Original Research Article

Comparative study of effects of tramadol and midazolam added to bupivacaine (0.25%) in supraclavicular brachial plexus block for upper limb surgeries

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Abstract

Background: Supraclavicular brachial plexus block is commonly used for upper limb surgeries due to its effectiveness, performance and margin of safety. To minimize the drawbacks of bupivacaine, adjuvants are usedto improve the quality and duration of action and postoperative analgesia. **Aim:** To compare the effects of tramadol and midazolam added to bupivacaine (0.25%) in supraclavicular brachial plexus block for upper limb surgeries. **Material and Methods:** A total of 60 adult cases from both sexes were randomly grouped into group I(received 40ml of 0.25% bupivacaine with 1mg/kg tramadol) and group B (Received 40ml of 0.25% bupivacaine with 25µg/kg midazolam preservative free). **Results:** The onset of sensory blockade was early in group II as compared to group I and statistically significant. The duration of postoperative analgesia was 12-14 hours in group II and was 6-8 hours in group I and was statistically significant. The changes in the pulse rate, blood pressure, respiratory rate were statistically significant in group II compared to group I. **Conclusion:** Midazolam with bupivacaine provides early and profound sensory and motor blockade as well as good postoperative analgesia without any side effects when compared with tramadol with bupivacaine.

Key Words: Upper limb surgeries, supraclavicular brachial plexus block, sensory and motor blockade, postoperative analgesia.

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INTRODUCTION

Brachial plexus block offers as optimal operating conditions for upper limb surgeries by producing complete muscular relaxation, maintaining haemodynamic stability and the associated sympathetic block. They also provide extended postoperative analgesia with minimal side effects. There are various approaches to block the brachial plexus namely the interscalene, supraclavicular, infraclavicular and axillary approach. Of these the supraclavicular technique is commonly used for upper limb surgeries due to its effectiveness, cost, performance, margin of safety.[1] It is carried out at the level of nerve trunks where it is more compact, resulting in homogeneous spread of anaesthetic throughout the plexus with a fast onset and complete block. Bupivacaine has been the local anaesthetic most frequently used.However, it has limiting factors like delayed onset, incomplete analgesia and moreover it has potential for cardiotoxicity. To minimize these drawbacks many drugs like neostigmine, opioids, hyaluronidase, midazolam, clonidine, etc., have been added to local anaestheticsas an adjuvantto improve the quality and duration of action and postoperative analgesia.[2-4] Tramadol is a weak central-acting opioid that has been shown to have Na^+ and K^+ channel-blocking properties and can block motor and nociceptive function similarly to

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local anesthetics.[5,6] Midazolam a water soluble, short acting benzodiazepine, produces analgesia by acting on gamma –amino butyric acid receptors (GABA). Extrasynaptic receptors for GABA are present on myelinated axons of peripheral nerves.[7] In the present study, the effects of tramadol and midazolam added to bupivacaine (0.25%) in supraclavicular brachial plexus block for upper limb surgeries were compared with respect to hemodynamic stability, sensory and motor blockade, analgesia duration and complications.

MATERIAL AND METHODS

After ethical committee approval and informed consent, 60 patients posted for routine or emergency forearm and hand surgeries were included in the study randomly.

Selection of Cases

Inclusion Criteria

1. ASA physical status I or II.
2. Age: between 18 to 50 years of age.
3. Sex: both males and females.
4. Posted for forearm and hand surgeries.

Exclusion Criteria

1. Rheumatic heart disease, ischemic heart disease, Hypertension
2. Respiratory diseases like COPD, Asthma.
3. Renal and hepatic derangements.
4. Disease of central nervous system.
5. Bleeding disorders.
6. Hypersensitivity/Allergy to any drug.

Patients under the study underwent through pre-operative assessment including detailed case history, physical examination and all necessary baseline investigations like Hb, BT, CT, urine routine etc.

