Original research article

Clonidine as an Adjuvant to Bupivacaine for Axillary Brachial Plexus Block in Patients Undergoing Orthopaedic Surgery of Forearm or Hand -A Non-Randomised Control Study

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Abstract

Introduction: Prolongation of axillary block is desirable in many instances to allow more prolonged or extensive surgery and decrease the requirement of further analgesics

Aims and Objectives: This trial was a non-randomised control study to examine the effect of adding clonidine to bupivacaine for Axillary block in patients undergoing orthopedic surgery of forearm or hand in prolonging the duration of analgesia.

Materials and methods: A total of 110 adult patients of ASA 1,2,3 class were alternately allocated to each of two groups. Group A received 0.25% Bupivacaine 40mL + 1 ml 150µg clonidine and Group B received 0.25% Bupivacaine 40mL + 1 ml 0.9% saline via perivascular Axillary block.

Results: The patient groups were comparable in terms of age, gender, co-morbidities and ASA class. In the bupivacaine clonidine group, analgesia was prolonged by a mean 208 minutes compared to bupivacaine alone. Onset of sensory and motor blockade was shortened by an average of 2.7 min and 3 min in the clonidine group. Duration of sensory block was a mean of 503.3 ± 125.9 minutes in bupivacaine- clonidine group, while in bupivacaine only group it was 287.1 ± 82.9 minutes. This shows a significant prolongation in the clonidine group by about 216.2 minutes. Mean duration of motor block in bupivacaine-clonidine group was 409.8 $\pm 89.3 \pm 89.3$ minutes while in bupivacaine only group it was 259.6 ± 74.8 minutes. This denotes a mean prolongation of 150.2 min in the clonidine group. Side effects noted in our study were hypotension, bradycardia and sedation incidence of which were 7.3%,9.1% and 36.3% respectively in the bupivacaine-clonidine group and 1.8%,3.6% and 9.1% respectively in the bupivacaine only group.

Conclusion: Clonidine is a useful adjuvant to bupivacaine for Axillary block. It significantly prolongs analgesia, duration of sensory and motor block. It also shortens the onset of sensory and motor block, although by a less significant amount.

Key Words: Axillary block, ASA, Bupivacaine and Clonidine

Introduction

Many drugs have been used by various investigators as adjuvants to local anesthetic medications for plexus blocks in an attempt to prolong the duration of block and analgesia[1,2]. Prolongation of block is desirable in many instances to allow more prolonged or extensive surgery and decrease the requirement of further analgesics. Clonidine has been used as an adjuvant to local anesthetic drugs since 1980s to extend the duration of block[1,3].

A number of studies have examined the effect of clonidine as an adjuvant to local anesthetic drugs in peripheral nerve and plexus blocks [4-13]. Most of these studies show that clonidine prolongs the duration of block and provides good analgesic effect[2,4-6,11-13]. However, majority of these studies used intermediate acting local anesthetic agents (mepivacaine, prilocaine, and lidocaine)[11-13.] Studies using clonidine as an adjuvant of Bupivacaine in plexus blocks are few [4,7,14,16]. Some studies report a significant prolongation of block, while others showed no significant prolongation[19]. Moreover there is lack of data regarding the effects in Asian population.

The aim of the present study is to study the effect of using clonidine as an adjuvant to Bupivacaine as compared to Bupivacaine alone for Axillary Brachial Plexus Block in patients undergoing Orthopedic surgery of forearm or hand in prolonging the duration of analgesia.

Materials and Methods

The study protocol of this trial was approved by the Institutional Research methodology and Human Ethical committee, Government Medical College, Thiruvananthapuram prior to commencing the study. A total of 110 patients of ASA I, II, III classes undergoing orthopaedic surgery of forearm or hand were enrolled in the study (55 patients in each group) after obtaining informed consent.

The sample size was calculated using an alpha error of 5% and based on the findings reported in previous studies. The minimum required sample size to detect a significant difference between the groups was 108 (54 in each group). The sample size was calculated for an alpha error of 5% and beta power of 80%. For the present study, the minimum sample size was calculated as 54 patients per each group totaling 108 patients. A total of 110 patients in the study , with 55 patients in each group

Patients with following characteristics were excluded from the study: Mallampati class 4 airway, Contraindication to axillary brachial plexus block or the study medications**,** Hemodynamic instability, H/o significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal or hepatic disease**,** Alcohol or drug abuse, Pregnant or lactating women, Patients taking medications with psychotropic or adrenergic activities, Patients on chronic analgesic therapy other than simple analgesics (NSAIDS)

Enrolled patients were allotted to one of the two groups (A or B) alternately. No premedication was given. No additional sedative medication was given. Axillary block was given by perivascular technique to deliver drugs as follows: Group A received 0.25% Bupivacaine 40mL + 1 ml 150µg clonidine. Total 41 mL solution. Group B received 0.25% Bupivacaine 40mL + 1 ml 0.9% saline. Total 41 mL solution The duration of analgesia, onset and duration of sensory block, onset and duration of motor block, heart rate, blood pressure and sedation were recorded at the first minute and at 5, 10, 30, 60,120, 180, 240, 360 and 480 min after completion of injection.

