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Original Research Article

Midazolam as Adjuvant: Comparison between Bupivacaine and Ropivacaine in Potentiation of Anaesthetic Effect in Supraclavicular Block: Hospital-Based Prospective Comparative Clinical Study

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Abstract:

Background: As recent trend in upper limb surgery is toward outpatient care, brachial plexus blocks have become very popular in effectively providing perioperative anaesthetic and analgesic requirement. Different agent has been added to local anaesthetic for a quicker and excellent intraoperative as well as postoperative analgesia and at the same time reducing the volume of total local anaesthetic used. As an adjuvant, midazolam is known to cause anti nociception and extend the effects of local anaesthetics with some inherent local anaesthetic properties. Purpose of the study was to assess the effect of midazolam as adjuvant, in potentiation of local anaesthetic effects in supraclavicular brachial plexus block. A hospital-based prospective comparative study was conducted after obtaining ethical committee clearance. 30 patients were included in each group using purposive sampling. Group A: Received ropivacaine with preservative free midazolam. Group B: Received bupivacaine with preservative free midazolam. The following parameters were noted: Onset of sensory block, onset of motor block, duration of sensory block, duration of motor block, duration of analgesia, haemodynamic variables, sedation score and complications were assessed.

Result: The onset of sensory and motor blockade was significantly faster in group B compared to group A. Again, the duration of sensory and motor blockade was significantly longer in group B compared to group A. The duration of analgesia was also significantly longer in group B compared to group A. Haemodynamic and sedition scores did not differ between the groups in the intra and post-operative period. Complications were almost negligible in both the groups and not significant.

Conclusion: In supraclavicular block with midazolam as adjuvant, bupivacaine has an advantage over ropivacaine in terms of early onset of sensory and motor blockade and helps in prolonging the duration of blockade as well as duration of analgesia.

Keyword: Bupivacaine, Ropivacaine, Midazolam, Supraclavicular Block.

Introduction

The use of regional anaesthesia in surgeries of the upper extremities is becoming extremely popular day by day. Brachial plexus blocks have become an important tool in effectively providing perioperative anesthesia and analgesia as the recent trend in upper limb surgery is toward outpatient care (Erickson JM et al., 2009).

The block is carried out at the level of trunk of brachial plexus where almost all the sensory, motor and sympathetic innervation of the upper extremity is carried in just three nerve structures confined to small surface area (Franco CD et al., 2017; Lanz E et al., 1984; Silverstein WB., 2000). Now a day's brachial plexus block is one of the extensively used methods for upper limb surgeries as a substitute to general anaesthesia. It can also combine with general anaesthesia to accomplish ideal operating conditions by maintaining stable haemodynamic status and producing muscular relaxation. Brachial plexus block can also provide intra-operative and post-operative analgesia and associated sympathetic blockade can reduce vasospasm as well as oedema (Pester JM et al., 2022).

Peripheral nerve blocks have become important in clinical practices due to their property of reducing post-operative pain leading to speeding up of patient recovery. Regional anesthesia also helps in minimizing the risks and side effects of general anaesthesia by avoiding it. Regional nerve blocks are based on the idea that nerve fibres can be

blocked wherever along their journey since pain is transmitted across them. Consequently, peripheral nerve blocking is now a widely accepted idea for complete anaesthetic care (Narendra BM et al., 2014).

The brachial plexus is constrained to its smallest surface area on the first rib, where block is established at the level of distal trunks and origin of divisions. These three trunks carry whole sensory, motor and sympathetic innervations of the upper extremity, with exception of uppermost part of medial side of arm (T2).

Different adjuvant, including clonidine, fentanyl, dexamethasone, midazolam, and dexmedetomidine, had been added to local anaesthetics to modify the block for a quicker onset and prolonged duration without any unfavorable systemic effects and also reduce the overall amount of local anaesthetic used (Bharti N et al., 2003).

Bupivacaine has been the most popular local anaesthetic for peripheral nerve blocks due to its lengthy duration of action and excellent quality of sensory blockade compared to motor blockade (Lew E et al., 2001). Ropivacaine is a more recent, long-acting local anaesthetic with neuronal blocking potential that appears to be on par with or better than Bupivacaine when used in peripheral nerve blockade (Lew E et al., 2001). Research demonstrates that it has a substantially higher safety margin than bupivacaine due to decreased CNS and cardiac toxicity, allowing for the use of higher dosages (Singelyn FJ., 2001).

