



Fentanyl and Clonidine with local Anaesthetics in Supraclavicular Brachial Plexus Block for Post operative Analgesia : A Comparative study

Dipti Mundhada¹, Janhavi Thatte², Deepak Phalgune³ *

1 Senior resident, Dept. of Anaesthesia, Poona Hospital & Research Centre, Pune, India.

2 Consultant, Dept. of Anaesthesia, Poona Hospital & Research Centre, Pune, India.

3 Research Consultant, Poona Hospital & Research Centre, Pune, India.

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*Corresponding author:

Email : dphalgune@gmail.com

Tel.: +91 9850434220

ABSTRACT

Role of Peripheral Nerve Block has expanded from operating suite into the arena of postoperative and chronic pain management. Single shot Brachial Plexus Block can provide analgesia only for period of action of local anaesthetic used. Keeping this in mind various drugs have been used as adjuvants to local anaesthetics with a view to increase analgesic efficacy and for extending duration of analgesia. The present study was undertaken to compare efficacy of adjuvant fentanyl and clonidine to local anaesthetics in Supraclavicular Brachial Plexus Block using nerve stimulator. Seventy patients aged 18 to 60 years scheduled for upper limb surgery in Poona Hospital & Research Centre, Pune between May 2014 and May 2015 under Supraclavicular Brachial Plexus Block and ready to participate were included. They were randomly divided into two equal groups of 35 each. Group C received 25ml 0.5% Bupivacaine + 1 µg/kg body wt of Clonidine whereas Group F received 25ml 0.5% Bupivacaine + 1 µg/kg body wt of Fentanyl. Mean onset of sensory and motor block, mean complete onset of sensory and motor block was significantly higher in Group F as compared to Group C. Mean duration of analgesia was significantly less in Group F as compared to Group C. Addition of Fentanyl and Clonidine to local anaesthetic mixture did not cause any significant cardiovascular or respiratory disturbances and incidence of complications and side effects were minimal. Clonidine was better adjuvant to local anaesthetics in Supraclavicular Brachial Plexus Block.

INTRODUCTION

Pain is an inevitable component of postoperative period. Although pain has teleological function in warning patients about potential injury, it also exerts deleterious effects on respiratory, cardiovascular, neuroendocrine, gastrointestinal and other systems of the body.[1] Hence, an effective pain relief after surgery is essential for optimal care of patient. Great advances have been made in management of surgical anaesthesia and analgesia using different modalities like systemic opioids, cyclooxygenase inhibitors, regional anaesthesia techniques, epidural analgesia, Transcutaneous Electrical Nerve Stimulation, and Peripheral Nerve Block (PNB) etc. Despite these technical advances, many patients continue to suffer due to inadequate control of pain. Major cause of pain includes inadequate knowledge regarding effective and

inadequate dosages of opioid due to fear of respiratory depression and addiction.[2]

Role of PNB has expanded from operating suite into arena of postoperative and chronic pain management. Typical features of PNB include rapid onset, predictable, dense anaesthesia and postoperative analgesia. PNB is achieved by injecting local anaesthetic solution around a nerve root to produce anaesthesia in distribution of that nerve.[3] Advantages of single shot PNB as compared to General Anaesthesia (GA) are many e.g. simple technique, early ambulation, avoidance of intubation and its complications, economic and safe for upper limb surgeries and post operative analgesia.[4,5] Among various PNB, Brachial Plexus Block (BPB) is one of the most common practiced.

Brachial plexus can be anaesthetized at sites above clavicle or

below clavicle. Supraclavicular approach of Brachial plexus block has favorable safety profile, ease of performance, and broad applicability for arm, forearm, wrist and hand.[3,6] Single shot BPB can provide analgesia only for period of action of local anaesthetic used. It is very short and unlikely to provide postoperative pain relief for a long time. Keeping this in mind various drugs have been used as adjuvants to local anaesthetics with a view to increase analgesic efficacy and for extending duration of analgesia.[7-9] Technique of BPB underwent several modifications with introduction of electronic devices and imaging technology, which are intended mainly to minimize risk of pneumothorax and achieve predictable, successful, complete block and minimizing risk of complications associated with blind techniques. One of such upgradation is introduction of nerve stimulator to locate brachial plexus prior to injection of anaesthetic agents. In the present study, mean onset of sensory block, mean onset of motor block, mean complete onset of sensory block, mean complete onset of motor block, and mean duration of analgesia were compared between fentanyl and clonidine groups in Supra Clavicular Brachial Plexus Block (SBPB).

MATERIALS AND METHODS

All the patients aged 18 to 60 years scheduled for upper limb surgery in Poona Hospital & Research Centre, Pune between May 2014 and May 2015 under SBPB and ready to participate were included. Permission was obtained from Institutional Ethics Committee and Scientific advisory committee of institution for this prospective, observational study as per inclusion and exclusion criteria detailed below:

Inclusion Criteria: Age > 18 years of either sexes, body weight \geq 40 kg, ASA physical status I and II.

