Original Research Article

A comparative study on the analgesic effects of clonidine and midazolam as an adjuvant to a mixture of local anaesthetics in supraclavicular brachial plexus block

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Abstract

Introduction: With the rapid increase in traffic accidents, victims present for upper limb surgeries. Brachial plexus block is a good substitute to general anaesthesia. The aim of this study was to compare the analgesic effects of clonidine and midazolam as adjuvant to a mixture of local anesthetics in supraclavicular brachial plexus block**. Material & Methods:** A randomized prospective double blind study conducted at Department of Anaesthesiology in a Tertiary care teaching hospital over a period of 6 months on 60 ASA- I and ASA II patients who fulfilled the inclusion and exclusion criteria. They were divided into 2 groups of 30 each based on computer generated randomization table, Group C received 150 µgm clonidine +Inj lignocaine 2% with adrenaline 15ml+Inj bupivacaine plain (0.5%) 15ml and diluted to 40ml and Group M received Inj midazolam 50µgm/kg adjuvant to the same mixture of local anesthetics and diluted to 40ml. Both the groups were compared based on the onset of sensory & motor block, duration of sensory & motor block, sedation measured by sedation score (Culebras). Total duration of sensory & motor analgesia & post-operative VAS score was recorded. **Results**: Onset of sensory and motor block was earlier in Group C, even duration of analgesia was significantly prolonged in Group C (619.53 ± 77.58 min versus 508.73 ± 89.83 min. in group M, the p value being < 0.001). VAS score was 0 upto 3hrs in Group C and 0.5hr in group M. And the maximum sedation score seen in Group C was 3(Sedated and responding to mild stimulus). In Group M the maximum score noted was only 2 (Sedated and responding to verbal commands)**. Conclusion:** Clonidine as an adjuvant in brachial plexus block for upper limb elective surgeries prolongs post-operative analgesia and also has high sedation score with no complications in either of the groups.

Keywords: Clonidine, Midazolam, post-operative analgesia, Sedation score, supraclavicular brachial plexus block, VAS score

Introduction

With the expeditious increase in road traffic accidents occurring each day. Accident victims present to us for upper limb surgeries. To cope up with this work load regional blocks become very much accepted as part of comprehensive anesthesia care. Introduced by Halsted and Hall[1] in 1885, Brachial plexus block is a good alternative to general anesthesia for upper extremity surgeries. Patient is free from side effects of general anesthesia drugs and also upper airway handling. Of the many techniques that are described and practiced, supraclavicular approach produces most complete block of all the branches of brachial plexus and hence is suitable for arm, forearm and hand surgeries.

Supraclavicular brachial plexus block (SBPB) is attractive due to its effectiveness, performance ease and margin of safety[2]. This block gives good and complete muscle relaxation, intraoperative hemodynamic stability also post-operative analgesia.

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Bupivacaine is longer acting and lignocaine has faster onset of action. These two are most frequently used local anaesthetics. But, even with long-acting bupivacine, the duration of postoperative analgesia is often inadequate. Many studies have been done to find a way to prolong the analgesia produced by local anaesthetics so that the patient remains pain-free in the post-operative period.

Adjuvants added to local anaesthetics reduce the total dose of local anaesthetics and prolong the analgesic effects without causing systemic side effects. Various studies have investigated several adjuncts, including, opioids, clonidine[3], neostigmine, hyaluronidase[4], bicarbonate, tramadol[5,6], fentanyl and midazolam[7]. The results have been inconclusive because of associated side effects or doubtful efficacy. Popular additives being used are clonidine, dexmedetomidine, buprenorphine, morphine, fentanyl and midazolam.

