Original Article

Effect of clonidine added to local anaesthetic in suparaclavicular brachial plexus block

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Abstract

Objective: objective of this study is to compare the onset, intensity and duration of sensory and motor block, the quality and duration of post operative analgesia and adverse effect if any in both control and clonidine group. **Method:** Present study was carried out on 100 patients which were divided into two group. One group (50 subjects) is control group and another group is Clonidine group (50subject) which received clonidine as an adjuvant to local anaesthetic in supraclavicular brachial plexus block with proper anaesthetic technique e. Duration of sensory block, motor block, duration of postoperative analgesia, sedation score and VAS score were obtained in both groups and values were compared with unpaired't' test. Values were consider statistically significant when p <0.05. **Result:** Present study state that there is statistically significant difference between mean values of onset and duration of sensory and motor block, duration of postoperative analgesia, sedation score and VAS. **Conclusion**: Clonidine added to local anaestheitic in supraclavicular brachial plexus block hastens the onset, prolongs the duration of sensoryand motor blockade, provides sedation and longer pain-free period without significant hemodynamic alterations.
Keyword: Supraclavicular block, Clonidine, Adjuvant to local anesthetic.

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INTRODUCTION

Merskey defined PAIN as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or expressed in terms of such damage. The word PAIN is derived from Latin word 'Poena' means suffering. Acute postoperative pain is the result of a complex physiological reaction to tissue injury. Local anesthetics administered as regional nerve blocks are utilized in providing postoperative pain relief in many surgical procedures by blocking signal traffic to the dorsal horn. Tramadol and fentanyl had been successfully used as adjuvants to local anesthetic in brachial plexus block.[2,3] The concurrent injection of alpha 2 adrenergic agonist drugs has been suggested to improve the nerve block characteristic of local anesthetic solutions through either local vasoconstriction[4] and facilitation of C fiber blockade[5] or a spinal action caused by slow retrograde axonal transport or simple diffusion along the nerve.[6] Clonidine is a selective 2 adrenergic agonist with some 1 agonist property. In clinical studies, the addition of clonidine to local anesthetic solutions improved peripheral nerve blocks by reducing the onset time, improving the efficacy of the block during surgery and extending postoperative analgesia.[7,8] The effect of clonidine is dose related between 0.1 and 0.5 µg/kg.[8] Clonidine possibly enhances or amplifies the sodium channel blockade action of local anesthetics by opening up the potassium channels resulting in membrane hyperpolarization, a state in which the cell is unresponsive to excitatory input.[9] Thus we decided to evaluate the effect of clonidine added to local anaesthetic in suparaclavicular brachial plexus block

MATERIAL AND METHODS

After approval from the Institutional Ethics Committee, informed written consent was obtained, a prospective randomized double blind study was conducted in the

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Department of Anaesthesiology, GMERS Medical College, Civil Hospital Gandhinagar. 100 patient of ASA physical status I or II scheduled for elective and emergency surgeries around elbow, forearm and hand were enrolled in this study. All the patients were subjected to detailed preanaesthetic evaluation with clinical history, systemic examination done. Routine investigation like Haemogram, RBS, Renal Profile, ECG for patient above 40 years of age, HIV and HBsAg and other specific investigation were done as per patient clinical evaluation. Patient Inclusion criteria were Patients coming for upper limb orthopaedic surgery,Patients aged 18-55 and ASA grade 1,2 physical status. And Exclusion criteria were Age <18 years, and >55 years, ASA grade >3(High risk patients eg. Cardiopulmonary disease, hepatic and renal dysfunction) Patients allergic to any anesthetic drugs, Patients on sedative and hypnotic medication, History of malignant hyperthermia, Pregnant patients. Patients having pregnancy, diabetes, recent drug intake (within 24 hours), previous nerve injury, contraindication to regional anaesthesia, opioid or benzodiazepines dependence, history of drug allergy, drug abuse, any major systemic illness and uncooperative patients were excluded from the study. Patients will be randomly divided into 2 groups— Group C and Group A. depending on the drugs given:

