Original Research Article

Comparison between intravenous dexmedetomidine and midazolam for sedation during upper extremity surgeries under supraclavicular brachial plexus block

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Abstract

Background: The search for an ideal sedative agent during surgery under brachial plexus block still goes on. Midazolam is commonly used as a intraoperative sedative but it has no impact on brachial plexus block. Dexmedetomidine is a new alpha 2 receptor agonist used widely for sedation. Our aim was to compare the efficacy of equivalent doses of dexmedetomidine infusion with midazolam on sedation,block characteristics and patient satisfaction. **Methods:** In this study, 100 American Society of Anesthesiologists (ASA) I and II patients posted for forearm surgeries under ultrasound-guided brachial plexus block were divided to receive either midazolam (Group M) or dexmedetomidine (Group D) infusion. They were administered an initial loading dose of the midazolam and dexmedetomidine over 10 min followed by a maintenance dose till the end of the surgery. Effect on sedation,block characteristics and patient satisfaction were monitored. $P < 0.05$ was considered statistically significant.
Results: Time of onset of sedation was earlier in dexemedetomidine group compared to midazolam group. Profile of block characteristics was better compared to midazolam group. Patient satisfaction score was greater in dexemedetomidine group compared to midazolam group.**Conclusion:** Dexmedetomidine may be a better alternative to midazolam for sedation in patients undergoing surgeries in brachial plexus block.

Keywords: brachial plexus block, dexmedetomidine, midazolam,sedation.

Introduction

Brachial plexus block(BPB) is a popular and widely employed regional nerve block of the upper extremity surgeries. Various approaches to brachial plexus block have been described but supraclavicular approach is the easiest and most consistent method for anaesthesia and perioperative pain management in surgery below the shoulder joint. It provides good surgical condition, prolongs analgesia and decreased opioid administration during postoperative period[1].

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Sedation should be administered along with BPB, which will provide amnesia, anxiolysis, freedom from recall of surgery, about the procedure and postural discomfort[2]. Loud noises, untoward remarks in the operating room perceived by the patients, may have long term undesirable psychological effects[3]. So administration of sedation is essential during surgeries performed under regional anesthesia[4].
Various drugs have been used for sedation during BPB, but the preferred drugs are those which produce sedation and also provide better BPB profile.
Midazolam is a commonly used drugs for sedation during BPB[5].Midazolam is a benzodiazepine with relatively early onset of action and early recovery time due to its short half life, as compared to diazepam. The primary drawback of midazolam is potential accumulation of drug that can cause prolonged sedation

and hangover effect when used as infusion over prolonged time.Dexmedetomidine is an imidazole derivative with adrenergic α1 to α 2 receptor selectivity ratio of 1:1600 making it a highly selective α 2agonist. This reduces the unwanted side effects involving α 1 receptors[6]. At therapeutic level it provides sedation, reasonable patient satisfaction, less opioid requirement and less respiratory depression without affecting cardio-vascular stability[7].

There are few studies comparing dexmedetomidine versus midazolam for sedation during surgeries under regional anesthesia. So this study was performed to compare sedation produced by intravenous dexmedeto-midine and midazolam in patients undergoing upper limb surgery under BPB.

Primary objectives of the study were to observe: Onset of sedation by using BIS(BispectralIndex) monitoring, Intra-operative sedation, by using BIS monitoring and Post-operative recovery time by using BIS and RSS(RamsaySedation Scale).

Secondary objectives of the study were to observe:Block characteristics (Onset of motor block and sensory block, Duration of motor block and duration of sensory block) ,patient satisfaction score using Likert Verbal Rating Scale and adverse effects during infusion of the studied drugs.

Methods

Ethics statement: The study was approved by the Institute Ethics Committee, SCB Medical College and Hospital. Written consent was obtained after informing the participants about the nature, scope and risks related to the study.

Duration and type of the study: This study was conducted from August 2017 to November 2019. A total of hundred consenting adult patients were included in this double-blind, randomized, comparative study.