Exclusion Criteria: Patients not willing for procedure, neurological lesion, diabetic neuropathy, psychiatric patients, history of allergy to local anesthetics, infection / swelling at proposed site of injection, bleeding disorders/patient on anticoagulation.

Based on previously published study,[10] setting an alpha error at 0.05, and power at 80%, sample size of 35 in each group was calculated by formula.[11] In all 70 ASA (American Society of Anaesthesiologist) grade I and II patients scheduled for upper limb surgery under SBPB were included in the study. They were randomly divided into two equal groups of 35 each, using computer generated randomization code. Randomization code was provided to an anaesthetist who prepared study medication. All other doctors, nurses and patients were blind as to group assignment.

Group C: 25ml 0.5% Bupivacaine + 1 μ g/kg body wt of Clonidine

Group F: 25ml 0.5% Bupivacaine + 1 μ g/kg body wt of Fentanyl

All patients underwent pre-anaesthetic check up and were assessed as per history and clinical examination. Investigations were conducted as per the protocol of the institution. Patients were explained about purpose, procedure and advantages of SBPB. Visual Analogue Scale (VAS) was explained to patients in detail. Patients were given tablet Alprazolam 0.25 mg orally night before surgery. All selected cases were advised to remain nil per orally for fluids and solids, at least six hours prior to performing block.

Only routine ongoing medications for systemic disease (if any) were continued as per schedule considering patients safety profile. Patient was made to lie down in supine position with head end of tilttable table elevated 30° and ipsilateral shoulder kept down with head turned to the opposite side. Patient was asked to keep arm to be blocked flexed at elbow and wrist was supinated to easily detect a twitch of fingers. Baseline parameters such as pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR), oxygen saturation (SpO₂), and ECG were continuously recorded. Supraclavicular region of side to be blocked was prepared according to hospital infection control protocol. Supraclavicular block was given as per standard protocol using nerve stimulator. Site of stimplex needle insertion was marked as per surface anatomical landmarks. After completion of injection needle was withdrawn completely and antiseptic dressing with little pressure was applied at site of puncture.

Following completion of Local Anaesthetic (LA) injection, time was noted (Time-0). Intra-operative PR, SBP, DBP, MAP, RR and SpO₂ were recorded at an interval of every 15 minutes from Time-0. Sensory block was evaluated by Hollmen scale and findings were recorded at an interval of every 2 minutes from time-0 till complete sensory block was achieved i.e Hollmen Score=4.[12]

Onset Time of Sensory Block (OTSB) was taken as time interval in minutes from time-0 till sensory block started appearing i.e Hollmen score > 1. Time for Complete Sensory Block (TCSB) was taken as duration of time in minutes from time-0 till complete sensory block was achieved i.e Hollmen Score=4.

Motor block was evaluated by using Modified Bromage Scale (MBS) for upper extremity and findings were recorded at an interval of every 2 minutes from time-0 till complete loss of motor power was achieved i.e MBS Score=3.[13]

Onset Time of Motor Block (OTMB) was taken as time interval in minutes from time-0 till motor block started appearing i.e MBS score \geq 1. Time for Complete Motor Block (TCMB) was taken as duration of time in minutes from time-0 till complete motor block was achieved i.e MBS score=3. Adequacy of block was evaluated by Allis clamp test before handing over patient to surgeon. Test was done by asking patients whether they felt any discomfort when pressure was applied with Allis clamp at area of surgical field. Reading was recorded as follows:

- a) Complete (Total comfort to patient)
- b) Inadequate (Discomfort: Requiring supplementation)

Block was considered to be failed if complete sensory and motor block was not achieved even after 45 minutes. Failed blocks were converted to GA and recorded. These patients were excluded from study. All patients were given intravenous (IV) injection midazolam 1-2 mg. Duration of surgery and type of surgical procedure done was recorded. Intra-operative complications / complaints (if any) such as Vessel injury, hematoma, inadequacy of block, nausea and vomiting, pruritus, dyspnea, fall in RR <10 per min, fall in SpO₂ < 90%, any symptom/sign of LA toxicity, any significant ECG changes etc. were recorded and managed accordingly. Intra-operative medication given (if any) was also recorded.

After completion of surgery patient was shifted to post operative recovery room. Patient was monitored till the time

patient did not demand analgesic or VAS Score ≥ 4 .[14] On reaching that point of time patient was given systemic analgesics Inj. diclofenec sodium 75mg IM or as per individual requirement. VAS was recorded at an interval of every one hour till the score ≥ 4 .

Time of first dose of postoperative systemic analgesic was on the basis of VAS score ≥ 4 or on demand made by patient (whichever was early).

In the present study, primary outcomes measures were mean onset of sensory block, mean onset of motor block , mean complete onset of sensory block, mean complete onset of motor block, and mean duration of analgesia whereas secondary outcome measures were mean heart rate , mean systolic blood pressure , mean diastolic blood pressure , mean SpO₂ , mean respiratory rate. Primary and secondary outcome measures were compared between the two groups.