Group C	Inj. Lignocaine 2% 10 ml with
(Control)	Inj. Adrenaline 1: 2,00,000 (5 mcg/ml)
	Inj. Bupivacaine 0.5% 20 ml
Group A	Inj. Lignocaine 2% 10 ml with
(Clonidine)	Inj. Adrenaline 1: 2,00,000 (5 mcg/ml)
	Inj. Bupivacaine 0.5% 20 ml
	Clonidine 0.5 mcg/kg

Preoperatively, adequate fasting hours (6-8 hours) were confirmed. Each patient was informed in detail regarding the nature and purpose of the study and were explained 0-10 point visual analogue scale (VAS) on sheet of paper where (0) labelled as (no pain) and 10 as (excruciating pain). Written informed consent was obtained after explaining the procedure to the patient.

Anaesthetic Technique

In pre anaesthesia preparation room baseline vital parameters (pulse rate, blood pressure, respiratory rate, SpO2) were recorded, intravenous line was secured on contra lateral arm and the patients were premedicated with Inj. Ranitidine 1mg/kg IV, Inj. Glycopyrolate 5 mcg/kg IV. Then patients were shifted to operation table. The patients were placed in supine position with ipsilateral arm adducted, roller pack was placed in between scapula and neck was turned slightly to the contra lateral side. Under all aseptic and antiseptic precaution local site was prepared. Just above the midclavicular point, subclavian artery was palpated 1 to 1.5 centimeter above the clavicle, immediately lateral to sternocleidomastoid muscle and was pushed medially by thumb, than 3 to 4 cm long 23 G hypodermic needle attached to a 2 cc syringe filled up with 2 cc sterile water held in pen holding position, was directed posteriorly, medially and caudally on first rib to locate paraesthesia which was felt as feeling of tingling at elbow and finger. Once the patient felt paraesthesia, it was suggestive that the needle was touching the brachial plexus and then 30 ml of study drug was given after careful negative aspiration. Baseline vital parameters were recorded. After giving the block, sensory and motor blockade was assessed for its onset and complete blockade as described later. Intra operatively, Pulse rate, blood pressure, respiratory rate, SpO_2, sensory and motor blockade as well as sedation score were observed at 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 45 minutes and than 1 hourly for 6 hours, 2 hourly upto 16 hours and 4 hourly upto 24 hours. Total duration of sensory blockade, motor blockade, and postoperative analgesia were recorded. Postoperative analgesia (VAS $\geq$5) was recorded at 1 hourly interval for first 6 hours and then 2 hourly up to 16 hours and then 4 hourly upto 24 hours. Complications of brachial plexus block e.g. pneumothorax, nerve injury, local site hematoma, surgical emphysema and side effects of Clonidine i.e. bradycardia, hypotension and respiratory depression were also observed. Postoperatively, whenever VAS $\geq$ 5 or patient complaint of pain, Inj. Diclofenac Sodium (1.5 mg/kg) 75 mg IM was given as rescue analgesic. Total requirement of rescue analgesics in terms of doses in 24 hrs postoperatively was also observed.

Assessment of sensory blockade

The sensory block was assessed with pin prick to 23 G hypodermic needle and graded as per score:

Score	Clinical description
0	Sharp pains on pin prick
1	Touch sensation on pin prick
2	Not even touch sensation

Palmar surface of index finger, little finger and dorsum of thumb were assessed to test for median, ulnar and radial nerve respectively. Onset of sensory blockade was taken as the time from the end of injection to touch sensation on pinprick. Complete sensory block was considered with score of 2. Duration of sensory blockade was described as the time from onset to sensory blockade to time when patient again developed touch sensation to pin prick (score 1).

Assesssment of motor blockade (bromage three point scale)

Motor blockade was assessed by asking patient to abduct/adduct the following

Score	Clinical description
0	Normal motor functions with full flexion and extension of elbow, wrist and fingers
1	Decreased motor strength with ability to move fingers only
2	Complete motor blockade with inability to move fingers also

Onset of motor blockade was considered as time from end of injection to the time when a score of 1 was achieved. Total duration of motor blockade was considered as time from onset of motor blockade to time of any decrease from highest motor score achieved.

