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Original Research Article

A Comparative Study between Dexmedetomidine and Fentanyl as Adjuvant with Epidural Levobupivacaine in Abdominal Hysterectomy

Anirban Kundu[1], Suchismita Pal[2], Souvik Saha[3], Sudipa Mandal[4]

[1]Assistant Professor, Anaesthesiology, Diamond Harbour Government Medical College and Hospital, Diamond harbour, West Bengal.
[2]Assistant Professor, Anesthesiology, Diamond Harbour Government Medical College and Hospital, Diamond Harbour, West Bengal.
[3]Assistant Professor, Anaesthesiology, Diamond Harbour Government Medical College and Hospital, Diamond Harbour, West Bengal.
[4]Specialist Medical officer, Gynecology and Obstetrics,Diamond Harbour Government Medical College and Hospital, Diamond Harbour, West Bengal.

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Corresponding author: Dr. Sudipa Mandal
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Abstract

Background: Objective of this study was to compare epidural dexmedetomidine or fentanyl with levobupivacaine in terms of onset of sensory block, peak height of sensory block, duration of analgesia, Onset, and duration of motor block, intra operative haemodynamic stability, surgeon's satisfaction regarding operating condition by VAS scale and untoward side effects

Methods: After the approval of the Institutional Ethics Committee this randomized, parallel group, double-blind controlled study was carried out under the Department of Anaesthesiology of a tertiary care centre in north India.

Results: Dexmedetomidine (50µg) is better adjuvant that fentanyl (50µg) in terms early onset of sensory and motor block. Dexmedetomidine provides longer duration of sensory and motor block than fentanyl. Both are comparable regarding maximum level of sensory block. Regarding haemodynamic parameter (Mean BP, Heart rate) and adverse effect (bradycardia, hypotension, nausea & vomiting, pruritus) dexmedetomidine is better alternative than fentanyl, though it cause more decrease of heartrate. Dexmedetomidine provides more satisfaction among surgeon than fentanyl.

Conclusions: Therefore, epidural dexmedetomidine is a feasible, safe, and more reliable adjuvant with levobupivacaine (0.5%) to provide smooth anaesthesia and analgesia with higher satisfaction to surgeon than epidural fentanyl in abdominal hysterectomy.

Keywords: Dexmedetomidine, Fentanyl, Adjuvant, Epidural Levobupivacaine, Abdominal Hysterectomy

Introduction

Regional anaesthesia is a popular method of anaesthesia for gynaecological surgery than general anaesthesia as it has so many advantages. Spinal, epidural anaesthesia are common options for gynaecological surgeries. Spinal anaesthesia is advocated because of its reliability and simplicity, but suffers the limitation of a single injection technique, longer discharge times, and a higher incidence of side effects than the other two techniques [1] (epidural and general anaesthesia). Epidural anaesthesia for gynaecological surgery is widely accepted for its greater advantages over general anaesthesia in terms of avoidance of laryngoscopic surge, better perioperative pain management and greater patient satisfaction. [2] Epidural anaesthesia also attenuates neuroendocrine response to surgery if given well ahead of surgical stimulus. [3] Many beneficial aspects of epidural anaesthesia have been reported, including better suppression of surgical stress, [4] positive effect on postoperative nitrogen balance. [5] It can be used to extend analgesia into postoperative period, where their use has been shown to provide better analgesia than can be achieved with parenteral analgesic.

Many local anaesthetic agents have been used for epidural anaesthesia. Bupivacaine is a well established long acting local anaesthetic which like all amide anaesthetic has been associated with cardiac toxicity when used in high concentration or when accidentally administered intravascularly. Levobupivacaine, the the s-enantiomer of 1-butyl-N-2, piperidine-2-carboxamide is a local anaesthetics with a chemical structure related to mepivacaine and bupivacaine. A number of studies suggest that levobupivacaine is associated with less central nervous system toxicity and cardiactoxicity with less motor block potency but anaesthesia and analgesic property is comparable with 6dimethyiphenyl bupivacaine. [6]

Gynaecological surgeries are sometimes associated with significant blood loss and there is greater incidence of hypotension. Epidural anaesthesia provides more stable cardiovascular haemodynamics, reduces blood loss, better peripheral vascular circulation [7,8] though it itself may cause hypotension. It is a major concern specially in aged patient population. In this scenario sedative drugs, either inhalational or intravenous, may potentiate the incidence of respiratory depression as well as hypotension. To avoid this and to have stable haemodynamics and postoperative analgesia, an effort has been made to administer various adjuvant in the epidural route along with local anaesthetics.