Procedure: Patient was made to lay supine with head turned to opposite side with ipsilateral arm adducted. After aseptic preparation, midpoint of clavicle and interscalene groove was identified. At a point 1-1.5 cm posterior to midpoint of the clavicle, skin wheal was raised with local aneasthetic. A 22 gauge 4 cm short beveled needle was passed through the same point in a caudal, slightly medial and posterior direction until paresthesia was elicited. Indication of correct placement of needle is either by fascial click, paraesthesia of forearm and hand or visible contraction of the muscles of the upper extremity. After negative aspiration for blood study the drug was then injected slowly after repeated aspirations. The patients were randomly assigned to two equal groups:

Group I (n=30): Received 40ml of 0.25% bupivacaine with 1mg/kg tramadol

Group II (n=30): Received 40ml of 0.25% bupivacaine with 25µg/kg midazolam preservative free.

All local anesthetic solutions and adjuvant drugs were prepared by an anesthesiologist not involved in the performance of brachial plexus block, patient care and data collection. Sensory blockade of each nerve was assessed by pinprick and compared on the contralateral arm. Sensory blockade was rated on a scale from 100% (normal sensation) to 0% (no sensation). Motor blockadewas evaluated by: a. Thumb abduction (radial nerve) b. Thumb adduction (ulnar nerve) c. Thumb apposition (median nerve) and d. Flexion of the elbow in supination and pronation of the forearm (musculocutaneous). Intra operatively baseline pulse rate, blood pressure and respiratory rate and SPO_2 were monitored. For continuous neurological evaluation, no sedative drugs were administered intra operatively. Additionally, adverse effects like nausea, vomiting, itching, urinary retention and respiratory depression were recorded.

RESULTS

Most of the patients are middle aged men and women in both the groups. The mean age of patients in Group I and II were 30.8and 32.1 respectively. There were 14 males and 16 females in Group I and II males and 17 females in Group 2.The mean weight in patients of Group I was 51.83 and in Group II it was 48.47. Most of the patients underwent ulna plating (22) followed byradius plating (19) and radius ulna plating (12).The demographic characteristics were comparable in both groups.

Pulse rate, systolic and diastolic blood pressure after taking patient on operation table were considered as baseline. Mean of these parameters were measured in both groups.

Table 1: Comparison of pulse rate between two Groups

Time Points	Pulse Mean ± SD		p value and Significance
	Tramadol	Midazolam	
Baseline	80±6.10	80.87±6.66	0.60 (NS)
1 min	80±6.10	78.80±6.03	0.45 (NS)
2 min	79.8±5.97	75.27±5.64	0.001 (HS)
5 min	79.47±5.92	73.73±5.96	0.001 (HS)
15 min	78.93±5.79	73.20±6.07	0.001 (HS)
60 min	78.13±5.46	73.07±5.67	0.001 (HS)
240 min	78.33±5.54	73.13±5.40	0.001 (HS)
480 min	79.47±5.35	73.40±5.15	0.001 (HS)
600 min	--	74.60±5.66	--
720 min	--	77.00±5.72	--
840 min	--	78.74±6.03	--

Test applied = Unpaired 't' test;p<0.05=Significant; p<0.01=Highly significant

It was observed that drop in pulse rate was significant at 2 minutes with midazolam which was not seen with tramadol. So, when these two values were compared the difference was significant. This shows that action of midazolam was earlier to that of tramadol.

Table 2: Comparison of Blood pressure between two Groups

Time Points	Blood Pressure (Mean ±SD)		p value andSignificance
	Tramadol	Midazolam	
Baseline	117±10.06	118.67±11.3	0.55 (NS)
1 min	117±10.06	116.00±9.41	0.69 (NS)
2 min	116.93±9.98	112.73±8.86	0.09 (NS)
5 min	116.47±9.68	111.27±7.92	0.03 (S)
15 min	115.93±9.61	110.80±7.66	0.03 (S)
60 min	115.53±9.49	110.80±7.64	0.04 (S)
240 min	115.53±9.49	107.77±19.4	0.05 (S)
480 min	117±9.78	111.13±7.31	0.01 (HS)
600 min	--	113.93±7.97	--
720 min	--	113.67±7.68	--
840 min	--	115.56±8.35	--