Assessment Ofsedation Score: Chernik *Et al* :[24]

Score	Clinical description
0	Awake and alert
1	Sleeping but easily arousable
2	Deep sleep but arousable
3	Deep sleep but not arousable

All the data regarding age, gender, height, weight, duration of surgery, ASA physical status, duration of surgery, Hemodynamic variables, onset and duration of sensory and motor blockade, VAS score, sedation score, complications of brachial plexus block and clonidine and the requirement of rescue analgesic were recorded. All the results were expressed as mean±SD (standard deviation). Statistical analysis was performed using Unpaired t-test. When p value is <0.05, it is considered as stsatistically significant.

Statistical Analysis

Results were expressed as mean SD (standard deciation). Statistical analysis was performed using unpaired student't' test. When p<0.05 it is considerd as statistically significant.

RESULTS

Differences in mean value of both groups (group C and group A) described below.

Table 1: Distribution of subject according to demographic profile and vitals

	Group C	Group A (Clonidine)	P value
Age	37.18 ±10.89	37.36 ± 9.79	p >0.05
Sex ratio (M/F)	28/22	26/24	p >0.05
Weight	54.52±4.68	56.42± 5.26	p >0.05
Height	158.32 ± 3.26	159.60 ± 3.61	p >0.05
ASA grade (I/II)	34/16	34/16	p >0.05
Duration of surgery	1.44 ± 0.46	1.54 ± 0.42	p >0.05
Base line heart rate (BPM)	82.34 ± 9.81	81.42 ± 14.32	p >0.05
Base line SBP (mm of Hg)	118.48 ± 10.52	118.36 ± 7.22	p >0.05
Base line DBP (mm of Hg)	77.04 ± 8.00	77.36 ± 6.68	p >0.05
Base line MAP (mm of Hg)	92.19 ± 8.62	91.69 ± 6.58	p >0.05
Base line SPO2 (%)	98.94 ± 0.42	98.82 ± 0.39	p >0.05

There was no statistically significant difference between the demographics (age, sex, height, weight, ASA grade, duration of surgery). Also there was no statistical significance in baseline parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and oxygen saturation. (Table I). No statistical difference was noted in the hemodynamic parameters (mean HR, MAP, Sp O2) before and after giving the block, throughout the surgery and postoperatively.

Table 2: Characteristics of sensory and motor block in group C and group A

	Group C Mean ±SD	Group A Mean ±SD	P value
Onset of sensory block (min)	9.1 ± 2.11	6.9 ± 1.37	<0.05
Onset of motor block (min)	12.24 ± 2.4	6.92 ± 2.04	<0.05
Duration of sensory block (min)	259.4 ± 33.88	311.6 ± 41.52	<0.05
Duration of motor block (min)	229.7 ± 30.70	270.9 ± 49.51	<0.05
Duration of analgesia (min)	320.6 ± 82.44	568.2 ± 120.43	<0.05
Requirement of rescue analgesic	2.92 ± 0.27	1.96 ± 0.20	<0.05

The onset of block was earlier in group A patients that was 6.9 ± 1.37 min for sensory block and 6.92 ± 2.04 min for motor block than those in group C 9.1 ± 2.11 min for sensory block and 12.24 ± 2.4 min for motor block, which was statistically significant ($P < 0.05$) (table 2) Mean duration of sensory block in group A was 311.6 ± 41.52 min and in group C was 259.4 ± 33.88 min. Patients belonging to group A had mean duration of motor block 270.9 ± 49.51 min and group C had a mean duration of motor block 229.7 ± 30.70 min which was statistically significant (table 2). The mean duration of postoperative analgesia was 320.6 ± 82.44 minutes in Group C while 568.2 ± 120.43 in Group A. Thus statistically significant prolongation of pain relief was noted in Group A. The mean requirement of analgesic doses was 2.92 ± 0.27 injections in Group C and 1.96 ± 0.20 in Group A, the

difference between the two groups was statistically significant (p <0.01). (Figure 1)