A water-soluble benzodiazepine called midazolam as adjuvant is known to extend the effects of local anaesthetics and because of intrinsic local anaesthetic properties (Bharti N et al., 2003). It is due to the fact that midazolam is known to cause anti nociception and improve the effects of local anaesthetics by acting on gamma amino butyric acid receptor located at peripheral nerves (Bharti N et al., 2003).

Methods

Aim of the study was to assess the role of midazolam as adjuvant while comparing anaesthetic effect of 0.5% bupivacaine versus 0.5% ropivacaine in supraclavicular block. Objective was to compare the onset and duration of motor as well as sensory blockade after addition of midazolam to 0.5% bupivacaine and 0.5% ropivacaine and also to compare the intraoperative hemodynamic changes and complications if any.

After obtaining prior permission from the institutional ethical committee the study was conducted in 60 patients of either sex with the age group of 18-60 years with weight between 50-70 kg under ASA grade I or II undergoing elective upper limb surgeries under supraclavicular block. All patients were explained regarding the type of anaesthesia and the procedure, and informed and written consent were taken from each patient and the patient's attendants. Patient refusing the procedure, with history of hypersensitivity to local anaesthetic, with bleeding disorder, pregnant or lactating mothers, and ASA grades III / IV were not included in the study. 30 patients were taken in each group using purposive sampling. Each patient was randomly allocated into one of the two groups. Group A received ropivacaine 0.5% (30 ml) with preservative free midazolam (50mcg\kg). Group B received bupivacaine 0.5% (30 ml) with preservative free midazolam (50 mcg\kg). After preparing all the drugs and the equipment's for the procedure patients were premedicated and under aseptic preparation, skin wheal with local anaesthetic was made. The point of insulated needle entry was about one inch lateral to insertion of SCM or one thumb breath lateral to SCM. The insulated short bevel nerve stimulation needle (Stimuplex® B-Braun) was use for peripheral nerve stimulator (B. Braun Stimuplex® HNS12). The stimulation was started with intensity of 1 mA and a pulse width of 0.1millisecond and frequency of 2 Hertz. Once the desired response was obtained, which was a muscle twitch of the fingers, current was gradually reduced to 0.5 mA and total volume of the anaesthetic solution was injected. The following parameters were noted: Onset of sensory block, Onset of motor block, duration of sensory block, duration of motor block, duration of analgesia, haemodynamic variable like HR, SBP, DBP, SPO_2 and sedation score, and any complications were assessed.

Assessment of sensory blockade - The sensory scale used for assessment was 4-point scale of Hollmen's scale (Lee ret al., 2012). Sensory block was assessed by pin prick with 22-gauge hypodermic needle in skin dermatomes C4-T2 once in every minute for initial 30 minutes and then every 30 minutes up to first 6 hours and hourly up to 24 hours from the time of complete block onset.

Onset of sensory block was the time interval between administration of drug and absence of sensation to pin prick (Hollmen's scale more than or equal to 3) (Kaur A et al., 2015). Duration of sensory block was defined by the time elapsed between loss of pin prick sensations to its reappearance (Hollmen's scale less than or equal to 2) (Kaur A et al., 2015).

Assessment of motor blockade – Motor block was graded using modified Bromage scale for upper extremities. Onset of motor block was assessed by the time interval between administration of drug and loss of flexion/extension movements in the arm (Modified Bromage scale 1) (Kaur A et al., 2015). Duration of motor block was defined as the time elapsed between injection of drug to complete

return of muscle power (Modified Bromage scale Grade 0) (Kaur A et al., 2015). This was assessed every minute till loss of finger movements, then every 30 min for first 6 hours and then hourly till finger movements regained.

Block was labelled as failed when there was absence of sensory blockade in all major nerves or presence of sensory block in only one of the nerves. In case of block failure, the patients were excluded from the study and the surgery was carried out under general anaesthesia. Ramsay sedation score (Ramsay MA et al., 1974) was employed for assessing the sedation in the groups.

Hemodynamic parameters were recorded during the basal period and for every 10 minutes throughout the surgery. After operation, all patients were transferred to the post anaesthetic care unit and monitored for 24 hours. The incidence of adverse events, i.e., shivering, hypotension (MAP < 65 mm Hg or SBP <100 mm Hg), bradycardia (HR< 100 mm Hg), nausea, vomiting were recorded during the stay in the post operation care unit (PACU). Post- operative pain at the incision site was assessed by visual analogue scale (VAS) at 0, 1, 2, 6, 12, 24 hours where VAS - 0 indicates the time at the end of surgery and VAS 10 – worst pain imaginable.

