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Role of midazolam as an adjuvant to local anaesthetic in supraclavicular brachial plexus block

Ravi N. Agrawal[1], Ritesh M. Karia[2], Parmila S. Jha[1], Dipsheekha C[1]

[1]Department of Anaesthesiology, Govt. Medical College & Sir T Hospital, Bhavnagar, Gujarat, India.

[2]Department of Physiology, GMERS Medical College & Hospital, Dharpur-Patan, Gujarat, India.

Abstract

Objective : objective of this study is to compare the duration of sensory and motor blockage, duration of post operative analgesia, request the first rescue analgesic, total doses required of post operative analgesia by the patient in both control and midazolam group. Present study also compare sedation score and visual analogue score (VAS) in both groups.

Methods : Present study was carried out on 100 patient which were divided in two groups. One group(50 subjects) is control group and another is midazolam group(50 subjects) which receive midazolam as an adjuvant to local anaesthetic in supraclavicular brachial plexus block. with proper anaesthetic technique duration of sensory block, motor block, duration of post operative analgesia, sedation score and visual analogue score were obtained in both groups and values were compared with 'unpaired t test'. Values were consider statically significant when $p < 0.05$.

Result : present study state that there is statically significant difference between mean values of duration of sensory and motor block, duration of post operative analgesia, sedation score and VAS.

Conclusion : the addition of midazolam to local anaesthetics in supraclavicular block improves the quality of blockade with stable haemodynamics and desirable sedation score without any adverse effects.

Key Words: Supraclavicular Block, Midazolam, Adjuvant To Local Anaesthetic.

INTRODUCTION

Asupraclavicular approach for blockade of the brachial plexus was first described by Kulenkampf in 1911.[1] Brachial plexus blocks are very useful alternative to general anesthesia for upper limb surgery. With the brachial plexus block we can achieve ideal operating conditions by producing complete muscular relaxation, maintaining stable intraoperative hemodynamics, and the associated sympathetic block. The sympathetic block decreases edema, postoperative pain and vasospasm [2,3]. So In recent years, the technique has gained importance as regional anaesthetic technique for surgical, diagnostic and therapeutic purposes in interventional pain management. Bupivacaine has long duration of action varying from 3 to 8 hours so it is most commonly used as a local anaesthetics' for brachial plexus block.[2-5] Any adjunct to brachial plexus block is supposed to prolong the analgesic effect without any systemic side effects or prolonged motor block, and should also reduce the total dose of local anesthetic. There are various studies which investigated several adjuncts, including opioids, clonidine, dexamethasone, neostigmine, hyaluronidase, and bicarbonate.[6-10] Midazolam is a water-soluble benzodiazepine and it is known to produce antinociception and to enhance the effect of local anesthetic when given epidurally or intrathecally. Midazolam produces this effect by its action on gamma aminobutyric acid-A (GABA-A) receptors.[11-12] Very little data is available on the effect of adding midazolam to a local anaesthetic solution. The objective of this study was to determine the dration of sensory and motor blockage and to determine analgesic efficacy of midazolam – bupivacaine combination compared to plain bupivacaine (0.5%) for supraclavicular brachial plexus block. Present study also compare sedation score and VAS in both groups.

Address for correspondence*

Ritesh M. Karia

Department of Physiology, GMERS Medical College & Hospital, Dharpur-Patan, Gujarat, India.

Email : riteshkaria@ymail.com

METHODOLOGY

After approval from the Institutional Ethics Committee and informed written consent from the patients, this, clinical study was carried out in 100 patients, aged 18-60 years, scheduled for elective and emergency upper limb orthopedic surgeries under supraclavicular brachial plexus block in the Department of Anaesthesiology, Govt. Medical College and Sir T. Hospital, Bhavnagar, Gujarat.

All the patients were subjected to detailed preanaesthetic evaluation with clinical history and systemic examination. Routine investigation like Haemogram, Random Blood Sugar, Renal Profile, ECG for patient above 40 years of age, HIV and HBsAg and other specific investigations were done as per patient clinical evaluation.

