Effects of addition of clonidine to bupivacaine in brachial plexus block

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Abstract

Clonidine has been used as an adjuvant to local anesthetics in order to extend the duration of analgesia in various regional and central neuraxial blockades. The present study was carried out on sixty patients of ASA (American Society of Anaesthesiologists) grade I and II, undergoing upper limb orthopaedic procedures. The study aimed to investigate the effect of addition of Clonidine to Bupivacaine in brachial plexus block with respect to the onset, and duration of sensory block and postoperative analgesic requirements. Patients were randomly divided in two groups, thirty each. Group A (n = 30) patients received 25 ml of 0.25% bupivacaine and 0.5 ml (75mcg) Clonidine, whereas group B (n = 30) received 25 ml of 0.25% Bupivacaine and 0.5 ml normal saline through a supraclavicular approach. Onset and duration of sensory blocks and side effects were recorded in both the groups. It was found that addition of Clonidine to Bupivacaine in brachial plexus block had faster onset of sensory block and also prolonged the duration of analgesia ,without any major side effects other than sedation, which is beneficial in clinical practice.

Key Words: *Analgesia, Brachial plexus, Bupivacaine, Clonidine, Supraclavicular approach.*

Introduction

Peripheral nerve blockade supplemented with monitored anaesthesia care is used as a primary and sole anaesthetic technique to facilitate a painless surgery. Amongst the various peripheral nerve blocks, brachial plexus block is widely used for upper limb surgeries. Local anesthetics administered as regional nerve blocks are utilized in providing pain relief in many surgical procedures by blocking signal traffic to the dorsal horn. Certain drugs may be used as an adjuvant to local anesthetics, to lower the doses of each agent and to enhance analgesic efficacy, while at the same time reducing the incidence of adverse reactions. Tramadol and Fentanyl had been successfully used as adjuvants to local anesthetic in brachial plexus block. Various studies have shown that concurrent injection of alpha 2 adrenergic agonist drugs like Clonidine, prolongs the duration of sensory block when added to local anaesthetics like mepivacaine and lignocaine in brachial plexus block.

We hypothesized that addition of Clonidine to Bupivacaine in brachial plexus block would prolong the sensory block and provide excellent postoperative analgesia for prolonged periods without major hemodynamic effects.

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Material and Methods

This prospective randomized controlled trial investigated the effects of adding Clonidine 75 μg to Bupivacaine in orthopaedic patients scheduled for upper extremity procedures. The study was conducted in a teaching institute. Sixty adult patients aged 18 to 60 yrs, of both sexes and ASA (American society of Anaesthesiologists) physical status I & II posted for upper limb surgeries were allocated into two groups: A and B, each of 30(n=30) using systematic random sampling method. Patients receiving chronic analgesic therapy, those with severe cardiopulmonary disease, thyroid disorders, diabetes mellitus, central or peripheral neuropathies, history of allergy to local anesthetics, or other contraindications to regional anesthesia were excluded from the study.

The procedures were of moderate duration (60-90 min.) and included implant removal, both bone plating, fixation of lower third of humerus and olecranon fixation.

Basic investigations recommended for ASA physical status I and II patients like complete hemogram, random blood sugar levels and electrocardiogram were reviewed.

Written informed consent of all the patients under study was taken.

Once the patient was brought to the operation theatre, standard monitoring was set up, including noninvasive arterial blood pressure, heart rate, and pulse monitoring. An 18-gauge intravenous (i.v.) cannula was inserted in the forearm and an i.v. infusion started. Under all aseptic precautions brachial plexus block, through supraclavicular approach was administered to all the patients with the help of a nerve stimulator. Group A patients received 25ml of Bupivacaine with 75 mcg (0.5ml) Clonidine while Group B received 25 ml of Bupivacaine with 0.5 ml of normal saline.

The time of onset of analgesia was assessed by three point score by pin prick method:

1. Grade 0: Sharp pain felt
2. Grade 1: Analgesia : Dull sensation felt
3. Grade 2: Anaesthesia : No sensation felt

Sensory score of 2 was taken as the time of onset of sensory block.

Similarly, the quality of intraoperative analgesia, was assessed and was graded as excellent when there was no need for any general anaesthetic supplementation intra operatively; good, if supplemented with general anaesthetics (patchy analgesia); and poor if the patient required general anaesthesia with controlled ventilation, after waiting for 20 min. following administration of block.