Data collected were entered in the Excel 2007 and analysis of data was done using Statistical Package for Social Sciences (SPSS) version 21.0. The comparison of quantitative variables between the groups such as mean age, mean weight , mean onset of sensory block, mean onset of motor block , mean complete onset of sensory block, mean complete onset of motor block, mean duration of analgesia, mean heart rate , mean systolic blood pressure , mean diastolic blood pressure , mean SpO₂ , mean respiratory rate was done using unpaired student's "t" test, whereas comparison of qualitative variables such as gender and ASA grade was done by using chi-square test. The confidence limit for significance was fixed at 95% level with p-value < 0.05

RESULTS

Between May 2014 and May 2015, 70 indoor patients undergoing upper limb surgery under SBPB were included in the study.

As shown in table 1. two groups were demographically comparable. There was no statistically significant differences with respect to mean age, sex distribution, mean weight and ASA distribution between two groups.

As depicted in table 2, mean onset of sensory and motor block , mean complete onset of sensory and motor block was significantly higher in Group F as compared to Group C. Mean duration of analgesia was significantly less in Group F as compared to Group C. There was no statistically significant difference in mean duration of surgery in two groups. As shown in Figure 1, by using unpaired t-test there was no statistically significant difference between mean heart rate, mean systolic blood pressure , mean diastolic blood pressure , mean SpO₂ and mean respiratory rate at baseline to end of surgery between group F and group C. Out of 35 patients from Group C, one patients had vessel injury which was managed by little withdrawal , pressure given for five minutes and repositioning of the needle. After completion of the block procedure antiseptic pressure dressing was applied. Four patients from Group F and three from Group C complained of nausea and vomiting in postoperative period. All these patients were given injection Ondansetron 4 mg intravenously. Two patient from Group F complained of pruritus.

DISCUSSION

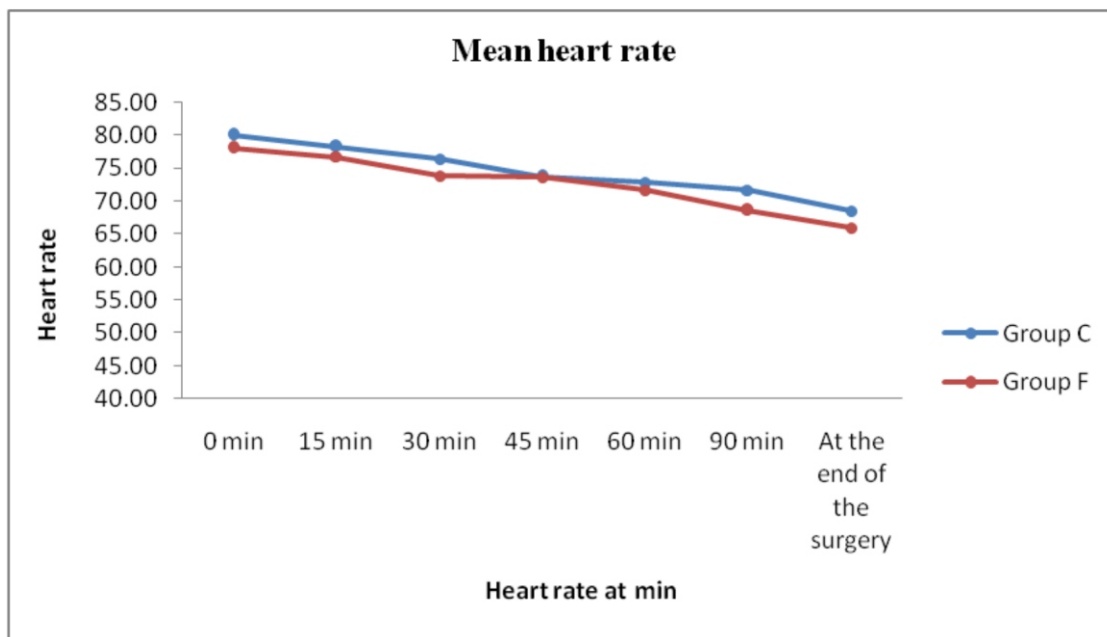
PNBs have become an integral part of surgical anaesthesia and postoperative analgesia , amongst which SBPB is widely practiced technique for upper extremity surgeries. Introduction of nerve stimulator for PNB has improved efficacy, success rate and safety of PNB. Addition of opioids to local anaesthetics improves quality of surgical anaesthesia and postoperative analgesia with an added benefit of no or minimal centrally mediated side effects.[15] Alpha blocker improves nerve block through local vasoconstriction, facilitation of C fibre blocked , spinal action