Patients were randomly divided into two groups of 50 patients each. Anaesthesiologist performing the block was blinded to the drug solution used.

Group C	Inj. Bupivacaine 0.5%, 20 ml
(Control)	Inj. Lignocaine 2%, 10 ml with
	Inj. Adrenaline 1: 2,00,000 (5µg/ml)
Group M	Inj. Bupivacaine 0.5%, 20 ml
(Midazolam)	Inj. Lignocaine 2%, 10 ml with
	Inj. Adrenaline 1: 2,00,000 (5µg/ml)
	Inj. Midazolam 50 **µ**g/kg (preservative free)

Preoperatively, adequate fasting of 6 hours was confirmed. Each patient was informed in detail regarding the nature and

purpose of the study and was explained 0-10 point visual analogue scale (VAS) on a sheet of paper where score of 0 labelled as no pain and 10 as worst possible pain.

Anaesthetic Technique

In pre anaesthesia preparation room, baseline vital parameters (heart rate, blood pressure, respiratory rate, SpO2) were recorded. Intravenous line was secured and the patients were premedicated with Ranitidine 1mg/kg, Glycopyrolate 5 **µ**g/kg intravenously 15 minutes prior to procedure. Then patients were shifted to Operation theatre.

On operation table, patient was given the position for brachial plexus block **:** Supine position with head resting on ring, ipsilateral arm adducted, shoulder depressed, roller pack placed in between scapula and neck turned slightly to the contra lateral side. Under all aseptic and antiseptic precaution local site was prepared. Subclavian artery was palpated 1 to 1.5 centimeter above the midclavicular point, immediately lateral to sternocleidomastoid muscle and was pushed medially by thumb. A hypodermic needle (23 G, 1inch) attached to a 2 cc syringe filled with sterile water was held in pen holding position, to be directed posteriorly, medially and caudally to elicit paraesthesia which was felt as feeling of tingling at elbow and fingers. Once the patient felt paraesthesia, it was suggestive that the needle was touching the brachial plexus and then 30 ml of study drug was given after careful negative aspiration. End of injection was considered as time 0. No sedation was given in intraoperative period.

After giving the block, Neurological assessment (sensory and motor), haemodynamic variables (Heart rate, blood pressure), effects on respiration (respiratory rate, SpO2) and sedation scores were recorded at the intervals of 1, 3, 5, 10, 15, 20, 30, 45 minutes than at hourly interval upto 6 hours, 2 hourly upto 16 hours and 4 hourly till 24 hours from the end of injection of local anaesthetic.

Sensory characteristics of the block were assessed using response to pinprick to 23 G hypodermic needle as per the criteria mentioned below

Score	
0	Normal sensations to pin prick
1	Dull response to pin prick
2	No response to pin prick

Palmar surface of index and little finger and dorsum of thumb were assessed to test for median, ulnar and radial nerve respectively. Duration of sensory blockade was taken as time duration of onset of sensory block to reappearance of dull response to pin prick (score 1).

Motor characteristics of block were assessed using Bromage three point scale as per the criteria mentioned below,

Score	
0	Normal motor functions with full flexion and extension elbow, wrist and fingers
1	Decreased motor strength with ability to move fingers only
2	Complete motor blockade with inability to move fingers

The duration of motor blockade was considered as time from onset of motor blockade to regression of bromage score to 1. Patients with inadequate blockade requiring supplementation were excluded from the study.

Sedation was assessed as per the criteria shown below [13]

Score	
0	Awake and alert
1	Sleeping but easily arousable
2	Deep sleep but arousable
3	Deep sleep and not arousable

Duration of postoperative analgesia was taken as time from onset of sensory block to the time of administration of first rescue analgesic. Postoperatively, VAS was recorded at hourly interval for first 6 hours and then 2 hourly up to 16 hours and then 4 hourly upto 24 hours. Whenever VAS = 5 or patient complaint of pain, Inj. Diclofenac Sodium (1.5 mg/kg) 75 mg IM was given as rescue analgesic.