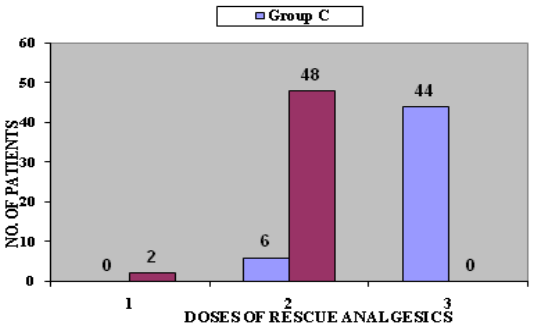

Figure 1: doses of rescue analgesic required in first 24 hours.

Figure 2 shows Sedation score was comparable in both the groups. Most of the patients in group A were calm and/or sleepy but easily arousable intraoperatively and postoperatively. There was statistically significant difference in sedation score starting from 15min to 4 hr between the two groups as group A patients had higher sedation score compare to group C patients (p<0.05).

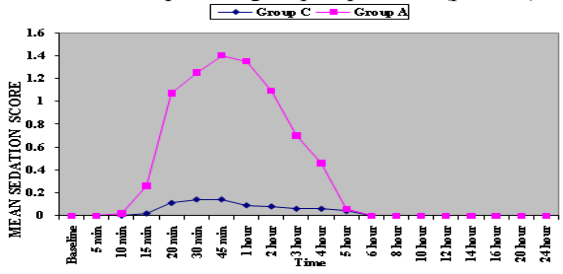

Figure 2: Sedation score

Figure 3: Shows VAS pain score was lower in group A at 1 hr to 16 hr and at 24 hr while pain score was statistically significantly higher in group C (p <0.05)

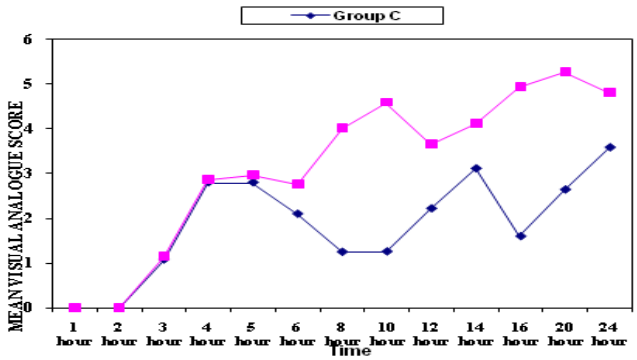

Figure 3: VAS score: VAS pain score was lower in group A at 1 hr to 16 hr and at 24 hr while pain score was statistically significantly higher in group C (p <0.05) There were no intropeative and postoperative complication recorded

DISCUSSION

Brachial plexus block provides both intraoperative anaesthesia and postoperative analgesia without any systemic side-effects.[1] Local anesthetics administered as regional nerve blocks are utilized in providing postoperative pain relief in many surgical procedures by blocking signal traffic to the dorsal horn. Certain drugs may be used as adjuvant to local anesthetics to lower doses of each agent and enhance analgesic efficacy while reducing the incidence of adverse reactions. Tramadol and fentanyl had been successfully used as adjuvants to local anesthetic in brachial plexus block.[2,3] The concurrent injection of 2 adrenergic agonist drugs has been suggested to improve the nerve block characteristic of local anesthetic solutions through either local vasoconstriction 4 and facilitation of C fiber blockade5 or a spinal action caused by slow retrograde axonal transport or simple diffusion along the nerve.[6]Clonidine is a selective 2 adrenergic agonist with some 1 agonist property. In clinical studies, the addition of clonidine to local anesthetic solutions improved peripheral nerve blocks by reducing the onset time, improving the efficacy of the block during surgery and extending postoperative analgesia.[7,8] The effect of clonidine is dose related between 0.1 and 0.5 µg/kg. 8 Clonidine possibly enhances or amplifies the sodium channel blockade action of local anesthetics by opening up the potassium channels resulting in membrane hyperpolarization, a state in which the cell is unresponsive to excitatory input. 9 The analgesic properties of clonidine when administered intrathecally or epidurally as adjuvant have been well demonstrated 10.They seem to be attributable to its α2-agonist properties. Its action on large no α2 receptors present in the central nervous system, at loecus coeruleus and dorsal horn of the spinal cord, is the main mechanism of centrally mediated sedation and analgesia[11]. Specific peripheral effects of clonidine appear less obvious because α2- adrenoreceptors are not present on the axon of the normal peripheral nerve[11]. It has been postulated that clonidine improved the duration of postoperative analgesia only when used as an adjuvant to intermediate-acting local anaesthetics and that it was not worthwhile to combine it with long-acting local anaesthetics. Various investigators like Murphy *et al.*[12] analyzed randomized trials that the usefulness of a variety of adjuvants, including clonidine added to local anaesthetics for brachial plexus block. On the basis of data from six trials (349 patients), they concluded that clonidine in doses up to 150 µg increased the duration of postoperative analgesia with minimal adverse effects. McCartney *et al.* 14 reviewed 27studies (1,385 patients) using clonidine as an adjuvant to local anaesthetics for a variety of peripheral nerve blocks. They concluded that clonidine