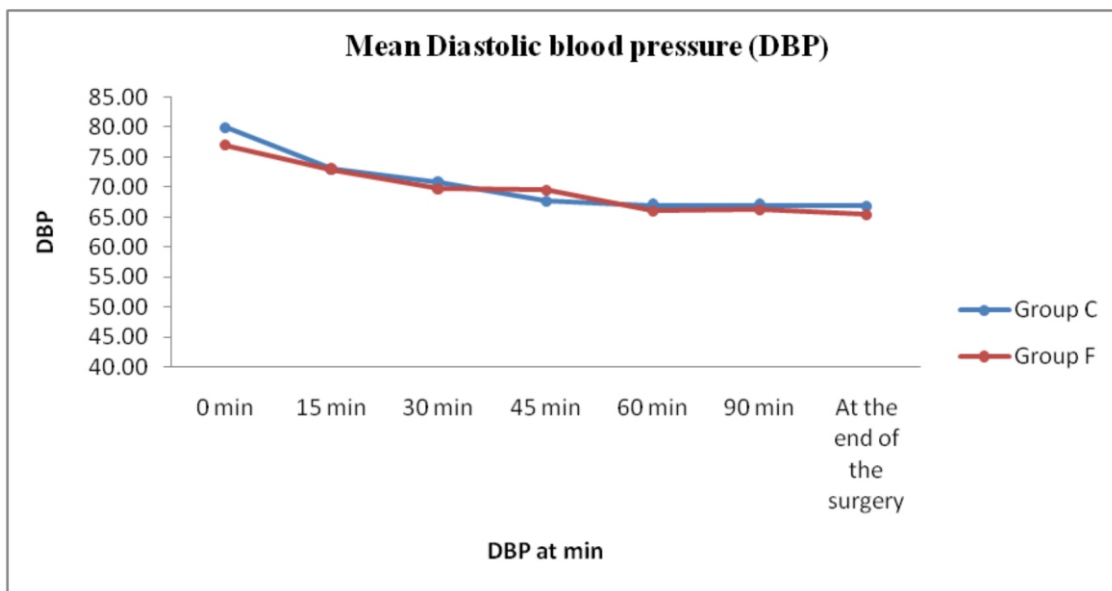
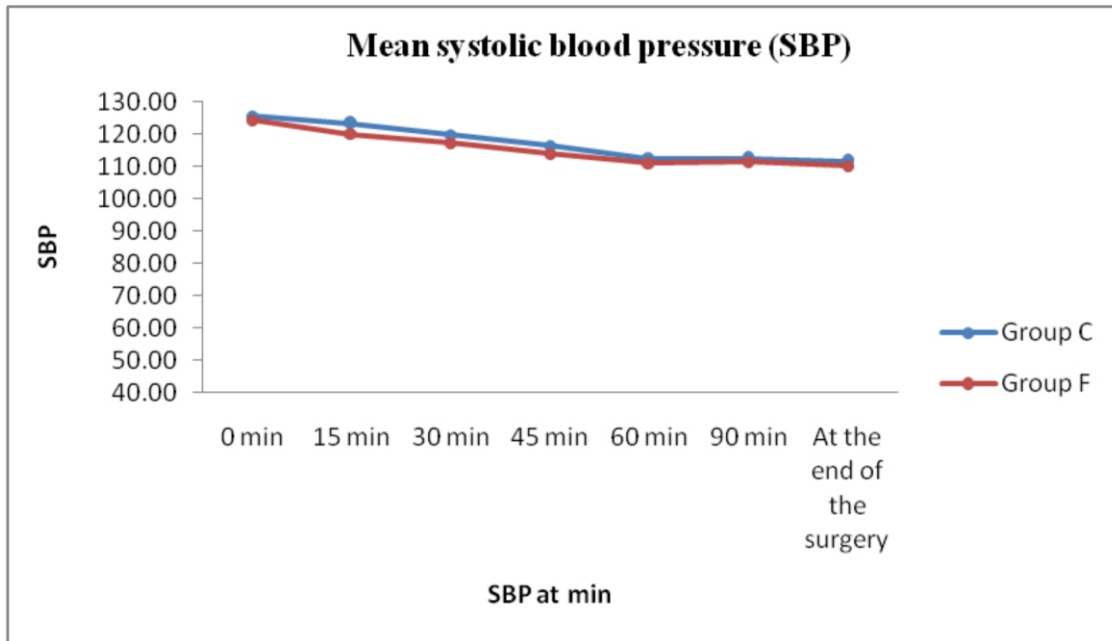
Table 1. : Demographic profile

Demographic characteristic	Group C (N = 35)	Group F (N = 35)	p value
Mean age in years (SD)	40.69 (± 15.38)	38.86 (± 13.35)	0.597
Gender , no (%)			
Male	21 (60.00)	19 (54.29)	
Female	14 (40.00)	16(45.71)	0.809
Mean weight in kg (SD)	62.20 (± 7.71)	65.29 (± 7.44)	0.093
ASA Grade (%)			
I	22 (62.86)	19 (54.29)	
II	13(37.14)	16(45.71)	0.628