Statical analysis

Results were expressed as **mean SD** (standard deviation). Statistical analysis was performed using unpaired student's t-test. When $p<0.05$ it is considered as statistically significant.

RESULTS

Differences in mean value of both groups (Group C and Group M) is described below.

Table 1 shows Characteristics of sensory block, motor block and post operative analgesia.

Duration (In Minutes)	Group C	Group M	p value
Sensory Block	269.6 ± 36.88	304.6 ± 40.52	<0.005
Motor Block	231.70 ± 40.70	266.90 ± 49.91	<0.005
Post Operative Analgesia	325.60 ± 81.44	573.20 ± 125.40	<0.005

From table 1 it is clear that mean value of sensory block duration in control group is 269.6 + 36.88 minutes, while in Midazolam group it is 304.6 + 40.52 and the difference is statically significant. Like wise duration of motor block and duration of post operative analgesia is also statically significant between control group and midazolam group.

Table 2 shows requirement of first rescue analgesic in both group.

Time of IM injection (hrs)	**Group C**		**Group M**	
	No. of patients	%	No. of patients.	%
4 to 5	13	26	0	0
5 to 6	17	34	1	2
6 to 8	10	20	0	0
8 to 10	10	20	10	20
10 to 12	0	0	26	52
12 to 14	0	0	10	20
14 to 16	0	0	2	4
16 to 20	0	0	1	2
20 to 24	0	0	0	0
>24	0	0	0	0
Total	50	100%	50	100%

From table 2 it is clear that in Group C, all the patients (100%) required rescue analgesic within 10 hrs of induction whereas in Group M, only 20% required rescue analgesic within 10 hrs of induction. 52% patients had postoperative analgesia of 10-12 hrs and remaining patients had postoperative analgesia of 12-16 hrs in Group M.

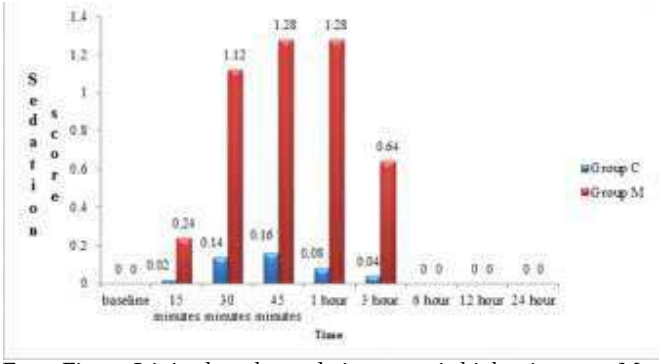
Table 3 shows requirement of total doses of rescue analgesic in 24 hours

No. of Analgesic doses	Group C		Group M	
	No. of Patients	(%)	No. of Patients	(%)
1	0	0	2	4
2	4	8	48	96
3	46	92	0	0
	50	100	50	100
Mean ± SD	2.92 ± 0.27		1.96 ± 0.20	
	P <0.05			

Figure: 1 shows comparison in Mean values of VAS in both group.

From Figure 1 it is clear that visual analogue score in both group is statically significant. (p<0.05)

Figure: 2 shows comparison of Mean Value of Sedation Score in both group.



From Figure 2 it is clear that sedation score is higher in group M

DISCUSSION

In recent years, the regional technique of brachial plexus block has gained importance for surgical, diagnostic and therapeutic purposes in interventional pain management. It includes blocking the brachial plexus using local anaesthetic agents where it is most compactly arranged. It provides ideal condition for surgery, maintains stable haemodynamics, decreases vasospasm, edema and postoperative pain along with early ambulation, return to work and other advantages of regional techniques which avoids general anaesthesia and its Complications.[14]

Among the commonly used local anaesthetics, lignocaine and bupivacaine, bupivacaine provides longer duration of blockade but the duration of postoperative analgesia is short when it is used alone.