Different drugs have been tried as adjuvant to local anaesthetic. Local anaesthetic with opioids demonstrate significant synergy, They provide excellent analgesia and prolongs the time of regression of sensory block. [9]

Since the introduction of epidural opioids into clinical practice of anaesthesia in 1979, it has gained widespread popularity and acceptance. Epidural administration of combination of opioids and levobupivacaine for postsurgical pain relief has resulted in better pain scores. Several authors have suggested that this combination may produce a synergistic effect, while reducing the incidence of side effects. [10,11]

Since hydrophilic opioids such as morphine, remain in the cerebrospinal fluid for long duration and may be responsible for undesirable side effects like delayed onset of peak analgesic effect and late respiratory depression, highly lipophilic opioids such as fentanyl have been used to reduce the side effects of extradural opioid administration. [12,13] Fentanyl, a potent opioid receptor agonist is largely used to provide analgesia for acute pain and to enhance the quality to epidural block for perioperative analgesia. [14]

α2 adrenargic agonist has both analgesic and sedative effect when administered in epidural route along with local anaesthetics. [15,16] The incidence of vomiting, prurtitus and respiratory depression is less frequent as compared with that seen after epidural opioid. Both dexmedetomidine and clonidine are α2 agonist used widely in clinical practice. Clonidine also have sedative and analgesic property. [17] It has Aδ and C fidres and intensifies local anaesthetic conduction block and also prolongs analgesia. [18] Dexmedetomidine, a denantiomer of medetomidine, has analgesic property and augmentation of local anaesthetic effect causing hyperpolarisation of nerve tissues by altering transmembrane potential and ion conduction at locus coeruleus in brainstem. The drug has sedative, hypnotic and analgesic effect [19] with limited respiratory depression with special property of easy arousability without cloudiness of mind and better haemodynamic control. Decreased oxygen demand due to enhanced sympathoadrenal stability [4] makes it very useful in the perioperative period as well.

With this previous review, this study was conducted to compare dexmedetomidine with fentanyl with epidural levobupivacaine in respect of perioperative anaesthesia and analgesia.

Aims and Objectives

Objective of this study was to compare epidural dexmedetomidine or fentanyl with levobupivacaine in terms of onset of sensory block, peak height of sensory block, duration of analgesia, Onset, and duration of motor block, intra operative haemodynamic stability, surgeon's satisfaction regarding operating condition by VAS scale and untoward side effects

Materials & Methods

After the approval of the Institutional Ethics Committee this randomized, parallel group, double-blind controlled study was carried out under the Department of Anaesthesiology of a tertiary care centre in north India from March 2015 to June 2016.

Inclusion Criteria

- ASA grade: I and II
- Age: 40 to 60 years
- Sex: Female
- Type of surgery: Elective gynaecological surgeries (Abdominal hysterectomy)

Exclusion Criteria

- Local infection in the lumbar region
- Known hypersensitivity to amide local anaesthetic
- Bleeding diathesis
- Spinal deformity
- Diabetes
- Preexisting neurological, cardiac, renal, metabolic, psychiatric disorder.

Written informed consent was obtained. Patients thus enlisted for the study were randomly allocated into two groups, group-A and group-B using a computer generated randomization chart.

Group-A (n=30): received 15 ml of 0.5% Levobupivacaine hydrochloride plus 50 µg dexmedetomidine

Group-B (n=30): received 15 ml of 0.5% Levobupivacaine hydrochloride plus 50 µg Fentanyl citrate.

Sample Size

60(30 in each group). For the purpose of sample size calculation the duration of analgesia was taken as primary outcome measure. It was estimated that n=27 subjects (recruitment target being 30 subjects per group) would be required per group in order to detect the difference of 30 minutes in the duration of analgesia between two groups with 80% power and 5% probability of type 1 error. This calculation assumes a standard deviation

of 45 minutes for the duration of analgesia parameters.

Statistical Methods

Data were entered in MS excel data base and were analyzed with the help of statistical package for social science (SPSS software version 16.0 for Windows, SPSS Inc.

Chicago). Numerical variables would be compared between groups by Student's unpaired ttest if normally distributed or by Mann-Witney U-test if otherwise. Categorical variables would be compared between groups by Chi-square test or Fisher's exact test as appropriate. Analysis would be two tailed and $p<0.05$ would be considered statistically significant.

Results

There was no statistically significant difference in age distribution among the study groups as (P value = 0.472). There was no statistically significant difference (p=0.517) between the Group-A and group-B in respect to the body weight.

There was no statistically significant difference (p=0.282) among the study groups (Gr. B) and the control group (Gr. A) in respect to the height. There was no statistically significant difference (p=0.222) among the Group-A and Group-B in respect to the duration of surgery in minutes. There was no statistical significance between the two groups with regard to ASA grading (P value = 0.800).