Table 2. : Post operative comparison

Post operative block characteristic	Group C (N = 35)	Group F (N = 35)	p value
Mean duration of surgery (SD)	79 min 34 sec (± 44 min 39 sec)	79 min 26 sec (± 43 min 27 sec)	0.989
Mean onset of sensory block (SD)	6 min 14 sec (± 50 sec)	7 min 4 sec (± 44 sec)	< 0.001
Mean onset of motor block (SD)	9 min 53 sec (± 1min 5 sec)	11 min 10 sec (± 52 sec)	< 0.001
Mean complete onset of sensory block (SD)	13 min 12 sec (± 1 min 5 sec)	13 min 53 sec (± 50 sec)	<0.004
Mean complete onset of motor block (SD)	17 min 10 sec (± 55 sec)	18 min 4 sec (± 1 min 8 sec)	<0.001
Mean duration of analgesia (SD))	13 hours 13 min (± 52 min)	11 hours 37 min (± 1 hour 7 min)	<0.001

**Fig 1.** : Line diagram showing mean heart rate, mean systolic blood pressure, mean diastolic blood pressure, mean SpO₂, mean respiratory rate between group F and C throughout surgery.

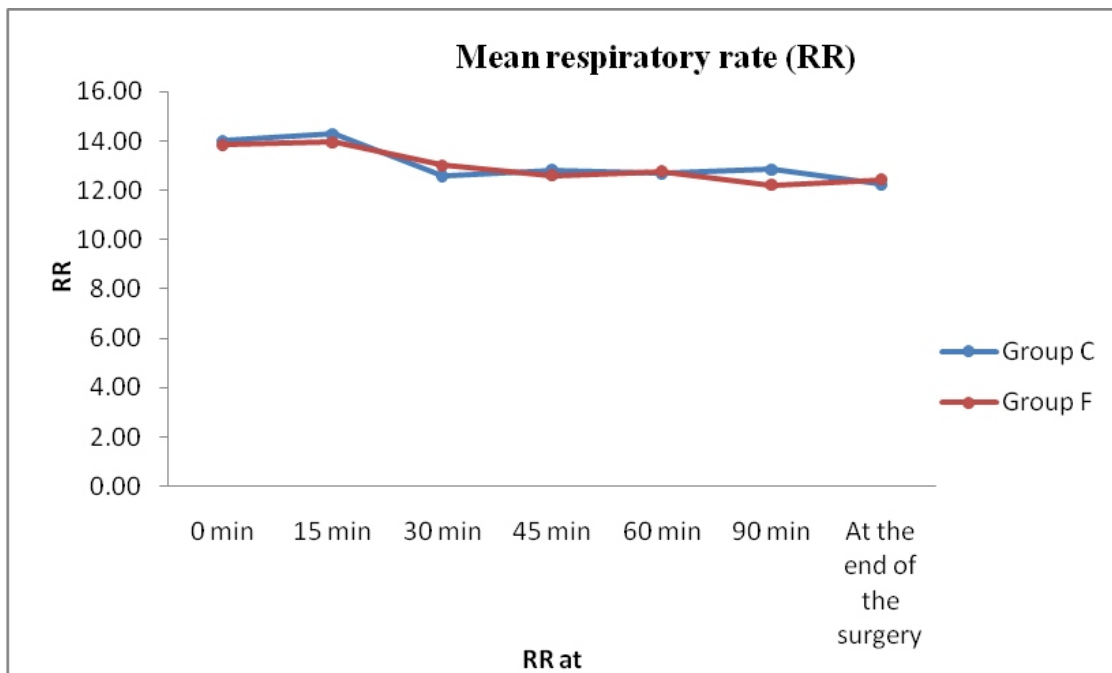
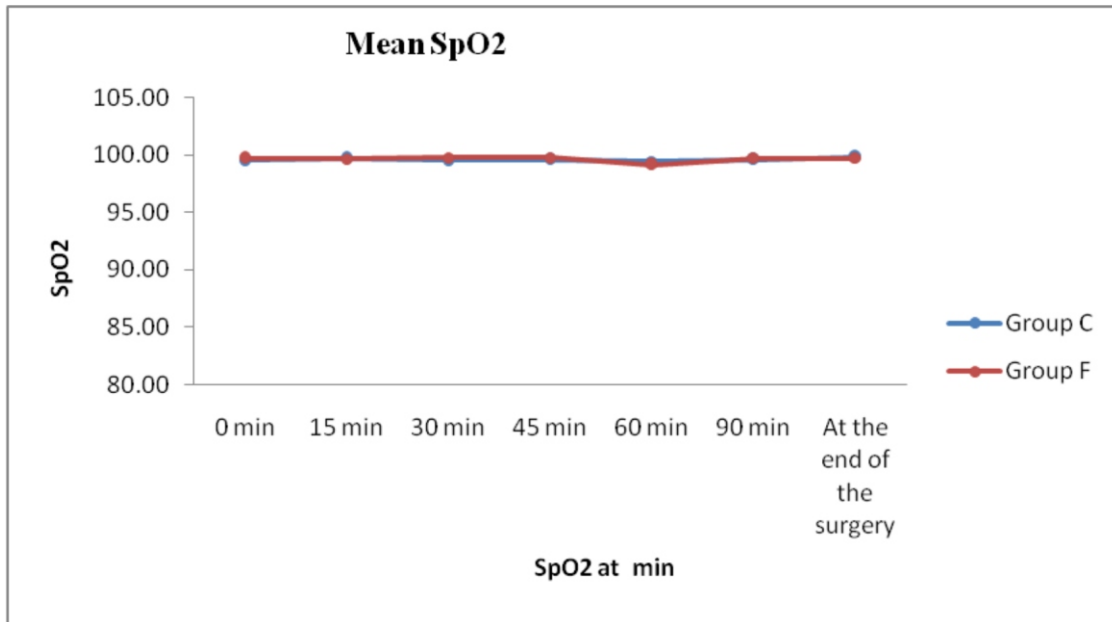