Study setting: SCB Medical College and Hospital

Study design: Double blinded randomized comparative study

Inclusion criteria:Patients of either sex,with ASAI/II, Age-18 to 50years and Patients undergoing upper extremity surgery under supra clavicular brachial plexus block

Exclusion criteria:Patients who refused to participate

Difficult airway anticipated in preoperative assessment.

Patients with known contraindications to brachial plexus block (coagulopathy or local infection)

Patients with known allergy to bupivacaine, midazolam or dexmedetomidine

Sample size: 100 (50 patients in each group). Sample assignment was done by sequential allocation using sealed opaque envelope in to 2 equal groups:

Group D (Dexmedetomidine Infusion), GroupM (Midazolam infusion)

Parameters of observation

Onset of sedation(time to reach BIS75)

Recovery from sedation(time to reach BIS90)

Intraoperative sedation- variation of BIS score was recorded and RSS of 3-4 was maintained until the end of surgery.

The Ramsay sedation scale is as follows: 1=anxious, agitated, restless; 2=co-operative, oriented, tranquil; 3=responds to commands only;4=brisk response to light glabellartapor loud noise; 5=sluggish response to a light glabellar tap or loud noise and 6=no response.

Block characteristics-Onset and duration of sensory and motor block

Patient satisfaction score by using Likert Verbal Rating Scale[7]-

1 - Extremely dissatisfied, 2 Dissatisfied, 3-Dissatisfied Somewhat, 4- Undecided Somewhat, 5- Satisfied somewhat, 6-Satisfied 7- Extremely satisfied.

Study technique: All patients were assessed for pre-anaesthetic check-up and airway assessment. A written informed consent was taken for enrolment in study after proper explanation of the procedure of the study and different aspects of BPB under peripheral nerve stimulator (PNS) guidance.All patients were premedicated with oral ranitidine 150 mg and oral alprazolam 0.25mg night before surgery.All were kept nil per oral 6 hour prior to surgery.On arrival to the operation theatre,intravenous access was established with 18G/20G cannula on the dorsum of the non-operative hand. Routine monitoring in the form of electro cardiography, non-invasivearterial pressure, pulse oximetry and respiration was done,and baseline values were noted. Oxygen at a rate of 5l/min through a facemask was administered to all patients. Group D patients were given 0.5 mcg/kg IV dexmedetomidine over 10min.bolus followed by 0.1mcg/kg/hr infusions as maintenance until the end of surgery. Group M were given 0.05 mg/kg IV midazolam over 10 min. bolus followed by 0.01mg/ kg/hr infusion as maintenance until the end of surgery. Variation of BIS scores after starting of infusion was recorded every 10mins till completion of surgery between the study groups. After starting of the infusion, when BIS score reaches down to 75, with prior aseptic preparation of the area, brachial plexus block was given with injection bupivacaine 0.5%plain by supraclavicular approach under ultrasound guidance. Surgeons were allowed to give incision, 30min after the block. Time to reach BIS score 75 was also noted and was considered as onset of sedation. Patient not having adequate block or requiring other

drugs as supplement and or conversion to general anaesthesia was excluded from the study. Hemodynamic parameters like MAP(Meanarterial pressure), Heart rate and SpO2 were recorded at the point of time when BIS reaches75 and in every10 mins,from the starting point of infusion to completion of surgery. Infusion was stopped at completion of surgery and Ramsey sedation score was recorded at that point. Duration of postoperative analgesia was recorded when the patient was complaining of pain, first time after surgery. Time to reach BIS score of 90(taken as recovery point from sedation) in both groups was recorded. At that point, Ramsay sedation score was recorded.Data were compiled and subjected to statistical analysis using the Statistical Package for Social Sciences (SPSS Inc.; Version 20.0. Chicago, IL,USA).Categorical variables were expressed as Number of patients and percentage of patients and compared across the group susing Pearson's ChiSquare test for Independence of Attributes. Continuous variables were expressed as Mean±Standard Deviation and compared across the 2groups using unpaired t test. P value was less than 0.05, was considered as statistically significant.