was beneficial only when added to intermediate-acting local anaesthetics. In this randomized, double-blinded trial, we compared clonidine as an adjuvant to bupivacaine in supraclavicular brachial plexus block, and found that there was significant decrease in onset and increase in duration of sensory and motor blockade in the clonidine group. In our study, Clonidine (5 mcg/kg) was added to local anaesthetics namely bupivacaine and lignocaine. In this study, except inj. Ranitidine and inj. Glycopyrrolate no other premedication was given for better assessment of intraoperative hemodynamic changes and postoperative analgesia. In our study, two groups were comparable with respect to age, gender, height, weight, surgical duration and ASA physical status. In our study, we did not find any statistically significant change in the pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, respiratory rate and SpO2. In present study, The mean time to onset of sensory block was 9.6 2.11 minutes in Group C and 6.9 ± 1.37 minute in Group A, while the mean onset of motor block was 12.24 ± 2.4 minutes in Group C and 6.92 ± 2.04 minutes in Group A. the difference between two Groups is statistically significant. ($p<0.05$) The mean duration of sensory block was 259.4 ± 33.88 minutes in Group C and 311.6 ± 41.52 minutes in Group A while the mean duration of motor block was 229.7 ± 30.70 minutes in Group C and 270.9 ± 49.51 minutes in Group A. the difference between two Groups was statistically significant. This suggests that when Clonidine added to local anaesthetics for supraclavicular brachial plexus block prolongs the duration of sensory and motor block. ($p<0.01$) Susmita Chakrabory, Jayanta Chakrabarti13 *et al* (2010), present randomized control trial clearly suggest that relatively low dose clonidine, as adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block, prolongs the duration of analgesia as well as motor block. Onset of times of block were also shown to be shortened though the study was not powered to measure these effects. Bernard and Macarie8 (1997), evaluating the effect of adding 30-300 µg clonidine to lognocaine for axillary brachial plexus block, reported that addition hastened the onset of the block and imporoved the efficacy of surgical anaesthesia. Danelli G *et al*. 15 evaluated the effects of adding 50 µg clonidine to 150 mg ropivacaine for superficial cervical plexus block in patients undergoing elective carotid endarterectomy. They opined that adding 50 µg clonidine to 150 mg ropivacaine for superficial cervical plexus block shortened the onset time and improved the quality of surgical anesthesia. Erlacher W *et al*.[18,19] in 2001 evaluated clonidine as adjuvant for mepivacaine,ropivacaine and bupivacaine in axillary plexus block and opined that clonidine prolonged both sensory and motor blockade of mepivacaine and bupivacaine but not ropivacaine. Antonucci S 20 evaluated effects of tramadol used as adiuvant in brachial plexus block and compared with clonidine and sufentanil. He used ropivacaine for block and concluded that tramadol as adiuvant provides a significative redution of onset time of sensory motor block and also provides a prolongation of anesthesia and analgesia with a quality of block similar that obtained with clonidine and sufentanil. El Saied *et al*. 21 conducted a study in which axillary brachial plexus blockade was performed in 50 patients using 40 ml ropivacaine 0.75 %. Group (A) had 150 µg clonidine and Group (B) 1ml normal saline added to the local anesthetic. There was no difference in onset of sensory motor blockade. They concluded that the addition of 150 µg of clonidine to ropivacaine, for brachial plexus blockade, prolongs motor and sensory block and analgesia, without an increased incidence of side effects. In respect to sedation score intraoperatively, most of the patients in Group A were calm and sleepy nut easily arousable whereas in Group C most of the patient were talkative. Postoperatively most of the patients were awake and talkative in Group C in comparison to Group A where calm and sleepy. There was statistically significant difference in sedation score starting from 15 minutes to 4 hours between two groups as Group A had higher sedation score compared to Group C. ($p<0.01$) The mean duration of postoperative analgesia was 320.6 ± 82.44 minutes in Group C while 568.2 ± 120.43 in Group A. Thus highly significant prolongation of post operative pain relief was noted in Group A. Most of the patients in Group C required first dose of rescue analgesic by 5 hrs postoperatively while most of the patients of Group A require first rescue analgesic dose by 10 hrs postoperatively. The mean requirement of analgesic doses was 2.92 ± 0.27 injections in Group C and 1.96 ± 0.20 in Group A. The difference between the two groups was statistically significant. ($p<0.01$) VAS was significantly lower in Group A as compared to Group C. The incidence of side effects was comparable in both groups. Singelyn[7] *et al* suggested that 0.5 µg/kg clonidine should be used. At this dose, significant prolongation of anaesthesia was achieved without undue sedation, hypotension and bradycardia. Giovanni Cucchiaro *et al*.[22,] evaluated the effects of clonidine on the duration of sensory and motor block and analgesia time in 215 children who underwent a variety of peripheral nerve block including brachial plexus block and concluded that the addition of clonidine to bupivacaine and ropivacaine can extend sensory block by a few hours, and increase the duration of motor blocks. Casati *et al*.[16] added low dose clonidine to ropivacaine (0.75%) in sciatic-femoral nerve block for foot surgery. They found that addition of 1 µg /kg clonidine to 0.75% ropivacaine prolongs the duration of postoperative