caused by slow retrograde axonal transport or simple diffusion along nerve.[16]

In present study, initial current of nerve stimulator was set to 1.0 mA and once desired response was obtained (muscle twitch of the fingers } , current was decreased to 0.4 mA if twitch still persisted drug solution was injected. This was in contrast to study by Franco CD et al , where after eliciting visible twitch at 0.9 mA and 0.5 mA, they injected LA solution by supraclavicular approach and found no difference in success rate of block.[17] Flexion or extension of wrist or fingers was considered as acceptable response to locate brachial plexus. We had a success rate of 100% and none of our patient had to be supplemented with general anaesthesia. This is comparable to study by Jeon DG et al wherein they compared twitch response between upper arm and wrist or finger in a supraclavicular block. They concluded that

elicitation of distal response was more effective in increasing success rate and reducing onset time than elicitation of proximal response in a single injection supraclavicular block using 40 ml of 1% mepivacaine. [18] Borgeat et al. reported success rates of 97% when distal response was elicited, and 44% when proximal response was observed in infraclavicular block.[14]Success rate in our study can be attributed to the fact that brachial plexus is more compact in supraclavicular region than in infraclavicular region. Secondly, in supraclavicular region, there are more nerve interconnections than in infraclavicular region.

In the present study , mean onset of sensory and motor block , mean complete onset of sensory and motor block was significantly higher in Group F as compared to Group C. Mean duration of analgesia was significantly less in Group F as compared to Group C. These results were comparable to study



conducted by Shirish G Chavan et al.[15] It was reported that anesthesia was more complete and prolonged when fentanyl is added to bupivacaine solutions for regional anesthesia.[19] Karkaya et al. stated that time for onset of sensory and motor block was 27.3 ± 1.6 min and 25.1 ± 1.8 min respectively. They further stated that the addition of $100 \mu\text{g}$ fentanyl to 40ml of 0.25% bupivacaine almost doubled duration of analgesia following axillary brachial plexus block when compared with 40ml of 0.25% bupivacaine alone.[20] Gormley et al. reported that addition of opioid alfentanil ($10 \mu\text{g}/\text{kg}$) to Lignocain($7\text{mg}/\text{kg}$)with adrenalin 1 in 200000 injection near neurovascular sheath in axillary brachial plexus block provided insufficient plasma concentration to produce systemic effects.[21] In our study, Group C had OTSB of 6.23 ± 0.84

minutes and OTMB 9.89 ± 1.08 minutes, TCSB and TCMB were 13.20 ± 1.08 and 17.17 ± 0.92 min respectively. Clonidine enhances both sensory and motor blockade of neuraxial and peripheral nerves after injection of local anaesthetic solution, without affecting the onset.[22-24]

Shivinder et al. reported that clonidine 0.150 mg in 40 ml of 0.25% bupivacaine significantly enhances quality of SBPB in upper limb surgeries by faster onset and prolonged duration of sensory and motor block, enhancing post-operative analgesia. They further stated that VAS scale was significantly lower in clonidine group than in control group up to 180 min, at 360 and 480 minutes.[25] These findings indicate faster onset of sensory block and prolongation of analgesia with use of clonidine. Prolongation of analgesia observed was consistent with other

trials performed at brachial plexus[26-28],popliteal block.[29]

Singh SP et al reported that duration of analgesia (7.28 ± 0.55 hrs) was significantly prolonged when 75gm of fentanyl was added to 30 ml of 0.25% bupivacaine.[30] Duration of analgesia in our study in fentanyl group was 11.62 ± 1.11 hr which was slightly longer than above study probably because nerve block was performed with help of nerve stimulator as against paresthesia elicited by them. Chakrabarti et al.reported analgesia duration was 415.4 ± 38.18 min in Clonidine Group compared to 194.2 ± 28.74 min in control.[16] In our study duration of analgesia was more($783 \text{ min} \pm 52 \text{ min}$).

