesthesiology (ASA) status-I and II.

Onset was measured in minutes following administration of supraclavicular block until the loss of pin prick sensation in the anaesthetized limb and was assessed every 2 minutes. Duration of analgesia was measured in hours and it was the time from administration of anaesthetic agent to patient's first complaint of pain (VAS  $> 4/10$ ). Pain was assessed every 30 minutes using the visual analog scale (VAS) where zero (0) represents no pain and 10 meant the worst possible pain. The administration of first post-operative analgesia was at VAS  $> 4$ .

## DATA ANALYSIS PROCEDURE

All the collected data was entered and analyzed through SPSS version 20. Numerical variables as age, duration of onset of sensory block and duration of analgesia have been presented by mean  $\pm$  SD. Categorical variables as gender has been presented by frequency and percentage. Independent sample t-test has been applied to compare the mean duration of onset of sensory block and mean duration of analgesia between the two groups taking  $p$ -value  $\leq 0.05$  as significant.

## RESULTS

The age of the patients ranged from 20 years to 60 years with a mean of  $38.90 \pm 11.92$  years. Majority ( $n=146$ , 55.3%) of the patients were aged between 20-40 years. There were 201 (76.1%) male and 63 (23.9%) female patients in the study group. Majority (79.2%) of the patients belonged to ASA Class-I followed by ASA Class-II (20.8%). There was no significant difference between the two groups in terms of mean age ( $p=0.967$ ), and age ( $p=1.000$ ), gender ( $p=0.665$ ) and ASA class ( $p=0.880$ ) groups distribution as shown in Table-I.

Mean time to onset of sensory block was significantly shorter with dexamethasone ( $10.02 \pm 1.26$  vs.  $11.07 \pm 1.38$  minutes;  $p < 0.001$ ) as compared to midazolam and this difference was significant across all age, gender and ASA groups as shown in Table-II.

Mean duration of analgesia was significantly longer with dexamethasone ( $19.11 \pm 1.32$  vs.  $13.07 \pm 1.43$  hours;  $p < 0.001$ ) as compared to midazolam and this difference was significant across all age, gender and ASA groups as shown in Table-III.

Characteristics	Participants n=264	Dexamethasone + Bupivacaine n=132	Midazolam + Bupivacaine n=132	P-Value
Age (years)	$38.90 \pm 11.92$	$38.87 \pm 11.97$	$38.93 \pm 11.92$	0.967
<b>Age Groups</b>				
20-40 years	146 (55.3%)	73 (55.3%)	73 (55.3%)	1.000
41-60 years	118 (44.7%)	59 (44.7%)	59 (44.7%)	
<b>Gender</b>				
Male	201 (76.1%)	102 (77.3%)	99 (75.0%)	0.665
Female	63 (23.9%)	30 (22.7%)	33 (25.0%)	
<b>ASA Class</b>				
Class-I	209 (79.2%)	105 (79.5%)	104 (78.8%)	0.880
Class-II	55 (20.8%)	27 (20.5%)	28 (21.2%)	

**Table-I. Baseline characteristics of study population**

Independent sample t-test and Chi-square test, observed difference was statistically insignificant

	Participants in both groups N	Dexamethasone + Bupivacaine n=132	Midazolam + Bupivacaine n=132	P-Value
Overall	132/132	$10.02 \pm 1.26$	$11.07 \pm 1.38$	$< 0.001^*$
<b>Age Groups</b>				
20-40 years	73/73	$9.89 \pm 1.39$	$10.96 \pm 1.48$	$< 0.001^*$
41-60 years	59/59	$10.19 \pm 1.06$	$11.20 \pm 1.24$	$< 0.001^*$
<b>Gender</b>				
Male	102/99	$10.00 \pm 1.19$	$10.96 \pm 1.43$	$< 0.001^*$
Female	30/33	$10.10 \pm 1.47$	$11.39 \pm 1.17$	$< 0.001^*$
<b>ASA Class</b>				
Class-I	105/104	$10.03 \pm 1.30$	$11.10 \pm 1.38$	$< 0.001^*$
Class-II	27/28	$10.00 \pm 1.07$	$10.96 \pm 1.40$	$0.006^*$