Technique

Standard perivascular Axillary block was performed in all cases with the patient in supine position with arm abducted and externally rotated[17] (Fig 2). Axillary pulse was identified and the area was disinfected. Under strict aseptic conditions. Injection area was subcutaneously infiltrated with 1mL 2% lignocaine. 22G short beveled, insulated, unipolar cannula connected to a nerve stimulator (Stimuplex, Braun, Melsungen, Germany) was inserted immediately above the artery until Brachial plexus was located. Brachial plexus location identified when a distal motor response was obtained with an output of less than 0.5 mA . Once the location was identified, the drug was injected. Negative aspiration was done before injection and after every 7-8 mL of drug was injected to avoid accidental intravascular injection. Time of injection was noted.

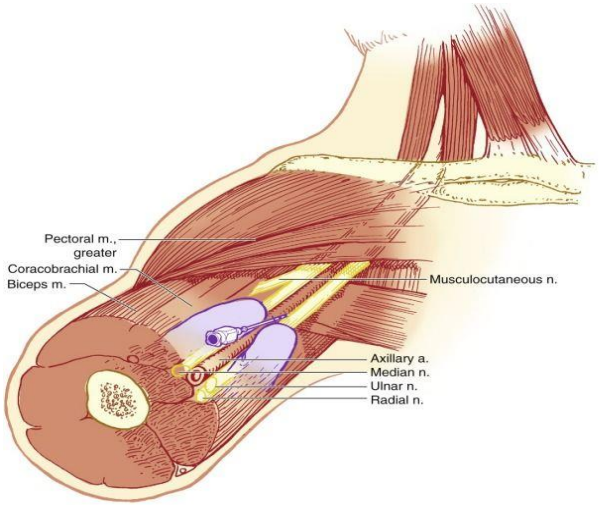

Fig.1: Positioning of the patient for Axillary block

Plexus block was considered successful if Vester-Andersen's criteria was fulfilled i.e., at least two out of four (radial, median, ulnar and musculocutaneous) nerve territories are effectively blocked[18].

Motor and sensory block of radial, median, ulnar and musculocutaneous nerves was determined at 1st minute and then at 5, 10, 30, 60,120, 180, 240, 360 and 480 min after completion of injection. Sensory block was determined by the pin prick test. Sensory block onset is defined as reduction in sensibility to 30% or less[14].

If, at the end of 30 minutes after injection, any of the major nerves involved in the area of planned surgical intervention had a sensibility of more than 30%, they were separately blocked or alternative method of anesthesia was chosen and the patient was excluded from further investigation under this study.

Duration of sensory block is defined as the time interval between injection and complete recovery of sensation[14]. Patients were asked to note the complete recovery of sensation, which was then verified by the anesthetist. Motor block were determined by modified British Medical Research Council rating scale ranging from 5(normal power) to 0 (complete paralysis).Movements checked were thumb abduction for radial n, thumb opposition for median n, thumb adduction for ulnar n and elbow flexion for musculocutaneous n. Motor block onset is defined as a reduction in power to 3 or less[14].

Analgesic effect was measured by the time of injection to the first demand of analgesic. Sedation score[20] ranges from 1 (alert) to 4(asleep, not arousable by verbal contact).

Sedation score 1 = awake
2 = drowsy
3 = asleep but arousable
4 = asleep but not arousable

The highest sedation score in first 2 hours after injection was taken as the sedation score of the patient for statistical purposes.

Occurrence of hypotension [19](fall of Mean Blood Pressure by >30% of baseline) anytime during the monitored period was classified as presence of hypotension.

Bradycardia(<45 bpm)[21,22] will also be monitored Analgesic effect was measured by the time of injection to the first demand of analgesic.

Data Analysis

Data was entered in a personal computer and analyzed using computer software, Statistical Package for Social Sciences (SPSS) version 10. Data is expressed in its frequency and percentage as well as mean and standard deviation. Following statistical analysis was employed to analyze the data: Chi square Analysis, Mann Whitney U test and Student's T test.

Results

Table 1: The patient characteristics of each group is depicted

Variables	Group A	Group B
No of patients, n	55	55
Age	43.13 ±12.64	40.24 ±12.41
Duration of Analgesia (min)	519.64±102.38	310.73 ±84.74
Gender	Male 36 ; Female 19	Male 40 ; Female 15
ASA	ASA 1- 37 ASA 2- 16 ASA 3 - 2	ASA 1- 39 ASA 2- 14 ASA 3 - 2
Sedation Score	Score 1 - 35 Score 2 -19 Score 3 - 1	Score 1- 50 Score 2- 5 Score 3 - 0
Hypotension , n	4	1
Bradycardia, n	5	2

Group A received 0.25% Bupivacaine 40mL + 1 ml 150µg clonidine. Group B received 0.25% Bupivacaine 40mL + 1 ml 0.9% saline. Total 41 mL solution.