Clonidine is centrally acting partial alpha 2 adrenergic agonist with selectivity ratio 200:1. Peripherally it prolongs the duration of analgesia by hyperpolarisation of cyclic nucleotide gated cation channels[8]. Midazolam (preservative free) a water soluble benzodiazepine produces its effect by action on GABA-A receptors. These GABA-A receptors are also found in the peripheral nerves[9,10].. It has been shown that the activation of peripheral GABA-A receptors decreases the transmission of nociceptive signals and this results in local analgesic effect[11-14]. The aim of this study was to compare both these adjuvants to a mixture of local anaesthetics in supraclavicular block with respect to onset of sensory and motor

blockade, duration of analgesia, duration of sensory and motor blockade, sedation score, complications and side effects.

Materials and Methods

This was a prospective, randomized double blind clinical study done at Department of Anaesthesiology in a Tertiary care teaching hospital over a period of 6 months after obtaining institutional ethics committee approval. Only patients who fulfilled the inclusion and exclusion criteria and who were fit after a thorough detailed pre anaesthetic checkup were included in the study. Sixty patients undergoing elective upper limb surgeries under SBPB were enrolled for the study. Written informed consent was obtained from all patients after thorough explanation regarding the study. Visual analogue scale was explained to the patient where a score of 0 was no pain and a score of 10 was worst pain.

Inclusion criteria

Patients aged between 20– 60yrs of either gender, weighing > 50kg, belonging to ASA- I and II, and scheduled for elective orthopaedic procedures around elbow, forearm and hand under SBPB were included in the study.

Exclusion criteria

Patients with h/o allergy or hypersensitivity of drugs under study, patient in circulatory instability, patient with known bleeding abnormality and systemic disorders, patient with cutaneous infection at the site of block, patient taking opiods, calcium channel blockers, clonidine and related compounds, pregnant patients, patients on anticoagulants, patients with partial block or who needed to be converted to GA were excluded from the study They were randomly allocated to one of two groups using a computer-generated randomization table.

Group- C: (n = 30) Patients received

- Inj. Lignocaine Hydrochloride 2% with Adrenaline(1:2,00,000) -15 ml
- Inj. Bupivacaine Hydrochloride 0.5% -15 ml
- Inj. Clonidine Hydrochloride 150µg (1ml)
- Normal Saline to make total volume 40 ml

Group- M: (n = 30) Patients received

- Inj. Lignocaine Hydrochloride 2% with Adrenaline(1:2,00,000) -15 ml
- Inj. Bupivacaine Hydrochloride 0.5% -15ml
- Inj. Midazolam 50 µg/kg (Preservative –free)
- Normal Saline to make total volume 40 ml

Care was taken to not exceed the upper safe dose limit of the drugs. The solution to be injected was made by an anaesthetist not involved in performing the block, patient care or data collection. The block was performed by a senior and experienced anaesthesiologist. Investigator was the anesthesia resident who checked the vital parameters and sensory and motor block. Investigator as well as the anesthesiologist who performed the block were blinded to the patient.

They were premedicated with Tab Ranitidine150mg oral with few sips of water on the morning of surgery. Adequate NPO status and consent were checked, IV access with 18 G cannula and RL started on the nonoperative hand prior to performing supraclavicular brachial plexus block in the pre-operative room. On arrival to the O.T, monitors were attached which included noninvasive blood pressure (NIBP), SpO2, ECG and capnography. Emergency drugs and equipments including facilities for GA were kept ready All patients were premedicated with 1mcg/kg Fentanyl i.v. After aseptic preparation The pulsation of subclavian artery was palpated with the thumb of one hand at 1cm above the midpoint of clavicle and the point of maximum pulsation was marked. The supraclavicular brachial plexus block was performed using subclavian perivascular technique described by Kulenkampff[15], modified by Winnie and Collins. After eliciting paraesthesia and following negative aspiration.40ml of the solution containing local anaesthetic combined with clonidine or midazolam as mentioned above was injected followed by a 3-minute massage to facilitate an even drug distribution. The onset and duration of sensory and motor blockade, duration of postoperative analgesia and untoward side effects, if any were observed.