Table 1: Distribution of Onset of Sensory Block and Onset of Motor Block

Duration of Sensory Block (min)	**Group A (N=30)**	**Group B (N=30)**
Minimum time	8	8
Maximum time	13	15
Mean	10.10	11.40
Std. Dev	1.373	1.886
Distribution of Onset of Sensory Block between Two Groups		
Duration of Motor Block (min)	**Group A (N=30)**	**Group B (N=30)**
Minimum time	14	16
Maximum time	22	25
Mean	17.53	21.37
Std. Dev	1.995	2.470
Distribution of Onset of Motor Block in Two Groups		

There was statistically significant difference (p=0.003) between the Group-A and Group-B in respect to the time for onset of sensory block. Patients in Group-A had early onset of sensory block than Group-B. Patients in the group-B had significantly earlier onset of motor block than Group-A (p=0.000).

There was no statistically significant difference in distribution of block height achieved in different patients between Group-A and Group B (P value=0.441 for T4 level, 0.292 for T5 level and 0.759for T6 level).

Table 2: Distribution of Duration of Sensory Block Onset of Motor Block and Analgesia

Duration (min)	**Group A (N=30)**	**Group B (N=30)**
Mean	157.33	138
Std. Dev	15.468	10.296
Distribution of Duration of Sensory Block (Two Segment Regression) between Two groups		
Duration (min)	**Group A (N=30)**	**Group B (N=30)**

Mean	250.37	213.97
Standard deviation	21.281	25.187
Distribution of Duration of Motor Block Between Two Groups		
Duration (min)	**Group A (N=30)**	**Group B (N=30)**
Mean	355.87	302.40
Std. Dev	18.846	37.736
Distribution of Duration of Analgesia (MIN) between Two Groups		

There was statistically significant difference (p=0.000) among the Group-A and Group-B in respect to the duration of sensory block. There was statistically significant difference (p=0.0000) among the Group-A and Group-B in respect to the duration of motor block.

There was a statistically significant difference (p=0.000) between the Group-A and Group-B in respect to the duration of analgesia. This was assessed on the basis of VAS score in the post-operative period (When VAS score≥4) or patient demand for analgesics in the post-operative period. Thus duration of analgesia was longer in Group-B (252.38 min) as compared to Group-A (231.25).

There was no statistically significant difference (p value >0.05) between the patients of Group-A and Group-B as per as mean arterial pressure (MAP) was concerned at any time in the study period.

Table 3: Comparison of Heart Rate between Two Groups

Time	Group-A (MEAN±SD)	Group-B (MEAN±SD)	Significance (p VALUE)
0 MIN	82.30±5.87	83.43±5.57	.446
5 MIN	80.60±6.86	83.67±4.79	.049
10 MIN	78.73±6.04	84.07±4.67	.000
15 MIN	77.80±6.16	86.80±4.83	.000
20 MIN	76.97±5.91	88.17±6.85	.000
25 MIN	78.37±6.99	89.80±7.09	.000
30 MIN	82.33±5.56	90.73±6.09	.000
45MIN	84.80±4.72	91.83±5.92	.000
60MIN	87.37±5.55	91.33±6.24	.014
75MIN	89.80±4.72	93.10±7.16	.039
90MIN	92.04±6.04	96.54±6.29	.011
105MIN	91.93±8.04	95.67±10.02	.492

Regarding the base line value no significant difference was noted between the two groups (p>0.05). Thereafter there was decline of heart rate from baseline value in group A after 10 min of administration of administration of epidural levobupivacaine and dexmedetomidine, which was statistically significant(p<0.05). It was continued upto 90 minutes. Thereafter heart rate become comparable between the two groups.

There was significant difference between group A (2.33) and group B (1.8) with regard to mean surgeon's satisfaction score (p value=0.000).

There was no significant statistical difference between the two groups with regard to side effects (p value > 0.05).

Discussion

The mean time of motor block were less in group A (17.53±1.99 minutes) than Group B (21.37±2.47 minutes). Appropriate statistical test shows, there was significant difference (p<0.05) in the time of onset of motor block between the two groups. Bajwa et al. [20] evaluated the addition of

dexmedetomidine or fentanyl to epidural ropivacaine in patient undergoing lower limb orthopaedic surgeries and they found that the onset of sensory analgesia and the establishment of the complete motor blockade was significantly earlier in the dexmedetomidine group. Gupta K, et al. [21] in their study with single shot epidural anaesthesia found that onset of complete motor block was 19.27± 4.7 minutes in group D (levobupivacaine + dexmedetomidine) and 22.78±5.5 minutes in group F (levobupivacaine+ fenanyl).