Test applied = Unpaired 't' test; p<0.05=Significant; p<0.01=Highly significant

Table 3: Comparison of respiratory rate between two Groups

Time Points	Respiratory Rate Mean ± SD		p value and Significance
	Tramadol	Midazolam	
Baseline	21.13±2.66	19±2.665	0.001 (HS)
1 min	21.13±2.66	17.4±1.831	0.001(HS)
2 min	20.93±2.77	16.33±1.061	0.001(HS)
5 min	20.00±2.57	15.87±0.730	0.001(HS)
15 min	18.47±2.21	15.93±0.365	0.001(HS)
60 min	17.13±1.94	15.93±0.365	0.001(HS)
240 min	16.73±1.70	15.93±0.365	0.001(HS)
480 min	17.40±2.04	16.13±0.507	0.001(HS)
600 min	--	16.00±0.000	--
720 min	--	16.33±0.758	--
840 min	--	16.44±1.013	--

Test applied = Unpaired 't' test; p<0.01=Highly significant

Table 4: Comparison of Sensory blockade between two groups

Time Points	Sensory Blockade (Mean ± SD)		p value and Significance
	Tramadol	Midazolam	
Baseline	100 ± 0	100 ± 0	0.001 (HS)
1 min	100 ± 0	66.67 ± 12.13	0.001(HS)
2 min	95.33 ± 8.19	26.33± 19.38	0.001(HS)
5 min	73.00 ± 13.9	3.33 ± 11.55	0.001(HS)
15 min	37.33 ± 19.9	0	0.001(HS)
60 min	4.67 ± 11.37	0	0.001(HS)
240 min	22.67 ± 13.3	0	0.001(HS)
480 min	7.00 ± 16.2	3.33 ± 8.44	0.001(HS)
600 min	--	15.67 ± 21.61	--
720 min	--	37.00 ± 25.88	--
840 min	--	62.22 ± 18.88	--

Test applied = Unpaired 't' test; p<0.01=Highly significant

Table 5: Comparison of motor blockade between two groups

Motor blockade	Tramadol	Midazolam	Significance
Onset (mins)	6.36 ± 1.22	3.63 ± 0.85	0.001 (HS)
Peak (mins)	14.26 ±3.70	6.53 ±1.43	0.001 (HS)
Duration (mins)	320 ± 65.13	564.00±37.29	0.001 (HS)

Test applied = Unpaired 't' test; p<0.01=Highly significant

The drop in blood pressure was significant with midazolam which was not seen with tramadol. So, when these value were compared the difference was significant. This showed that action of midazolam was earlier to that of tramadol. The decrease in respiratory rate was significantly earlier with midazolam as compared to tramadol. But it could be measured only up to 8 hours as with tramadol the effect of block weared off early (Table 3).

When the two groups were compared the SpO_2 was observed to be within normal limits throughout.

There was a significant decrease in the pain score with midazolam at 1 minute as compared with tramadol. Also the comparison could be conducted upto 8 hours only as most of the patients in the tramadol group required rescue analgesics Midazolam group has profound analgesia. This showed that analgesia in the midazolam group lasts much longer than in the tramadol group.