Onset of Sensory Block

Sensory block was assessed by pin prick method using 24G hypodermic needle, every minute till peak effect occurs. Patient was asked to answer questions and grading of sensory effect was done as follows.

Grade-0: Normal sensation (Sharp pain felt), **Grade-1**: Blunted sensation (Dull sensation or slight heaviness), **Grade-2**: No pain perception (State of anaesthesia)

Assessment of sensory block was done along the distribution of median nerve, radial nerve, ulnar nerve and musculo-cutaneous nerve. **Time to sensory onset**-was considered as the time duration between injection of drug to time for blunted sensation over any one of the nerve territories. **Duration of sensory block**-was taken as the time from the onset of grade 2 block to the return of grade 1 block. Motor block was assessed by using following grading scale as described by Bromage. Grade – 0: Normal muscle tone with full flexion and extension of elbow, wrist and fingers. Grade – 1: Decreased motor strength (with weak grip) i.e Paresis. Grade – 2: Complete motor block with inability to move the fingers.

Onset of motor block- was taken as the time elapsed between injection of drug and attainment of grade 1 block. **Duration of motor block-** was taken as the time from development of grade 2 block to return of grade 1 block.

Patient was observed for sedation according to following score as mentioned in the study **by Culebras et al[16] (2001)**

1. Awake and alert
2. Sedated and responding to verbal commands
3. Sedated and respondingto mild stimulus
4. Sedated and responding to moderate to severe physical stimulus
5. Not arousable.

All vital parameters were monitored throughout the procedure later in post-operative ward also. Intraoperative sedation score was noted at 0min, 5min, 10min, 15 mins and there after every 15 minutes till 2 hours. Post-operative VAS score was noted at 30 min.1 st hour, 2nd hour, 3rd hour, 6th hour, 9th hour, 12th hour, 18th hour and 24th hour. The rescue analgesia was given in the form of Inj. Diclofenac Sodium 1.5 mg/kg intramuscularly when VAS score was noted as 4 or more than 4 and number of rescue analgesics over a period of 24 hours was also noted.

Statistical Analysis

All the qualitative and quantitative data were analysed by using chi square test and unpaired t-test respectively. Results were expressed as Mean ± SD. 'P' values < 0.05 were taken as statistically significant and values < 0.001 were taken as highly significant.

Results

Both the groups, group C and group M were comparable with no statistically significant difference with respect to demographic data and ASA physical status of patients as shown in table 1.

Table 1: Demographic Data

Parameter	Group C	Group M	P value
Number of patients	30	30	
Age (in years,Mean±SD)	35.10±6.73	34.26±6.94	>0.05
Sex (Male:Female)	20:10	21:9	>0.05

Weight (in kg, Mean ± SD)	56.33±4.33	57.1±4.14	>0.05
ASA Status			
I	19 (63.33%)	18 (60%)	>0.05
II	11 (36.67%)	12 (40%)	>0.05

It was observed that the onset of sensory block in Group C (11.32±1.31 Mins) was significantly earlier than Group M (12.97±1.30 Mins) respectively, with P value of 0.001 which was highly significant. Also, the total duration of sensory block was longer with Group C than Group M. (502±67.68 Mins Vs 461.2±73.23) to a significant extent value <0.05 as seen in Table-2

Table 2: Different Parameters observed

PARAMETERS OBSERVED TIME IN MINUTES(MEAN±SD)	GROUP -C NUMBER OF PTS (30)	GROUP- M NUMBER OF PTS (30)	P-VALUE
Onset time of sensory block	11.32±1.31	12.97±1.30	<0.001
Total duration of sensory block	502.8±67.68	461.2±73.23	<0.05
Onset time of motor block	7.83±1.09	8.47±1.27	<0.001
Total duration of motor block	442.10±48.11	392.87±41.71	<0.001
Total duration of post operative analgesia	619.53±77.58	508.73±89.83	<0.001