Highest level of sensory block was achieved in both the groups was up to T4 dermatome and lowest level was up to T6 dermatome. Among the patient of group A 47% found to have a height of sensory block up to T4 dermatome, 30% up to T5, 23% up to T6 and in the patient of group B 37% up to T4,43% upto T5, 20% upto T6 dermatome. There was no significant difference between the two groups according to block height. Soliman R et al [22] also concluded that both the group in his study were comparable according to maximum sensory block height, also supported our study.

The duration of sensory block was calculated by counting time required to two segment regression of sensory block after surgery under epidural anaesthesia. The mean duration of sensory block was more (157.33±15.46 minutes) in group A than in group B (138±10.29 minutes). Gupta S et al. [21] in their study with single shot epidural anaesthesia found that two segment regression time was more for levobupivacine and dexmedetomidine than levobupivacine and fentanyl, which was stasistically significant ($p<0.05$), also supported our study.

The mean duration of motor block (250.37± 21.28 minutes) was more in group A in than group B (213.97±25.18 minutes). Gupta S et al. [21] in their study with single shot epidural anaesthesia found that mean duration of motor block was more in group LD (213.97±25.18 minutes) than group L (199±12.95 minutes) also supported our study.

Duration of analgesia was assessed from onset of sensory block to first request for resque analgesic or vas score >4(0=no pain and 10= worst possible pain). The mean duration of analgesia was 355.87±18.84 minutes in group A, in group B 302.40±37.73 minutes. The difference between two groups were statistically significant in respect to duration of analgesia. Hanoura SE et al. [23] in their study also found that time for first analgesic dose was more in DBF group in (321±19 mins) than in BF group (174±15.7 mins).

In the present study the baseline values of mean BP were similar in both the groups. Reduction of mean BP from their baseline values were noted following epidural dexmedetomidine as well as epidural fentanyl. We have noticed episode of hypotension in the intraoperative period in some patients of both the groups which was also statistically insignificant. Intra operative mean BP remain stable after 30-45 minutes. Gupta K et al.84 found no statistically significant episode of hypotension either in dexmedetomidine or fentanyl groups which also supported our study. [24]

Decrease in the intraoperative heart rate is known clinical effect of opioids but dexmedetomidine has similar chronotropic action in a exaggerated manner. They are α2 agonist, decrease heart rate due to postsynaptic activation of α2 adrenoreceptors in the central nervous system, resulting in decreased sympathetic activity. In the present study baseline heartrate was similar in both the groups. But decrease in the heart rate was more prominent in the dexmedetomidine group than fentanyl which was aiso statiscally significant($p<0.05$). Intraoperative heartrate become stable in both the group around 75-90 minutes. Soliman R et al. [22] also found stastically significant difference in intraoperative heartrate in

both the group ($p<0.05$) which also supported our study.

There was no statistical difference ($p=0.126$) between the two groups with regard to number of patients suffer from the episodes of hypotension. Bajwa et al. found no difference in the incidence of bradycardia or hypotension in the two groups.

Surgeon's satisfaction score ($p=.000$) were significantly higher in group A, which proved clearly that dexmedetomidine was superior adjuvant than fentanyl to provide satisfactory sensory-motor block when administered with 0.05% levobupivacaine in epidueal anaesthesia.

Five patients in group A and eight patient in group B had incidence of nausea and vomiting. Four patients in group B complaint about pruritus, while none in group A. Three patients in either group had shivering. Two patient in group A and one patient in group B had headache. There was no incidence of respiratory depression and urinary retention in any group. The side effects such as nausea and vomiting, pruritis, were lower in the dexmedetomidine group compared to fentanyl group and a similar result was shown by Gupta et al.[21]

Conclusion

Dexmedetomidine(50µg) is better adjuvant that fentanyl (50µg) in terms early onset of sensory and motor block. Dexmedetomidine provides longer duration of sensory and motor block than fentanyl. Both are comparable regarding maximum level of sensory block. Regarding haemodynamic parameter (Mean BP, Heart rate) and adverse effect (bradycardia, hypotension, nausea & vomiting, pruritus) dexmedetomidine is better alternative than fentanyl, though it cause more decrease of heartrate. Dexmedetomidine provides more satisfaction among surgeon than fentanyl. Therefore, epidural dexmedetomidine is a feasible, safe and more reliable adjuvant with levobupivacaine (0.5%) to provide smooth anaesthesia and analgesia with higher satisfaction to surgeon than epidural fentanyl in abdominal hysterectomy.