Statistical Analysis: Data from the case proforma was entered into Microsoft Excel spreadsheet version 2021 and analysis was performed using IBM-SPSS version 26. For determining of categorical data (percentage), a Chi-square test was applied. To calculate normally distributed continuous data (mean SD), a student t-test was applied. P value <0.05 was considered as statistically significant.

Results

Mean demographic data (age, weight, height, and gender) and the ASA grade, duration of surgery of patients in both groups were comparable (Table1).

Table 1: Demographic characteristics (Mean ± SD)

	Group A (n=30)	Group B (n=30)	P value
Age (yrs)	39±11	34±10	0.5692
Sex (M : F)	18:12	21:9	0.4962
Weight (kg)	62.3±11.9	60.9±10.1	0.238
Height (cm)	162±6	163±7	0.4519
ASA (I/II)	16/14	19/11	0.9658
Duration of surgery (min)	74±22	76±26	0.498

Onset of sensory block was significantly shorter in group B (9.56±1.6 minutes) compared to group A (16.5±2.3 minutes), p <0.05 (Table 2). Onset of motor block was significantly shorter in group B (10.8±1.9 minutes) compared to (18.6±3.1 minutes) in group A, p<0.05 (Table 2). Duration of sensory block was (12.4 ± 2.5) hours in group B was significantly longer than group A (10.2 ± 1.4) hours, p <0.05 (Table 2). Duration of motor block in group B (7.01±1.6) hours was significantly longer compared to group A (6.1 ± 0.85) hours, p <0.05 (Table 2). Duration of analgesia/ time taken for first request of post-operative (rescue) analgesic in group B was (13.4 ±1.5) hours which was significantly longer than group A (11.6±1.01) hours, p <0.05 (Table 2).

Table 2: Block characteristics (Mean±SD)

	Group A	Group B	P value
Onset of sensory block (min)	16.5±2.3	9.56± 1.6	0.0001
Onset of motor block (min)	18.6±3.1	10.8±1.9	0.0035
Duration of sensory block (hrs)	10.2±1.4	12.4±2.5	0.0004
Duration of motor block (hrs)	6.1±0.85	7.01±1.6	0.0325
Duration of analgesia(hrs)	11.6±1.01	13.4±1.5	0.0068

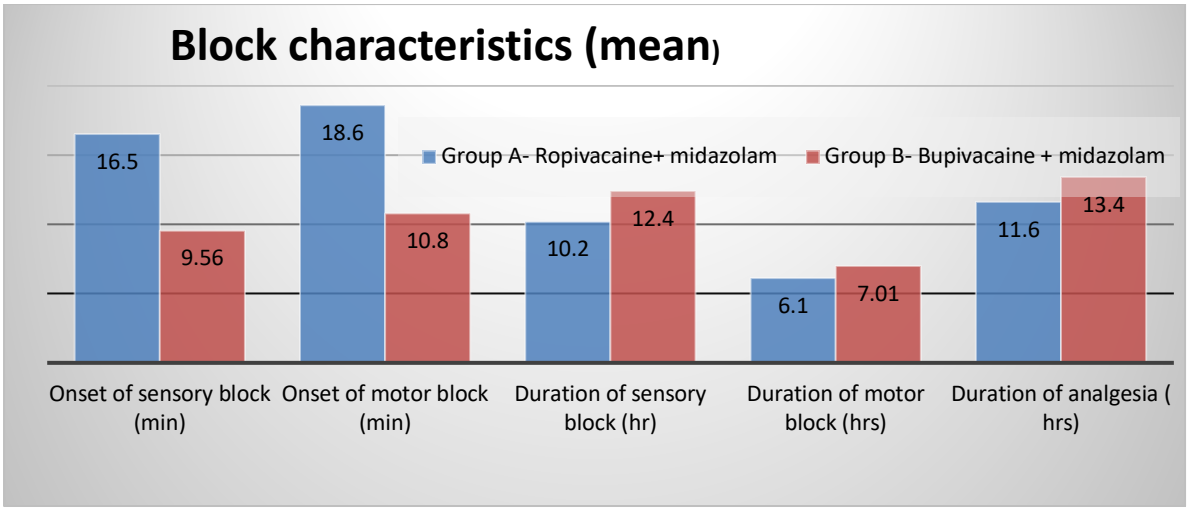

Figure1: Showing mean value of block characteristics.

In both groups sedation corresponding to score 2 was observed in some patients between 10 minutes from time of injection to 60 minutes. 13.3% patients in group B and in group A 16.7% at 10 minutes, 30.0% patients in group B and in group A 26.7% at 30 minutes and 6.7 % of patients in group B and in group A 10.0% at 60 minutes had sedation score of 2.