Onset of motor block was longer in Group C than Group M (7.83±1.09 Mins ,8.47±1.27 Mins respectively). P value<0.05. The total duration of motor block was longer in Group C (442±48.11 Mins) than Group M (392.87±41.71 Mins) to a highly significant extent <0.001. (Table-2)
The total duration of postoperative analgesia was 619.53 ± 77.58 min in group C and 508.73 ± 89.83 min. in group C, the p value being < 0.001. Thus total duration of post operative analgesia was significantly longer in group C patients compared to group M patients. (Table-2, figure1)

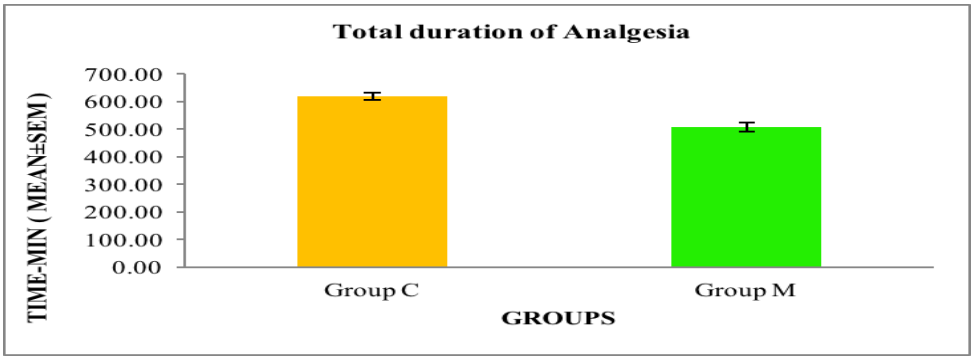

Fig 1:Total duration of analgesia

Table 3: Intraoperative Sedation score (mean score ± sem)

Time interval (in minutes)	Group C (Mean +SD)	Group M (Mean +SD)
0	1	0
5	1	0
10	1	0
15	1.73±0.08	1.27±0.08
30	2.33±0.11	1.43±0.09
45	2.47±0.10	1.67±0.09
60	2.40±0.14	1.67±0.09
75	2.73±0.08	1.63±0.09
90	2.83±0.07	1.70±0.10
105	2.77±0.09	1.87±0.06
120	2.67±0.11	1.50±0.09

This table-3 shows the intra operative sedation score in both the groups. It was noted that in Group C sedation score of 2 was seen by 30 minutes. And the maximum sedation score seen in Group C was 3(**Sedated and responding to mild stimulus) (**Figure2).

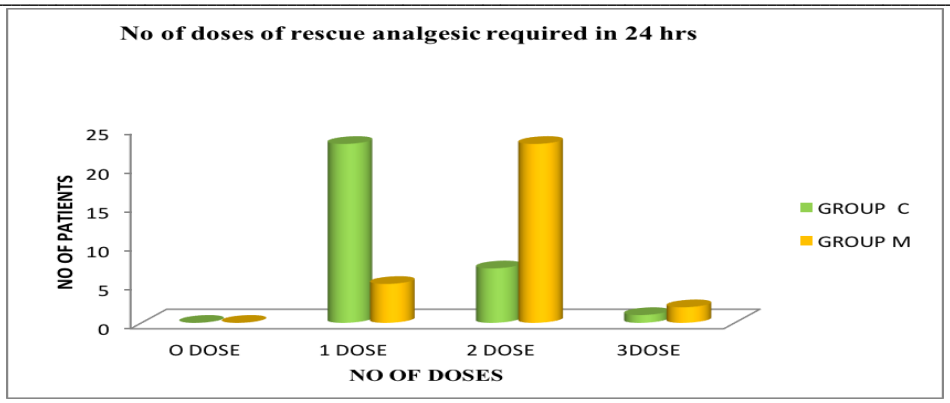

Fig 2:No.of dose of rescue analgesic required in 24 hrs

In Group M the maximum score noted was only 2 (**Sedated and responding to verbal commands)**. This shows that Group C patients were more sedated intraoperatively in comparison to Group M. This was statistically highly significant P value<0.001.(Figure 2)