The duration of analgesia was noted in both groups by noting the time of analgesic request postoperatively in the recovery room. All patients received inj. Tramadol 100 mg. for postoperative pain relief on demand.

Expected effects were bradycardia and sedation, but in addition, few patients had hypotension intra operatively.

Sedation score was assessed by using sedation scale (described by Culebras) for 8 hours postoperatively[18]:
Group 1: Awake and alert.
Group 2: Sedated, responding to verbal commands.
Group 3: Sedated, responding to mild physical stimulus.
Group 4: Sedated, responds to moderate or severe physical stimulus.
Group 5: Not arousable.
Motor block was not assessed in this study.

Data was summarized as mean ± standard deviation or as percentages. Statistical analysis was done using "Microsoft office Excel" software and SPSS version 17.0 and student 't' test, was applied for analysis of onset and duration of sensory block, while chi- square test was applied for quality of intra operative analgesia parameter. '*P*' values were calculated, $P<0.05$ was considered significant.

Results:

The age, sex distribution, body weight, and duration of surgery in the two groups were found to be comparable.

Table 1: Demographic data

Patients characteristics	Group A	Group B	P value
Age(yrs.)	43.56±5.34	43.02±6.75	>0.05
Weight (kg.)	55.04±5.79	54.4±5.18	>0.05
Duration of surgery(min)	94.6±8.4	92.8±7.2	>0.05
Sex(M/F)	18/12	20/10	>0.05

$p<0.05$ considered statistically significant
Onset and duration of sensory blocks have been presented in Table 2.

Table 2: Characteristic of sensory block

Characteristics of block(min.)	Group A	Group B	P value
Time of onset of sensory block	3.4 ± 0.67	7.1 ± 0.98	< 0.001
Time of complete sensory block	10.4 ± 0.48	17.3 ± 1.73	< 0.001
Duration of analgesia	386± 38	198± 28	< 0.001

It was found that the time of onset of sensory block was significantly shorter whereas duration of analgesia was significantly greater in the group receiving Clonidine.

The time of onset of sensory block was 3.4 ± 0.67 min in Clonidine treated group and was 7.1±0.98 min in control group i.e. the onset of analgesia was earlier by 3.7 min in Clonidine treated group. This difference was highly significant ($P < 0.001$) statistically as well as clinically. Similarly the time for complete sensory block was also earlier in Clonidine treated group by 6.9 min.

The duration of analgesia was 386 ± 38 min in Group: A while it was 198 ± 28 min. in Group: B. This difference was statistically significant ($p<0.001$)

The quality of analgesia was excellent in 85% patients while it was good in 15% patients of Group A whereas the quality of analgesia was excellent in 66% patients, good in 24% patients and poor in 10% patients of Group B.(Diag. 1 and 2). This difference was also highly statistically significant ($p<0.001$)

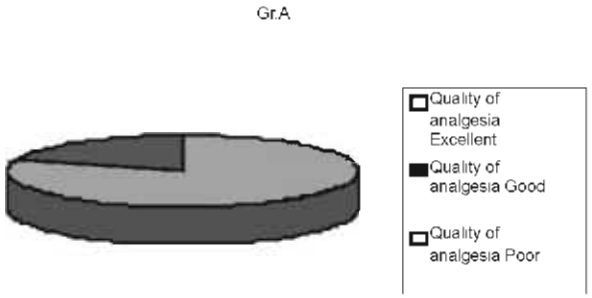

Fig. 1 : Quality of analgesia in Group A

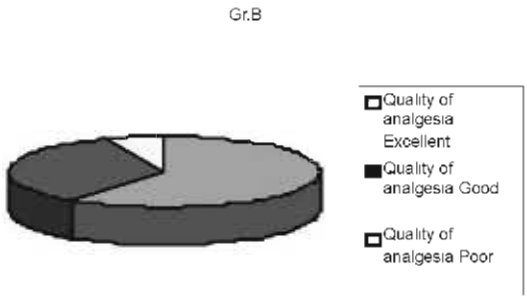

Fig. 2 : Quality of analgesia in Group B

Table no 3: Intraoperative side effects

Side effects	Group A	Group B	P value	P value	
Bradycardia (H.R.<60 beats/min)	01	0	>0.05	0	1.00
Hypotension (SBP fall of > 25% of baseline)	06	04	>0.05	04	0.766
Oxygen saturation < 90%	0	0		0	
Sedation score (mean ± SD)	2.24 ± 0.67	1.7 ± 0.61	>0.05	1.7 ± 0.61	<0.001

No statistically significant difference was observed in heart rate, blood pressure, and oxygen saturation between the two groups. The incidence of clinically relevant bradycardia and hypotension were comparable between groups (Table 3). Although patients who received Clonidine were found to be more sedated in comparison to those who did not, this finding was beneficial intra operatively .