After 60 minutes all patient's sedation score were 1. None of the patients had sedation score of 3 and above during the study period. Statistical analysis of sedation score by chi square test showed that the difference in Ramsay sedation score was not significant ($p > 0.05$) between the groups.

Haemodynamic parameters did not differ between groups in the intra and post-operative period. VAS was significantly lower in group B, at 6, 12 and 24 hours than group A, $p<0.05$. One subject in B group had bradycardia and one in each group had hypotension. Adverse effects in both the groups were almost negligible and clinically not significant, $p>0.05$(Figure2).

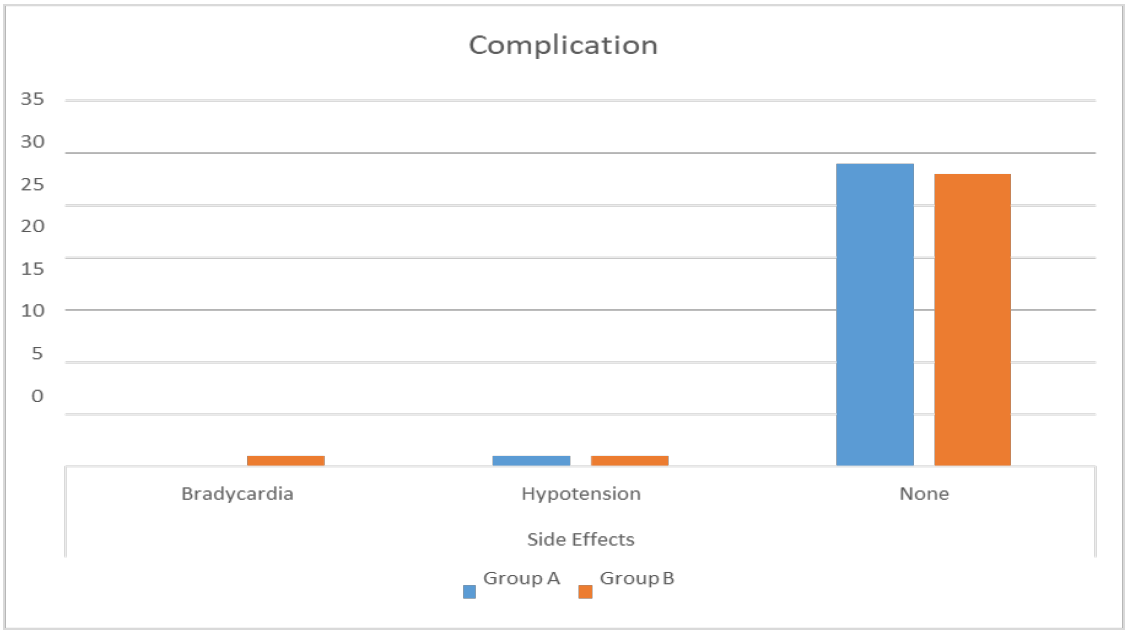

Figure 2: Bar diagram showing complications in each group

Discussion

In comparison to general anaesthesia, peripheral nerve blocks offer excellent hemodynamic stability and optimal operational circumstances. The development of local anaesthetics with improved safety profiles and longer half-lives enables better anaesthetic care to be given to even high-risk patients (Pester JM et al., 2022).

The S (-) enantiomer is the principal agonist because it possesses true local anaesthetic activity, whereas the R (+) enantiomer not only possesses less local anaesthetic activity, but with greater

toxicity. Ropivacaine is a pure S (-) enantiomer, unlike bupivacaine, which is a racemate, developed for the purpose of reducing potential toxicity and improving relative sensory and motor blockade profiles (Vaghadia H et al.,1999).

The mean time from onset of block to request of analgesics was taken as total duration of analgesia. The duration of analgesia was longer after adding midazolam as additives in B group in comparison with A group. Regarding the duration of analgesia, our results are similar to previous studies like Jarbo K et al, who also found the similar findings (Jarbo K et al., 2005). In their study they also add midazolam as additives and compared it with plain bupivacaine. Gulec S et al in 1998 found that a bupivacaine and midazolam combination prolonged postoperative analgesia compared to a bupivacaine-morphine combination when administered caudally (Gulec S et al., 1998).