Results

Hundred patients were enrolled and randomized to either of the two groups,50 patients in each. The demographic profile of the patients in the two groups was comparable. Haemodynamic parameters, i.e., heart rate and mean arterial pressure, in both the groups were comparable.

Table 1: Block characteristics

Block characteristics	Group D (Mean ±SD)	Group M (Mean±SD)	*P* Value
Onset of sensory block (min)	16.7 ±1.9	19.9 ±1.7	<0.001
Onset of motor block (min)	19.6 ±2.8	23.7 ±1.4	<0.001
Duration of sensory block (min)	733.0 ± 57.9	303.9 ±40.8	<0.001
Duration of motor(min)	636.3 ± 92.5	266.1 ± 28.5	<0.001

The onset of sensory and motor block was quicker in the dexmedetomidine group than in the midazolam group(table 1).The mean sensory block onset time was16.7±1.9 min in the dexmedetomidine group and19.9±1.7 min in the midazolam group (p<0.001).The mean motor block onset time was 19.6 ±2.8 min in the dexmedetomidine group and 23.7±1.4 min in the midazolam group (p<0.001) (Table 1).The duration of sensory as well as motor block was more prolonged in the dexmedetomidine group than in the midazolam group. The duration of sensory block in the dexmedetomidine group was 733.0±57.9 min,where as in the midazolam group, it was 303.9±40.8 min(p<0.001). The duration of motor block in the dexmedetomidine group was also prolonged;it was 636.3±92.5 min in the dexmedetomidine group and 266.1± 28.5 min in the midazolam group (p<0.001) (Table 1).

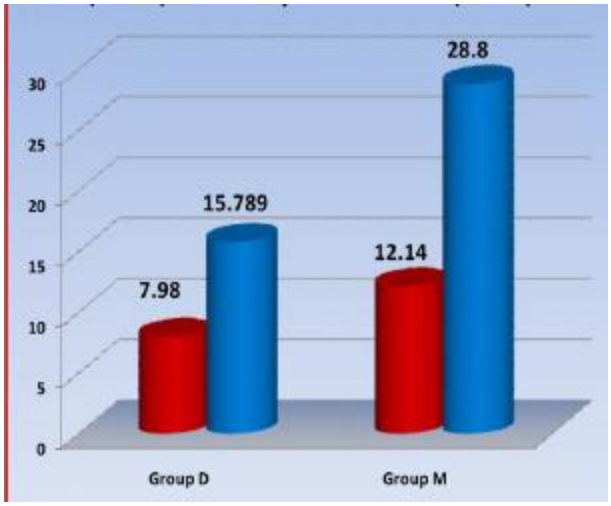

Fig1:Time of onset of sedation (BIS75-red)&recovery from sedation(BIS90-blue)

Significantly more time was required to reach BIS value75in group M patients as compared to group D.(fig1)

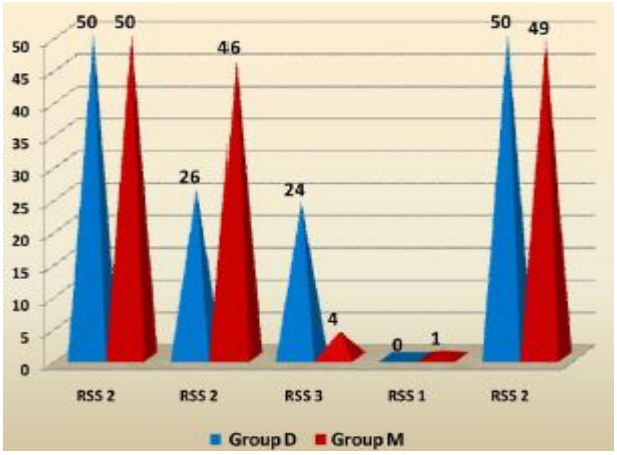

Fig 2: RSS (Ramsay sedation scale) at different time intervals.