Table 4: Number of rescue analgesia doses

No. of Doses	Group C (No of pts)	Group B (No of pts)	P value
0	0	0	<0.001
1	22	5	<0.001
2	7	23	<0.001
3	1	2	<0.001

This Table-4 shows that Rescue analgesic doses of Group C and Group M. There is a strong association between rescue analgesic doses and the treatment groups, P-value<0.001. Rescue analgesic in the form of Inj Diclofenac 75 mg I.M., was given. In Group C majority of patients (n=22) required only 1 dose of rescue analgesic in 24 hrs, While majority of patients(n=23) in Group M required 2 doses of rescue analgesic in 24 hrs. VAS score was 0 up to 3hours in group C and 0.5 hours in group M. The VAS score of 4 or more than 4 was attained by 12 hours in Group C and by6 hours in group M. Thus rescue analgesic was given at 12hours in group C patients while rescue analgesic was given at 6 hours in group M.

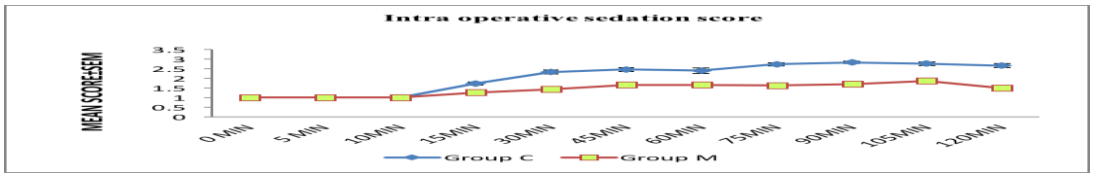

Fig 3:Intra operative sedation score

(Figure 3) Thus, Group-C (Clonidine group) patients had longer duration of pain relief in post- operative period. VAS score was highly significant, P value<0.001. (Table-5, Figure 4)

Table 5:Postoperative VAS score (mean ± sem)

Time interval (in hours)	Group C	Group M
0.5Hr	0±0	0
1 Hr	0±0	0.37±0.09
3 Hr	0±0	2.23±0.20
6 Hr	1.63±0.23	4.33±0.22
9 Hr	3.40±0.09	6.10±0.41
12 Hr	5.90±0.25	4.23±0.31
18 Hr	3.57±0.20	4.67±0.48
24 Hr	4.33±0.46	5.40±0.56

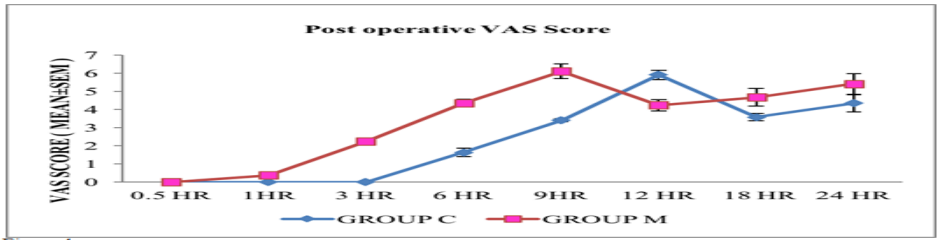

Fig 4:Post operative VAS Score

Discussion

Brachial plexus is a good alternative to general anesthesia for upper extremity surgeries. Of the many techniques described and practiced, supraclavicular approach produces most complete block. Use of adjuvant made the work easy as the dose of local anesthetics reduced and post operative analgesia duration increased. This helped the patients have a longer pain free post operative period. Our study compared the analgesic effects of clonidine and midazolam as adjuvant to a mixture of local anesthetics in supraclavicular brachial plexus block in patient undergoing upper limb surgeries.