Discussion

Local anaesthetics used for administering regional nerve blocks are at times ineffective or provide poor quality of analgesia. Certain drugs are added to local anaesthetics to enhance their efficacy, likewise, in subarachnoid blockade, Tramadol and Fentanyl had been successfully used as an adjuvant to local anesthetic in brachial plexus block[2,3].

The primary outcome of the present randomized controlled trial clearly suggests that relatively low-dose (75 mcg) Clonidine, as an adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block, prolongs the duration of analgesia. The limitation of the present study is its difficult to define the duration of analgesia (as it is a subjective finding and depends on the tolerance of the patient).

Onset time of the sensory blocks and the time of complete sensory block was found to be shortened. Similary side effects, such as sedation was more in Clonidine treated group. This finding was beneficial intraoperatively. These findings were also observed in various clinical studies, in which addition of Clonidine to local anaesthetics improved peripheral nerve blocks by reducing the onset time, improving efficacy of the block during surgery and extending the postoperative analgesia[7,8].

Bernard and Macarie also found that addition of 30-300 mcg. of Clonidine to Lignocaine for axillary brachial plexus block hastened the onset and improved the efficacy of surgical analgesia[8].

However there are some studies which do not support our finding like the study by Duma et al, which showed no difference in analgesia after addition of Clonidine 0.5 µg/kg to levobupivacaine in axillary block[15]. Similarly Culebras et al also had findings contradicting our study[18]. Probable explanation for this inconsistency may relate to inter-patient variations in the anatomy of the plexus sheath and difference in the spread of local anesthetics in the plexus sheath depending upon the block technique.

Clonidine is an alpha-2 adrenergic agonist, which, it has been suggested, improves nerve block characteristics of local anaesthetic solutions through local vasoconstriction and facilitation of 'c' fiber blockade or spinal action caused by slow retrograde axonal transport or simple diffusion along the nerve[4,5,6].

Clonidine possibly enhances or amplifies the sodium channel blockade action of local anaesthetics by opening the potassium channels, resulting in membrane hyper polarization to excitatory input[9].

A number of studies have focused on the effect of Clonidine as adjuvant to either Lignocaine or Mepivacaine and these studies used 150 mcg of Clonidine. Therefore it was decided that the study would use Bupivacaine and in slightly less dose so as to reduce the incidence of its adverse effects[7,8].

It has been widely demonstrated in different studies that subcutaneous/intramuscular injection of Clonidine is not as effective as perineural administration, there by suggesting that local anaesthetic prolonging action of Clonidine is primarily mediated locally at the neuron[10,11]. Injecting Clonidine as a sole analgesic in brachial plexus sheath does not provide clinically relevant analgesia but many authors belive that Clonidine exerts its local anaesthetic effect by prolonging its action on nerve fibers as a result of complex interactions between Clonidine and axonal ion channel/receptors[5,10,12,13].

Peripheral antinociception induced by Clonidine has also been related to alpha-2 adrenoceptor mediated local release of enkephalin like substance[14].

One of the controversy likely to arise in this study is that clonidine hastened the onset of sensory block despite being a vasoconstrictor. This finding has also been observed in other different studies[7,8]. The mechanism remains unknown, and has not been explained satisfactorily.

The dose of Clonidine used in this study was sufficient to prolong the duration of analgesia without producing significant hemodynamic compromise in patients. Similar observations was also made by Colin McCartney who found that addition of Clonidine in low doses upto 150mcg. produces minimal or no hemodynamic alterations. However, some patients were sedated in their early stay in the recovery room but this number was not statistically significant[16]. All patients were stable intraoperatively which shows that Clonidine does not alter hemodynamics.

Finally, to conclude, Clonidine, when added to local anaesthetics in smaller doses hastens the onset of sensory block in addition to prolonging the duration of sensory block, there by offering better quality of intra-operative analgesia without any significant side effects other than sedation.

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