Significantly more number of patients had higher sedation score in group M compared to group D. (Fig 2)

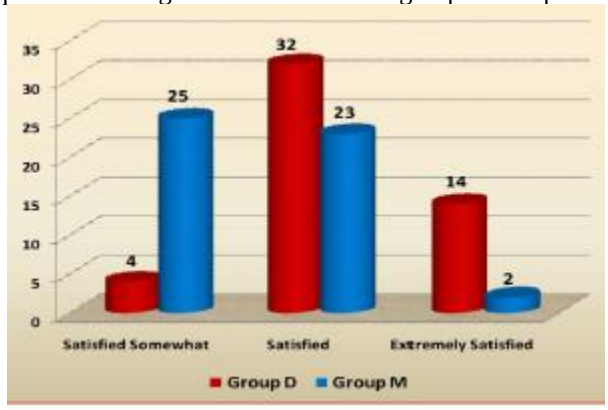

Fig 3:Patients satisfaction score

Significantly more number of patients had higher patient satisfaction score in D group. (Fig 3)

Discussion

Supraclavicular brachial plexus block is widely employed regional nerve block to provide anaesthesia and analgesia for the upper extremity surgery. Supraclavicular block provides a rapid, dense and predictable anesthesia of the entire upper extremity in the most consistent manner of any brachial plexus technique[8]. Sedation during regional blocks is routinely employed. It would be beneficial if such an agent also prolonged the duration of block. Various studies had been performed to compare dexmedeto-midine and midazolam for intraoperative sedation. Propofol produces rapid onset and offset of sedation. However, it produces hypotension, respiratory depression and airway obstruction[9]. So this study was conducted to compare dexmedetomidine and midazolam for intra operative sedation during upper limb surgeries under BPB.We chose a loading dose of 0.5 mcg/kg of dexmedetomidine based on previous literature and studies. Reports suggest that on administration of low or moderate doses and slow rates of infusion of dexmedetomidine, α2 agonist effects are observed but not α 1 effect[10]. In view of its short distribution half-life of 5min, dexmedetomidine necessitates that it be given as a maintenance infusion. The loading dose of midazolam 0.05 mg/kg was chosen based on a recent study by Eren et al[11] that this dose is comparable to dexmedetomidine0.5mcg/ kg in terms of sedation. We aimed to compare equivalent doses of both the drugs to avoid any bias in our results. Dexmedetomidine has both sedative and analgesic properties and has been used as a single agent in many painful procedures[12]. The onset and intraoperative sedation and recovery from sedation was compared between dexmedetomidine and midazolam. Time to reach BIS 75 was considered as onset of sedation which was significantly ($p < 0.001$). Earlier in group D (7.98±1.41min) in comparison to group M (12.14 ± 2.36min) . At BIS 75 RSS(RSS-I) was also recorded which was comparable between the groups. This finding was also supported by study performed by Jo et al comparison between intravenous

dexmedetomidine and midazolam for bispectral index guided sedation during spinal anesthesia[13]. Intra operative sedation was assessed byBIS value at 10 min interval. Most of the values were significantly lower in group D ($p < 0.05$) in comparison to group M. BIS value at 20, 50, 60 and 70 min in group D were also less in comparison to group M but values were not statistically significant ($p > 0.05$).At the end of the surgery infusion of the study drugs were stopped and recovery was assessed by BIS value and RSS. Immediately after discontinuation of the study drugs, RSS (RSS-II) was evaluated. At this point RSS 2 (co-operative, oriented, tranquil) was observed in 26 patients of group D. However this score was observed among 46 patients in groupM. RSS 3 (responds to command) was found among 24 patients in group D where as this score was observed among 4 patients of group M.Time to reach BIS value90 was earlier in group D(15.78±2.74)in comparison to group M(28.8±5.21)which was statistically significant ($p <0.01$). At that time RSS was also assessed. RSS (RSS-III) was comparable($p=0.315$)between the groups when BIS value was 90. In this study we observed that intra operative BIS value was lower with dexmedetomidine infusion in comparison to midazolam infusion. This findings corroborates with other studies like study by Liang Y et al who compared dexmedetomidine and midazolam for sedation in gynaecologic surgery underepidural anesthesia showing dexmedetomidine significantly reducing fentanyl requirement and both drugs showing similar patient and surgeon satisfaction scores and no difference in time to recovery[14].