The onset of motor blockade was earlier with midazolam (3.63±0.85) as compared with tramadol (6.36±1.22).Also the duration of motor blockade was more with midazolam (564±37.29) as compared with tramadol (320±65.13). Patients were observed for number of analgesics which patients consume in the first 24 hrs post-operatively. Every patient in group I received more than 3 analgesics in first 24 hours while the patients of group II received 2 or less than 2 analgesics. In group I, 11 (36.67%) required more than 5 analgesics in first 24 hours post-operatively 5 (16.67%) required 3 analgesics while maximum 18 (60%) received 4 doses for analgesia. In group II, 10 (33.33%) patients required 2 analgesics in first 24 hours post-operatively while maximum 20 (66.67%) patients received only one dose of analgesic in first 24 hours post-operatively. Mean analgesic doses requirement for group I was 3.7 ± 0.59 while same for group II was 1.3 ± 0.46 within first 24 hours. ($p< 0.0001$). The mean duration of post-operative analgesia was 6.637 hrsin Group I and 16.912 hrs in Group II. Thus, midazolam produces significantly longer post-operative analgesia duration than tramadol. Group I had one episode of nausea and one episode of vomiting. Group II also has one episode of nausea and one episode of vomiting. These episodes were relieved by intravenous injection of Ondansetron 0.08 mg/kg. No patient in both the groups showed any incidence of respiratory depression. No significant difference was found in both the groups with respect to intra and post-operative complications. The patients in group I were all awake throughout the intraoperative and post-operative period. 25 patients in group II showed sedation score of 1 after 15 minutes post-operatively. The sedation score was maintained till 60 minutes. Patients were maintaining oxygen saturation with ventimask during this period. 5 patients in group II showed sedation score of 2 after 15 minutes post-operatively and was maintained till 60 minutes.

DISCUSSION

From time to time, man has resorted to many methods in his search for relief of pain. Painless surgery is probably the greatest boon that has been granted to the patients and indirectly to surgeons. Opioids have been administered for many years to allay anxiety and to reduce pain associated with surgery. Midazolam produces this additive effect on local anesthetics by its action on the GABA- A receptor complexes present in the spinal cord. The mean onset of analgesia in group I was 6±3minutes.The mean onset of analgesia in group II was 2± 1 minutes. The difference in onset of analgesia in group II is statistically and clinically very significant. ($p< 0.001$).Batra*et al* in their study also found early onset of analgesia with midazolam which correlates with our study.[8] The mean duration of analgesia in group I was 390±120 minutes. The mean duration of analgesia in group II was 1014±120 minutes.The difference in duration of analgesia in group II is statistically and clinically very significant. Batra *et al*,[8] in their study found duration of analgesia of approximately 24 hrs with midazolam-bupivacaine combination. Nishiyama T *et al*[9] concluded that midazolam improves post operative epidural analgesia with continuous infusion of local anaesthetics. Shaikh SI *et al*[10] found that Addition of midazolam 50mcg/kg to 30ml of bupivacaine 0.5% for supraclavicular brachial plexus block prolonged sensory blockade and post-operative analgesia without increasing the risk of adverse effects. These studies included different approaches of midazolam use. Our study with use of midazolam in perineural approach also provided good quality and duration of analgesia as in above studies. Present study found that duration of postoperative analgesia is longer with midazolam. The postoperative analgesia was so profound in the study group II that patients were very comfortable and absolutely devoid of pain. Midazolam added to local anesthetic in brachial plexus block did cause a significant alteration in pulse rate within 2 minutes which was statistically significant. It may be due to elimination of anxiety and pain but there was no evidence of bradycardia. In group II there was statistically significant, alteration in the systolic blood pressure which may be due to elimination of anxiety, pain and additional effect of sedation which is dose related though there was no evidence of hypotension. There was statistically significant decrease in the mean respiratory rate in group II after 2 mins post block upto 10-14hours postoperatively but no evidence of respiratory depression. The onset of motor blockade in group II was in 3.63±O.85 minutes which lasted for duration of 564±37.19 minutes whereas the onset of motor blockade in group I was 5.36± 1.11 which lasted for only 320±65.l3 minutes. The difference is statistically and clinically very significant. Batra *et al*[8], in their study, found duration of motor blockade of approximately 18 hrs with midazolam. Nishiyama *et al*[9], Shaikh *et al*[10] when used midazolam bupivacaine combination found increased duration of motor blockade. Their results correlate well with our study result. Duration of sensory blockade in group II was up to 14 hrs and in group I upto 8 hrs in our study. Batra *et al* [37]decided to use this drug in brachial plexus block. Duration of sensory blockade in this study i.e. approximately 24 hrs correlates well with our study. Patients were observed for number of analgesics which patients consume in the first 24 hrs post-operatively. Every patient in group I received more than 3 analgesics in first 24 hours while the patients of group II received 2 or less than 2 analgesics. Mean analgesic doses requirement for group I was 3.7 ± 0.59 while same for group II was 1.3 ± 0.46 within first 24 hours. ($p< 0.0001$). The prolonged duration of analgesia provided by midalzolam reduced the consumption of analgesics and thus reduced not only the overall cost of patient care but also makes it more convenient for nursing patient who is pain free for long time post-operatively. No significant difference was found in both the groups with respect to intra and post-operative complications. In our study we found of that patients in group I were all awake throughout the intraoperative and post-operative period. 25 patients in group II showed sedation score of 1 after 15 minutes post-operatively. The sedation score was maintained till 60 minutes.5 patients in group II showed sedation score of 2 after 15 minutes post-operatively and was maintained till 60 minutes. Batra *et al*[8] also found out in their study higher sedation score in bupivacaine-midazolam group, but clinically significant sedation was not present. This may have been due to partial vascular uptake of the drug and its transport to the central nervous system where it acts on GABA receptors and produces sedation. The limited duration of sedation could be explained by the fact that midazolam is highly lipophilic and diffuses faster into the blood vessels and by its rapid clearance and short half-life (1.7-2.6 hrs). Our study results correlate with their findings. This sedation in fact was useful in calming down the patient in post-surgical unit. To conclude, midazolam in the dose of 25µg/kg with bupivacaine provides early and profound sensory and motor blockade as well as good postoperative analgesia without any side effects when compared with tramadol 1mg/kg with bupivacaine.