**Table-II. Comparison of mean time to onset of sensory block (minutes)**

Independent sample t-test, \* observed difference was statistically significant

	Participants in both groups N	Dexamethasone + Bupivacaine n=132	Midazolam + Bupivacaine n=132	P-Value
Overall	132/132	19.11±1.32	13.07±1.43	<0.001*
<b>Age Groups</b>				
20-40 years	73/73	19.11±1.31	12.95±1.56	<0.001*
41-60 years	59/59	19.12±1.35	13.22±1.23	<0.001*
<b>Gender</b>				
Male	102/99	19.06±1.38	13.04±1.38	<0.001*
Female	30/33	19.30±1.12	13.15±1.56	<0.001*
<b>ASA Class</b>				
Class-I	105/104	19.13±1.29	13.00±1.39	<0.001*
Class-II	27/28	19.04±1.48	13.32±1.54	<0.001*
<b>Table-III. Comparison of mean duration of analgesia (hours)</b> Independent sample t-test, * observed difference was statistically significant				

## DISCUSSION

Brachial plexus block has become a viable alternative to general anesthesia for the surgeries on the upper limb as it provides adequate muscle relaxation and an excellent intra- and postoperative analgesia.<sup>11</sup>

The advent of ultrasonography (USG) guidance for locating the brachial plexus has increased the success rate and has renewed the interest in brachial plexus block.<sup>11</sup> It also helps to reduce the total volume of drug required to be injected for anesthetizing the plexus, thereby decreasing the chances of systemic toxicity of local anesthetics.

Majority studies available in literature have evaluated the individual effects of different additives to bupivacaine in improving its efficacy and less data is available to look for the comparative effect. This study compared the additional effect of dexamethasone versus midazolam as an adjuvant to bupivacaine for the mean duration of onset of sensory block and duration of analgesia for ultrasound guided supraclavicular block.

This study shows that the mean time to onset of sensory block was significantly shorter with dexamethasone (10.02±1.26 vs. 11.07±1.38 minutes; p<0.001) as compared to midazolam. Our observation is in line with that of El-Baradei et al. who also observed notably less time to

onset of sensory block with dexamethasone (10.4±4.2 vs. 11.5±1.6 minutes; p<0.05) as compared to midazolam.<sup>11,12</sup> Alarasan et al, Meitei et al and Islam et al had similar observations for mean time to onset of sensory block on addition of dexamethasone to bupivacaine for brachial plexus block i.e., (10.36±1.99 minutes), (9.52±4.14 minutes) and (9.89±1.97 minutes) respectively.<sup>13-15</sup> Results of several studies as Rastogi et al. in 2016 (12.19±1.45 minutes), Dalvi et al. in 2016 (12.3±1.35 minutes), Dash et al. in 2014 (12±2.9 minutes) and Nalwaya et al. in 2014 (11.6±1.39 minutes) reported similar mean time to onset of sensory block with midazolam previously.<sup>16-19</sup>

Similarly, a significant longer mean duration of analgesia was observed with dexamethasone (19.11±1.32 vs. 13.07±1.43 hours; p<0.001) as compared to midazolam. Baradei et al. also reported comparable difference in mean duration of analgesic with dexamethasone (19.4±2.2 vs. 13.2±2.6 hours; p<0.05) and midazolam.<sup>11</sup> A similar mean duration of analgesia i.e., 22.4 hours was reported previously by Dash et al in patients receiving brachial plexus block with addition of dexamethasone.<sup>18</sup> Raghu et al. also reported the mean duration of analgesia with addition of midazolam to be 13.65±2.01 hours, corresponding to our patients receiving midazolam.<sup>20</sup>

The present study is first of its kind in local population and concludes the addition of dexamethasone to bupivacaine to be superior to midazolam in terms of early onset of sensory block ( $10.02 \pm 1.26$  vs.  $11.07 \pm 1.38$  minutes;  $p < 0.001$ ) and longer duration of pain control ( $19.11 \pm 1.32$  vs.  $13.07 \pm 1.43$  hours;  $p < 0.001$ ) for ultrasound guided supraclavicular brachial plexus block in patients undergoing upper limb surgery. Thus the results of the present study advocate for the future practice that dexamethasone should be used as an adjunct to bupivacaine particularly in cases where longer duration of analgesia is required.

The limitation to the study is that we did not compare the onset and duration of motor block and the side effects of dexamethasone and midazolam when used with bupivacaine which should be considered before adopting dexamethasone plus bupivacaine in routine practice. Such a study is highly recommended in future research.

## CONCLUSION

Addition of dexamethasone to bupivacaine in ultrasound guided supraclavicular brachial plexus block resulted in rapid onset of sensory block and prolonged analgesia as compared to midazolam in patients undergoing upper limb surgery irrespective of patient's age, gender and ASA status.





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