Intraoperative MAP values were comparable between the two groups. Given its anxiolytic and sedative properties,midazolam has negative inotropic activity in atrial tissues mediated by the inhibition of L-type calcium channels.

However, although dexmedetomidine and midazolam reduce blood pressure and heart rate, a previous comparative study demonstrated lower heart rate and blood pressure during third molar surgery for dexmedetomidine compared to midazolam during monitored anesthesia care. The additional findings of the present study are that systematically administered dexmedetomidine(a)shortens the onset of motor and sensory block, (b)prolongs the duration of motor and sensory block and(c) does not cause any significant side effect compared to midazolam sedation during supraclavicular brachial plexus block.It has been suggested that the spinal mechanism is the principal mechanism for the analgesic action of dexmedeto-midine-even though there is clear evidence for the supraspinal and peripheral sites of action[15]. When added as an adjuvant, it may directly act on the nerve or due to central action after absorption through the block site into systemic circulation. Based on these observations, it appears that the central and peripheral mechanisms were in play in our patients, resulting in block prolongation.In a randomized controlled study, Kathuria et al evaluated dexmedetomidine as an adjuvant toropivacaine in supraclavicularbrachial plexus block[16].Perineural addition and intravenous co-administration of dexmedetomidine both led to a decrease in the onset time and an increase in the duration of motor and sensory blockade. They observed that these effects were more prominent in patients who had received dexmedetomidine perineurally. Agarwal S et al[17]. evaluated the effect of perineural dexmedetomidine added to 0.325% bupivacaine compared to that of bupivacaine solution with normal saline. Perineural dexmedetomidineasan adjuvant significantly shortened the onset and prolonged the duration of sensory and motor blockade[13].A recent study by Abdallah F et al[18] in a comparison of intravenous and perineural dexmedetomidine in interscalene block,they suggested that intravenous dexmedetomidine along with ropivacaine 0.5% in inter scalene brachial plexus block prolongs the analgesic duration and reduces cumulative 24 hour morphine consumption without prolonging motor blockade and intravenous dexmedetomidine was found noninferior to perineural dexmedetomidine groups for these outcomes. Rutkowska K et al[19] investigated the effect of dexmedetomidine sedation on brachial plexus block in patients with end- stage renal disease in comparison to our study that included only patients with ASA I and II. They used 0.375% bupivacaine in their study, whereas 0.5%bupivacaine was used in our study.They also used midazolam sedation for the control group. However, the infusion of both study drugs was started after the establishment of the block, incontrasttoour study where infusions started before block placement. The duration of sensory(9.4±3.4 h) and motor block(11.9±3.8h)was significantly prolonged, but longer duration of motor block than of sensory block is not desirable in the postoperative period. They also attributed the overall result of their study to the generalized peripheral analgesic effect of dexmedetomidine. Higher patient satisfaction score was found in group D in comparison to group M, which was statistically significant. A possible limitation of this study could be that amnesia scoring &cognitive function testing for psychomotor impairment was not done. Dexmedetomidine infusion resulted in stable haemodynamic parameters with a better block profile,

without significant side effects. This was in agreement with the findings of other studies where dexmedetomidine was found to be a valuable addition for sedation in patients undergoing upper limb surgeries under brachial plexus block[20].

Conclusion

The onset of sensory and motor block was quicker in the dexmedetomidine group than in the midazolam group. The duration of sensory as well as motor block was more prolonged in the dexmedetomidine group than in the midazolam group,So we can conclude that dexmedetomidine is a superior sedative agent as its onset and offset of action is earlier than midazolam without producing hypotension and desaturation, during BPB

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