The American Society of Anesthesiologists physical status scores (ASA scores) across the two groups More than two-thirds of the patients in each of the groups were of ASA class 1 (67.3% in group A and 70.9% in group B). ASA 2 patients were 29.1 % in group A and 25.5% in group B. In both groups there were 2(3.6%) patients each of class 3.
Chi square analysis of these figures showed that there is no statistically significant difference among the two groups.
The above data and statistical analysis shows that the two groups (A&B) are comparable in terms of patient characteristics such as age, gender, comorbid conditions and ASA status.

Table 2: Outcome measures.

	Group A	Group B	**t value**	**p value**
Sensory Block - Onset (min)	9.04 ± 4.99	11.73± 6.06	- 2.543	< 0.05
Sensory Block - Duration (min)	503.27 ± 125.99	287.09 ± 82.95	10.628	< 0.001
Motor Block - Onset (min)	13.33 ± 4.41	15.36 ± 5.92	- 2.046	< 0.05
Motor Block - Duration (min)	409.82 ± 89.29	259.64± 74.76	9.564	< 0.001
Duration of Analgesia (min)	519.64±102.38	310.73 ±84.74		< 0.001

Group A received 0.25% Bupivacaine 40mL + 1 ml 150µg clonidine. Group B received 0.25% Bupivacaine 40mL + 1 ml 0.9% saline. Total 41 mL solution.

Side effects

1. Sedation: The sedation scores of the patients in each group is shown in the table 1. It shows that 20 patients (36.4%) of group A had a sedation score of 2 or more although no other sedative medications were administered. Only 5 patients (9.1%) of group B had a sedation score of 2 or more. Chi square analysis yielded a p score of <0.01 which shows a highly significant difference.

2. Hypotension: Hypotension was present in 4 patients (7.3%) of group A while it was seen only in 1.8% of patients of group B. (table 9, fig 13)
Although the figures seem to be of clinical importance, Chi square analysis showed no statistically significant difference between the two groups.

3. Bradycardia: Bradycardia was seen in 5 patients (9.0%) of group A and 2 patients(3.6%) of Group B. chi square analysis showed a p value >0.05 which means there is no statistically significant difference between the groups.

Discussion

This study examined the effect of adding clonidine to bupivacaine for Axillary block in patients undergoing orthopedic surgery of forearm or hand in prolonging the duration of analgesia.

Patient characteristics

Only patients of ASA class 1,2 and 3 were included in the study . class 4 was excluded to avoid morbidity due to the reported side effects of clonidine like hypotension and bradycardia. Most studies reported results in ASA 1, 2 & 3 class. In our study, majority (96.48%) of the patients were of ASA class 1 and 2.

Mean age of the group A was 43.1 years and that of group B was 40.24 years. Majority of the patients were males (65.5% in group A and 72.7% in group B. this pattern of age and sex distribution is understandable as all were undergoing orthopedic surgery for fractures sustained by road traffic accidents. Patients attending the hospital due to road traffic accidents have a similar age and sex distribution. The study by Duma et al[14] has a similar distribution(60% males and mean age 43.3 yrs(bupivacaine-clonidine group) and 36.7 yrs(bupivacaine only))
Comorbid conditions seen in the patients of two groups were diabetes, hypertension, and bronchial asthma. These conditions were evenly distributed with no significant difference between the groups as analyzed using chi square test.

The patient characteristics of the two groups were comparable when analyzed using chi square test.

Post operative analgesia

Post operative analgesia, defined as the time until first analgesic request, was significantly longer in the bupivacaine clonidine group (519.6102.4 minutes) while in bupivacaine group it was 310.784.7 minutes indicating a mean prolongation of 208 minutes. Popping et al[19] analyzed thirteen trials testing 17 comparisons .Thirteen comparisons showed that clonidine prolonged the analgesia. Fang et al[15] reported a mean prolongation by 188 minutes in the clonidine group.

Studies suggest that perineurally injected clonidine has an analgesic effect through systemic reabsorption. Only two studies compared clonidine across routes. In one, patients received 150 micrograms of clonidine subcutaneously or added to mepivacaine for brachial plexus block[6]. The duration of postoperative analgesia was longer in patients receiving clonidine into the plexus sheath. In the second, 140 micrograms of clonidine was added to ropivacaine for sciatic-femoral nerve block or was injected intramuscularly[37]. In that trial, clonidine had no impact on quality or duration of postoperative analgesia through either route.
In our study clonidine prolonged the analgesia and demand for analgesic supplement by about three and half hours. This may be a beneficial effect leading to use of a decrease of total dose of analgesics needed post operatively.