In present study there were no significant variations in haemodynamic and respiratory parameter at different intervals of time as compared to baseline in any of the groups. These findings were similar to other studies.[9,12,30,31] In our study, vessel injury had occurred in only one patient. Kothari D reported that 6% had vessel puncture using lateral approach for SBPB. Chances of piercing vessels are remote as they lie medial to nerves.[32] In present study, only 7(11.7%) patients complained of nausea and vomiting in postoperative period.Out of 7, four patients were from Group F and three were in Group C. Systemic effect indicated partial systemic resorption. This absorption could explain longer duration of analgesia in both groups. These side effects were observed during first six hours. This suggests that blood level become very low after this time. Two patients developed pruritus both were from fentanyl group.The serious potential risk of opioid administration is respiratory depression. In the present research, we did not observe any respiratory depression possibly because the dose of opioids used was $1 \mu\text{g}/\text{kg}$.

Limitations of the study : USG guided nerve block should have been used for success rate of the block.

Future research: Present study was conducted as a single shot technique, the use of continuous infusion by catheter may be considered for postoperative pain relief. Different doses of clonidine and fentanyl should be studied to decide maximum safe dose which can be used with no haemodynamic changes and longer duration of action. Other long acting opioids like(buprenorphine, nalbupine)and alpha agonist dexmetomedine need to be studied for duration of post operative analgesia.

CONCLUSIONS :

Technique used for SBPB with aid of nerve stimulator was easier to perform, had better efficacy with a success rate of 100%, provided dense surgical anaesthesia, reasonably safe with no complication like pneumothorax and with minimal incidence of vessel injury. There was no neurological deficit in any patient as the current was 0.4mA and there was no intraneural injection. Mean onset of sensory and motor block, mean complete onset of sensory and motor block was significantly higher in Group F(Fentanyl) as compared to Group C(Clomidine). Mean duration of analgesia was significantly less in Group F as compared to Group C. Addition of Fentanyl and Clonidine to LA mixture did not cause any significant cardiovascular or respiratory disturbances and incidence of complications and side effects were minimal.

REFERENCES

1. James D, Justins D. Acute postoperative pain. In: Healy Tej, Knight PR, editors. Wylie and Churchill Davidson's A Practice of Anesthesia. 7th ed. London: Arnold; 2003.

- pp.1213-34.
2. Hurley RW, Wu CL. Acute postoperative pain. In: Miller RD,editor. Miller's Anesthesia. 7th ed. Philadelphia: Churchill Livingstone; 2010. pp.2757-81.
 3. Wedel DJ, Horlocker TT. Nerve Blocks. In: Miller RD,editor. Miller's Anesthesia. 7th ed. Philadelphia: Churchill Livingstone; 2010.pp.1639-74.
 4. Pollard BJ, Norton ML. Principles of airway management. In: Healy Tej, Knight PR, editors. Wylie and Churchill Davidson's A Practice of Anesthesia. 7th ed. London: Arnold; 2003. pp. 443-64.
 5. Mayfield JB, Rosow CE. Anesthesia for the outpatient. In: Healy Tej, Knight PR, editors. Wylie and Churchill Davidson's A Practice of Anesthesia. 7th ed. London: Arnold; 2003.pp. 1021-36.
 6. Tsui BC, Rosenquist RW. Peripheral Nerve Blockade. In: Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC. Clinical Anesthesia. 6th ed. Philadelphia:Lippincott Williams & Wilkins; 2009.pp.955-1004.
 7. Prithviraj P, Andrés JD, Grossi P, Banister R, Sala-Blanch X. Aids to Localization of Peripheral Nerves. In: Prithviraj P,editor. Textbook of Regional Anesthesia. 1st ed. Philadelphia: Churchill Livingstone; 2003. pp. 289-335.
 8. Winnie AP, Collins VJ. The subclavian perivascular technique of brachial plexus anesthesia. Anesthesiology. 1964; 25:353-63.
 9. Khosa DS, Thind SS, Gupta HK, Jain S. Effects of adding potassium chloride to lignocaine and bupivacaine solutions on the onset time and duration of brachial plexus block. Indian J. Anaesth. 1990; 38:119-22.
 10. Ahmed N, Hossain M, Akhtaruzzaman, Mondol M, Khatun U H. Addition of clonidine or fentanyl with bupivacaine for supraclavicular brachial plexus blocks in upper limb surgery - a randomized comparative study. Journal of Bangladesh Society of Anaesthesiologists.Jan2011; 24: 3-7.
 11. Charan J,Bijwas T. How to calculate sample size for different study designs in medical research. Indian J psychological medicine 2013April- June;35:121-26.
 12. Jadon A, Panigrahi MR, Parida SS, Chakraborty S, Agrawal PS, Panda A. Buprenorphine improves the efficacy of bupivacaine in nerve plexus block: A double blind randomized evaluation in subclavian perivascular brachial block. J Anaesth Clin Pharmacol.2009; 25:207-10.
 13. Cline E, Franz D, Polley RD, Maye J, Burkard J, Pellegrini J. Analgesia and effectiveness of levobupivacaine compared with ropivacaine in patients undergoing an axillary brachial plexus block. American Association of Nurse Anesthetists. 2004; 72: 339-45.
 14. Borgeat A, EkatoDRAMIS G, Dumont C. An evaluation of the infraclavicular block via a modified approach of the Raj technique. Anesth Analg.2001; 93:436-41.
 15. Chavan S, Koshire A, Panbude P. Effect of addition of fentanyl to local anaesthetic in brachial plexus block on duration of analgesia. Anaesthesia: Essay and research 2011 Jan Jun,5;39-42