analgesia by 3 h, with only a slight and short-lived increase in the degree of sedation and no hemodynamic adverse effects. Casati *et al*.[17] has done a prospective, randomized, double-blind study in which he evaluated the effects of adding 1 μg/kg clonidine to 20 ml of ropivacaine 0.75% for axillary brachial plexus anesthesia. They concluded that adding 1 μg/kg clonidine to 20 ml of ropivacaine 0.75% for axillary brachial plexus anesthesia provided a 3 hour delay in first analgesic request postoperatively, without clinically relevant effects on the degree of sedation and cardiovascular homeostasis. Brummett CM *et al*. 23 found that dexmedetomidine when added to ropivacaine in peripheral nerve block caused approximately a 75% increase in the duration of analgesia. Above studies show that selective α2-adrenoceptor agonist like clonidine or dexmedetomidine when added as adjuvant to ropivacaine in different peripheral nerve blocks potentiates the sensory motor blockade. The mechanism is not clear. Probably peripherally, α2-agonists produce analgesia by reducing release of norepinephrine and causing α2-receptor-independent inhibitory effects on nerve fibre action potentials. Centrally, α2-agonists cause analgesia and sedation by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neurone and by activation of α2- adrenoceptors in locus coeruleus 5. So the action of clonidine would then more likely be via a synergistic mechanism of action in combination with the local anesthetic resulting in the prolonged effect.

CONCLUSION

Clonidine added to local anaestheitic in supraclavicular brachial plexus block not only hastens the onset, but also prolongs the duration of sensory motor blockade and provides a longer pain-free period without significant hemodynamic alterations. As it has more sedative potential, it can reduce patient anxiety and provide optimal intraoperative and postoperative patient comfort.

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