LIMITATIONS OF THE STUDY

Being small sample size, the results obtained from the study may be insufficient to draw conclusion on firm grounds. This study needs further evaluation on a larger

sample size. Hence, this study can be considered as only a beginning.

REFERENCES

1 Kothari D. Supraclavicular brachial plexus block - a new approach. Indian J Anaesth 2003;47(4):287-88.
2 Bazin JE, Massoni C, Bruelle P, Fenies V, Groslier D, Schoeffler P. The addition of local anaesthetics in nrachial plexus block: The comparative effects of morphine, buprenorphine and sufentanil. Anaesthesia 1997; 52:858-62.
3 Bone HG, Van Aken H, Brooke M, Burkle H, Brooke M, Burkle H. Enhancement of axillary brachial plexus block anaesthesia by coadminiatration of neostigmine. RegAnesth Pain Med 1999; 24:405-10.
4 Keeler JF, Simpson KH, Ellis FR, Kay SP. Effevt of addition of hyaluronidase to bupivacaine axillary brachial plexus block. Br J Anaesth 1992; 68:68-71.
5 Guven M, Mert T, Gunay I. Effects of tramadol on nerve action potentials in rat: comparisons with benzocaine and lidocaine. Int J Neurosci. 2005; 115(3):339–49.
6 Sarsu S, Mizrak A, Karakurum G. Tramadol use for axillary brachial plexus blockade. J Surg Res. 2011; 165(1):e23–7.
7 Edwards M, Serrao JM, Gent JP, Goodchild CS. On the mechanism by which midazolam causes spinally mediated analgesia. Anesthesiology 1990; 73:273-7.
8 Batra YK, Jain K, Chari P, Dhillon MS, Shaheen B, Redy GM. Addition of intrathecal midazolam to bupivacaine produces better post-operative analgesia without prolonging recovery. Int J ClinPharmacolTher 1999; 37:519-23.
9 Nishiyama T, Matsukawa T, Hanoaka K. Effects of adding midazolam on postop analgesia with two different doses of bupivacaine. J ClinAnesth. 2002; 14(2):92-7.
10 Shaikh SI, Veena K. Midazolam as an adjuvant in supraclavicular brachial plexus block. Anaesth Pain and Intensive Care 2012; 16(1):7-11.

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