16. Chakraborty S, Chakrabarti J, Mandal M C, Hazara A, Dass. Effect of clonidine as adjuvant in Bupivacain induced supraclavicular brachial plexus block. *Indian journal of pharmacology* 2010 April;42:74-7
17. Franco CD, Domashevich V, Voronov G, Rafizad AB, Jelev TJ. The supraclavicular block with a nerve stimulator: To decrease or not to decrease that is the question. *Anesth Analg.* 2004;98:116771
18. Jeon DG, Kim WI. Comparison of a supraclavicular block showing upper arm twitching response with a supraclavicular block showing wrist or finger twitching response. *Korean J Anesthesiol.* 2010;58:464-7
19. King MJ, Bowden MT, Cooper GM. Epidural fentanyl and 0.5% bupivacaine for elective caesarean section. *Anaesthesia* 1990;45:285-8.
20. Karakaya D, Duyukgoz F, Bars S, Guldogus F, Tur A. Addition of fentanyl to bupivacaine prolongs anesthesia and analgesia in axillary brachial plexus block. *Reg Anesth Pain Med* 2001; 26(5):434-8.
21. Gormley WP, Murray JM, Fee JPH, Bower S. Effect of the addition of alfentanil to lignocaine during axillary brachial plexus anaesthesia. *Br J Anaesth* 1996;76:802-5
22. El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, El-Ozairy HS, Boulis SR. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. *Br J Anaesth.* 2009;103:26874.
23. Bhatnagar S, Mishra S, Madhurima S, Gurjar M, Mondal AS. Clonidine as an analgesic adjuvant to continuous paravertebral bupivacaine for post-thoracotomy pain. *Anaesth Intensive Care.* 2006; 34:58691
24. Gabriel JS, Gordin V. Alpha 2 agonists in regional anesthesia and analgesia. *Curr Opin Anaesthesiol.* 2001;14:7513
25. Shivinder Singh, Amitabh Aggarwal A randomized controlled double-blinded prospective study of the efficacy of clonidine added to bupivacaine as compared with bupivacaine alone used in supraclavicular brachial plexus block for upper limb surgeries. *Indian Journal Anaesth* 2010; 54: 552-57
26. Casati A, Magistris L, Beccaria P, Cappelleri G, Aldegheri G, Fanelli G. Improving postoperative analgesia after axillary brachial plexus anesthesia with 0.75% ropivacaine. A doubleblind evaluation of adding clonidine. *Minerva Anesthesiol.* 2001; 67: 40712.
27. Erlacher W, Schuschnig C, Koinig H, Marhofer P, Melischek M, Mayer N, et al. Clonidine as adjuvant for mepivacaine, ropivacaine and bupivacaine in axillary, perivascular brachial plexus block. *Can J Anaesth.* 2001;48:5225.
28. Iskandar H, Guillaume E, Dixmérias F, Binje B, Rakotondriamihary S, Thiebaut R, et al. The enhancement of sensory blockade by clonidine selectively added to mepivacaine after midhumeral block. *Anesth Analg.* 2001;93:7715.
29. YaDeau JT, LaSala VR, Paroli L, Kahn RL, Jules-Elysée KM, Levine DS, et al. Clonidine and analgesic duration after popliteal fossa nerve blockade: randomized, double-blind, placebo- controlled study. *Anesth Analg.* 2008;106:191620.
30. Singh SP, Singh V, Kaushal D, Jafa S. Effect of alkalized bupivacaine and fentanyl mixture in supraclavicular brachial plexus block-A randomised double blind controlled trial. *J Anaesth Clin Pharmacol.* 2009; 25: 25-8.
31. Nishikawa K, Kanaya N, Nakayama M, Igarashi M, Tsunoda K, Namiki A. Fentanyl improves analgesia but prolongs the onset of axillary brachial plexus block by peripheral mechanism. *Anesth Analg.* 2000; 91:384-7.
32. Kothari D. Supraclavicular brachial plexus block: A new approach. *Indian J. Anaesth.* 2003; 47: 287-8.