In our study, the duration of sensory and motor blockade in group B was significantly longer than group A. Similarly, McGlade D P et al in 1998 while comparing 0.5% ropivacaine and 0.5% bupivacaine for brachial plexus block noted that the quality of anaesthesia was similar, however motor blockade lasted significantly longer when bupivacaine was used (McGlade D P et al., 1998). In the study conducted by Mathew S et al in 2018, midazolam when added to 30 ml of ropivacaine for supra clavicular brachial plexus block, duration of sensory and motor blockade was significantly prolonged when compared with equal volumes of plain ropivacaine (Mathew S et al., 2018). Our results showed that sensory blockade last longer as compared to motor block which agrees with the observation by De Jong RH et al (De Jong RH et al., 1963). These authors explained that large fibres require a higher concentration of local anaesthetic than small fibres. The minimal effective concentration of local anaesthetic for large (motor) fibres is greater than for small (sensory) fibres. Thus, motor function return before pain perception and duration of motor block is shorter than the sensory block (De Jong RH et al., 1963).

In our study, we observed that onset time for sensory blockade was quicker in group B than group A. In the study conducted by Narendra BM et al in 2014, "A comparative study of bupivacaine 0.5% and ropivacaine 0.5% for supraclavicular brachial plexus block" (perivascular approach), it was found that the onset of sensory and motor blocks was significantly faster in patients who received 0.5% bupivacaine than 0.5% ropivacaine (Narendra BM et al., 2014). All local anaesthetics block C fibres at the same rate, however the rate at which A fibres are blocked depends on physiochemical characteristics like pKa and lipid solubility. Even though the pKa of ropivacaine and bupivacaine are similar, Ropivacaine is less lipid soluble than bupivacaine and hence, it takes more time to block A fibres than bupivacaine. Ropivacaine also has less motor blockade than bupivacaine (Markham A et al., 1996; Kuthiala G et al., 2011).

In the study conducted by Jarbo K et al in 2005, it was found that the onset of sensory and motor blockade was significantly faster in patients who received a combination of midazolam and 0.5% bupivacaine than plain 0.5% bupivacaine (Jarbo K et al., 2005). This could be due to a local anaesthetic property of midazolam and its synergistic action with that of local anaesthetics.

In the study conducted by Mathew S et al and Jarbo K et al, it was found that hemodynamic parameters were remained stable in both the groups during supraclavicular brachial plexus block when adding midazolam to bupivacaine and ropivacaine (Mathew S et al., 2018; Jarbo K et al., 2005). Jarbo K et al concluded that midazolam when used in brachial plexus block in combination with 30 mL of bupivacaine (0.5%) accelerated the onset of sensory and motor blockade, and improved postoperative analgesia without producing any significant adverse consequences (Jarbo K et al., 2005). We concluded that the side effects / complication rates were almost negligible in both the groups if the necessary dosages applied and adequately deposited, and unintended intravascular injection were avoided.

In our study, sedation score using Ramsay sedation score was higher in patients in both the groups, receiving 50mcg/kg midazolam (preservative free) starting from 10 minutes to 60 minutes from the time of injection of drug (Ramsay MA et al., 1974). None of the patients in both the groups had sedation score 3 or above during the course of the study period. This could be due to partial vascular uptake of midazolam and its transport to CNS, where it acts and causes sedation. Adding midazolam not only provides prolonged post-operative analgesia but also causes sedation as in study described by Nishiyama T et al in 2002 (Nishiyama T et al., 2002).

In the study, pain score was recorded post-operatively according to visual analogue score. There was no difference in VAS score between the two groups till the 2nd post-operative hour. The VAS score in the group B was significantly lower at 6th, 18th and 24th hour in post-operative period compared to the patients in group A. In this study pain score was significantly lower in patients who received midazolam in addition to both bupivacaine and ropivacaine. The rescue analgesic requirement (inj. tramadol 1 mg/kg) was lower in B group compared to group A because duration of analgesia is more with 0.5% bupivacaine then ropivacaine 0.5%.

Conclusions

From the study, it was observed that in supraclavicular block after preservative free midazolam addition as adjuvant speeds the onset of sensory and motor blockade. The combination produces improved analgesia, prolonged anaesthetic effect and reduced requirements for rescue analgesics and minimum complication. Again, at equal volumes, bupivacaine 0.5% has an advantage over ropivacaine 0.5% after addition of midazolam. However, the sedation scores were comparable in both the groups. Hence, midazolam can be considered as a safe additive to local anaesthetic solution for brachial plexus block.

List of abbreviations:

- ASA: American Society of Anesthesiology
- CNS: Central nervous system
- SBP: Systolic blood pressure
- DBP: Diastolic blood pressure
- HR: Heart rate
- PACU: Post anaesthesia care unit
- SD: Standard deviation
- SCM: Sternocleidomastoid
- VAS: Visual analog score

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