The discovery of opioid receptors,[15,16] in spinal cord in dorsal horn neurons, served as gateway of many studies to find out effect of opioid given epidurally and intrathecally. Later research showed axonal GABA receptors in mammalian peripheral nerve Trunks,[17] especially on normal and regenerated sensory fibres.[16] Various studies in animals,[11,12,18-20] and humans,[21-25] have demostrated that antinociceptive action of benzodiazepine when used intrathecally to be mediated by GABA receptors, opioid receptors and benzodiazepine receptors in spinal cord.

Depending on the presence of opioid and benzodiazepine receptors in peripheral nerves, researchers conducted various studies using either local anaesthetic alone or various combination of local anaesthetic with one of the adjuvants, opioids,[26-29] (tramadol, fentanyl, sufentanil, buprenorphine) or non – opioids,[30] (clonidine, ketamine, dexamethasone, neostigmine) in order to potentiate the action of local anesthetics and prolong the duration of postoperative analgesia with lesser systemic side effects.

Benzodiazepines have desirable properties[31] of stable haemodynamics, sedation, less respiratory depression, along with potentiating and prolonging duration of analgesia through its antinociceptive action on GABA receptors, in contrast to opioids which are prone to cause varieties of side effects[16] e.g. nausea, vomiting, itching and respiratory depression.

Midazolam is a potent, water soluble short acting benzodiazepines. Very few studies [32-34] are available wherein midazolam was used as an adjuvant to local anaesthetic in peripheral nerve block, with the claim that this combination provides earlier onset, longer duration and better quality of analgesia in comparison to local anaesthetic used alone. There is need for future research in this field which prompted us to carry out this prospective, randomized, double blind, controlled, clinical study wherein midazolam is used as an adjuvant to local anaesthetic solution in brachial plexus block through supraclavicular route for upper limb orthopaedic surgeries.

In this study, the onset of sensory and motor block was significantly faster in patients who received combination of local anaesthetic and midazolam. This could be due to synergistic action of midazolam with that of local anaesthetic.

In this study, duration of sensory and motor block was statistically significantly prolonged in midazolam group.

In this study, the mean duration of post operative analgesia was 573.20 min (9.43 hrs) in Group M which was prolonged by 4 hrs as compared to Group C and was statistically significant (p<0.005).The increased duration of postoperative analgesia found in Group M produced clinically and statistically lower VAS scores in postoperative period while 80% of the patients in Group C required rescue analgesic in first 8 hrs. Majority of the patients in Group M (94%) were pain free for 12 hrs postoperatively resulting in significantly decreased in total dose and frequency of rescue analgesic requirement in 24 hrs postoperatively.

In this study, mean sedation score was higher in Group M as compared to Group C starting at 15 min from the time zero and remained so for next 4 hrs (p<0.05) . This could be due to systemic absorption of midazolam and its effect on central nervous system

to produce sedation. The limited duration of sedation could be explained by the fact that midazolam is highly lipophilic and diffuses faster into the blood vessels by its rapid clearance (6-11 ml/kg/min) and short half life (1.7- 2.6 hrs).[31]

In this study, SpO_2 remain fairly stable and comparable in both the groups and none of the patient in either group needed supplemental oxygen. This shows striking safety of midazolam with sedation, as none of the patient required supplemental oxygen or any airway assistance.

CONCLUSION

Midazolam prolongs the duration of sensory and motor blockade.It prolongs the duration of postoperative analgesia. It reduces the number of doses and frequency of rescue analgesics required in postoperative period.Midazolam provides stable haemodynamics without any respiratory depression with sedation of desirable magnitude. In conclusion, the addition of midazolam to local anaestheitcs in supraclavicular block improves the quality of blockade with stable haemodynamics and desirable sedation score without any adverse effects.

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