The results of our study were similar to the observation made by A.H.El Saied et al[17] in which the onset of motor block occurred earlier than sensory block. Our study results showed that the sensory block tended to last longer as compared to motor block, which agrees with the prediction made by Erlacher.W, Schushcing .C et al[18]. The total duration of sensory block was significantly prolonged in Group C. Our results are in full agreement to those of Singelyn F Jet al 1996[19], in which they used clonidine 5µgm/kg in axilliary brachial plexus block along with local anesthetics and found that clonidine significantly prolonged the duration both anaesthesia & analgesia and had no adverse effects.

The prolongation of sensory block is said to be dose dependent as reported by Buttner et al[20] and Bernard et al[21]. However they also reported an increase in the incidence of side effects with corresponding increase in the dose of clonidine. Increase in the duration of motor block was seen in EL Saied et al[17]and W. Erlacher etal[18]. However, no explanation has been given by these authors for prolongation of motor effect in clonidine group.

Pulse rate, blood pressure & saturation (Spo2) were recorded regularly throughout the period of study and post operatively. These was no significant difference in Pulse rate, Blood pressure & Spo2.

Our results match with those of Eledjam et al 1991[22], Singelyn et al 1992[23], Erlacher W et al 2001[18]. Contrary to these studies blood pressure decreased significantly in 90µgm & 300µgm clonidine in the study of Bernard JM et al[21] 1997.

Duma. B. Urbanekc et al[24] in 2004 –conducted a study on clonidine as an adjuvant to local anesthetics ,randomized ,controlled, double blinded with 4 groups of 20 patients each ,Group A=40ml 0.5% levobupivacaine +150 µgm clonidine, Group B=40ml 0.5% levobupivacaine +1ml saline .Third Group C =40ml of 0.5% Bupivacaine +150 µgm clonidine. Fourth group Group D =40ml of 0.5% Bupivacaine +1ml saline. Onset of block was significantly higher & duration of block was prolonged in clonidine groups with no significant hemodynamic changes.

Popping, Baried M at al[25] in 2009 conducted a metanalysis of 20 RCT suggested that clonidine may be a useful adjuvant to local anesthetics for peripheral nerve blocks. Koj Jarbo, Yatindra Kumar Batra et al 2005 conducted a prospective, randomized double blind study on 40 ASA & 2nd Group B (n=20) were given 30ml of 0.5% bupinacine and Group B(n=20) were given 30ml of 0.5% bupinacine with midazolam 50µmg/kg. It was concluded that midazolam hastened outset of sensory and motor block and improved postop analgesia without any adverse effects.

Trivedi. V. Patel N et al[26] (2010) conducted a randomized clinical study on 60 ASA 1st & ASA 2nd patients undergoing upper limb, orthopaedic surgeries group C clonidine n=20 and Group M(n=30), to a mixture of local anesthetics. It was observed that clonidine provides better analgesia and more sedation than midazolam. The results of this study are comparable to an study.

Prakash Kelika and Jamkan Maya Arun[27] (2017) conducted a study of clonidine as an adjuvant to brachial plexus block and its comparison with tramadol. It was concluded that clonidine in a dose of 1.5µmg /kg body provided fastest outset of sensory as well as motor block & the longest duration of post of analgesia and is thus good addictive to local anesthetics mixture for brachial plexus blocks.

Conclusion

Thus we conclude from our study that addiction of clonidine in comparison to Midazolam as an adjuvant to a mixture of local anesthetics in supraclavicular brachial plexus block, hastens the onset of sensory & motor block, Prolongs duration of sensory & motor block, prolongs the duration of post-operative analgesia and reduces the requirement of rescue analgesia. It does not produce significant or alarming sedation or affect vital parameters nor any increase in the evidence of complication .Thus clonidine 150µgm can be safely added to local anesthetics in brachial plexus block for early onset & prolonged duration of anaesthesia & post-operative analgesia.

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