Onset of sensory and motor block

Onset of sensory and motor block was shortened by the addition of clonidine by an average of 2.7 min and 3 min respectively. This has statistical significance as analyzed by t test. However, whether a difference of 2.7 min and 3 min is any clinical relevance is doubtful. Fang et al[15] found a shortening of sensory block onset time and motor block onset time by 1.3 min each in the clonidine group. Popping et al[19] in the meta-analysis of randomized trials reported that in 5 out of 11 comparisons clonidine shortened the sensory block onset time.

This finding of our study is in contrast to the most other reported series. In the Duma et al[14] series there was no statistically significant difference between the two groups with respect to onset of block. In fact, the median motor block onset in the bupivacaine clonidine group was longer (30min) compared to bupivacaine alone group (10 min). Median time of sensory block onset was 10 min in both groups. Erlacher et al[38] also reported a prolongation in block onset time in the bupivacaine clonidine group.

Duration of sensory and motor block

Mean duration of sensory block in the bupivacaine clonidine group was 503.3125.9 minutes while in bupivacaine only group it was 287.182.9 minutes. This shows a significant prolongation of the duration of the sensory block in the clonidine group by about 216.2 minutes. Popping et al[19] reported prolongation of the duration of sensory block in 10 out of 13 comparisons in a meta-analysis. They found that clonidine significantly prolonged the duration ($p<0.001$). Fang et al[15] reported a prolongation of sensory block by a mean duration of 68 min in the bupivacaine clonidine group.

Mean duration of motor block in group A was 409.8 minutes while in group B it was 259.674.8 minutes. This denotes a mean difference of 150.2 min. Fang et al[15] reported a prolongation of motor block by a mean duration of 242 minutes in the bupivacaine- clonidine group. Erlacher[38] reported a prolongation in the clonidine group by a mean of 244 minutes. Meta analysis of randomized trials by Popping et al[19] reported seven trials that tested eleven comparisons of duration of motor block. Of this nine were significantly longer with clonidine group

Side effects

Hypotension: In our study, arterial hypotension was present in 4 patients (7.3%) of group A while it was seen only in 1 (1.8%) patient of group B. Out of the 4 patients in the clonidine group two required the use of vasopressors Although the figures seem to be of clinical importance, Chi square analysis showed that there is no statistically significant difference between the two groups.

Popping et al[19] analyzed seven studies which reported on the presence or absence of arterial hypotension. They reported an incidence of 4.1% in the control group while in the clonidine group it was 13.1%. Bhatnagar et al[39] reported a significantly higher incidence of hypotension in bupivacaine clonidine group compared to bupivacaine only group in a study which examined the use of these drugs in continuous paravertebral block for post thoracotomy pain. Clonidine causes hypotension by central and peripheral attenuation of sympathetic outflow. The incidence of hypotension in 7.3% of our patients is less than the most reported series but nevertheless is important.

Bradycardia: In our study, bradycardia was seen in 5(9%) patients among the bupivacaine-clonidine group and 2(3.6%) patients in the bupivacaine only group. Popping et al[19] in the meta-analysis reported the incidence of bradycardia in seven studies. In controls, the average incidence of bradycardia was 4.1%, and with clonidine it was 8.5%. however these studies used heterogenous criteria for defining bradycardia.

Sedation: In our study, 20 patients in group A (36.3%) and 5 patients (9.1%) in group B had a sedation score of 2 or more. One patient in group A had a score of 3 and none had a score of 4. This difference is statistically significant. However it is unlikely to be of any adverse clinical implications as it rarely lasted more than 8- 10 hours. It may help to avoid the use of other sedative medications during the intraoperative and immediate post operative period.

Sedation is a widely reported side effect of clonidine. In Popping et al[19] meta analysis, four studies reported on at least one episode of sedation during surgery using specific definitions. In controls, the average incidence of sedation was 32.4%, and with clonidine it was 55.8%. Duma et al[14] reported no significant difference between the bupivacaine and bupivacaine-clonidine groups.

These side effects were not unexpected and are most likely the result of systemic absorption of the drug. The incidence of these side effects is minor. However it is important for the anesthesiologist to be aware of these side effects
Other reported side effects of clonidine like fainting and respiratory depression were not seen in our study

Conclusions

Clonidine is a useful adjuvant to bupivacaine for Axillary block. It significantly prolongs analgesia, and duration of sensory and motor block. It also shortens the onset of sensory and motor block, although by a less significant amount. The side effects like sedation may be advantageous
to a patient undergoing surgery under regional anaesthesia and other side effects like hypotension and bradycardia are not significant enough to limit its clinical usefulness.

Conflict of Interest: No

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