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Original Research Paper

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Anaesthesiology

A COMPARATIVE STUDY OF RAMOSETRON AND GRANISETRON FOR PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING LAPAROSCOPIC GYNECOLOGICAL SURGERIES UNDER GENERAL ANESTHESIA

Dr Suchismita Pal — Assistant Professor, Diamond Harbour Government Medical College And Hospital, Diamond Harbour, South 24 Parganas

Dr Jayanta Bhattacharya* — Professor, Vivekananda Institute Of Medical Sciences, Ramakrishna Mission Seva Pratisthan, 99, Sarat Bose Road, Kolkata-700026 *Corresponding Author

ABSTRACT

INTRODUCTION: Post-operative nausea and vomiting (PONV) is one of the most distressing and common complaint that patients have following general anesthesia. Laparoscopic gynecological surgery is associated with high incidence of post-operative nausea and vomiting. Granisetron is a selective competitive $5HT_3$ receptor agonist having both central and peripheral actions. Ramosetron is another $5HT_3$ receptor antagonist of newer generation with prolonged duration of action. This study compared the efficacy of prophylactic use of granisetron and ramosetron for prevention of PONV following laparoscopic gynecological surgery.

METHODS: In a prospective randomised study, 80 adult females received either granisetron(2.5mg) or ramosetron(0.3mg) (N=40 in each group) by the intravenous route at the end of the surgery. The treatment groups were similar in patient characteristics, surgical procedures and anesthetic management. Observation was done upto 48 hours post-operative.

RESULTS: Even though the incidence of nausea in the last 24 hours of observation was statistically significant in the ramosetron group vs granisetron (p=0.019) but the total response of 48 hours duration for both the groups were observed to be statistically insignificant (p=0.237).

CONCLUSION: In conclusion, prophylactic therapy with Ramosetron is equally effective as prophylactic therapy with Granisetron for the prevention of PONV in laparoscopic gynecological surgery.

KEYWORDS : postoperative nausea and vomiting (PONV), Granisetron, Ramosetron, laparoscopic gynaecological surgery

INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the most distressing and common complaint that patients have, following general anaesthesia. Kapur P.A described PONV as "the big little problem"[1] and considered it to be one of the major challenges faced by the anesthesiologists in their day to day practice. The phenomenon of PONV can lead to increase in the risk of wound dehiscence, bleeding from operative site, pulmonary aspiration of vomitus, esophageal tears (Mallory Weiss syndrome), muscle fatigue, fluid and electrolyte imbalance and also enhances psychological effects like anxiety and apprehension. In general, the incidence of emesis is highest in female patients of child bearing age and after certain surgical procedures including cholecystectomy, gynecological surgery and laparoscopy[2]. The highest incidence of post operative nausea and vomiting was reported in women undergoing laparoscopic ovum retrieval (54%) and the next highest occurred after laparoscopy (35%)[3]. A number of pharmacological agents like antihistaminic, phenothiazine derivatives, butyrophenones and dopamine receptor antagonists have been used as routine prophylaxis against PONV. However, these drugs have unwanted side effects like dysphoria, dry mouth, restlessness, tachycardia and extra pyramidal symptoms[2]. Recently introduced 5-HT_3 receptor antagonists are devoid of such side effects and have been proved highly efficacious in both preventing and treating PONV in gynecological surgery[4]. Granisetron is a selective competitive 5-HT_3 receptor antagonist, having both central and peripheral action, is in use as an anti emetic for a long time in gynecological surgery[4]. Ramosetron is another newer addition to selective 5-HT_3 receptor antagonist that have been proved to be an effective agent in preventing PONV in gynecological surgeries. This study was undertaken to evaluate and compare the efficacy of granisetron and ramosetron, given prophylactically, in preventing postoperative nausea and vomiting in the long term following laparoscopic gynecological surgery.

MATERIALS AND METHODS:

This comparative study was conducted with 80 female patients of 25-60 years of age who underwent laparoscopic gynaecological surgery under anesthesia. The study protocol was reviewed and approved by the hospital ethical committee and a written informed consent was obtained from each and every patient recruited in this study. Each group consists of 40 patients. Group A received i.v. Granisetron (2.5mg) and Group B received i.v. Ramosetron (0.3mg). The drugs were given at the end of surgery during skin closure. Subject exclusion criteria were unwilling patients, those with history of pulmonary, cardiovascular, metabolic, gastrointestinal disorders, motion sickness, previous PONV, pregnant and menstruating females as well as patients who have taken anti-emetic medication within 24hrs before the surgery and patients with history of allergy to study drugs.

Each of the patients selected for the study was visited and examined on the day before surgery, was counselled and written informed consent was taken. A thorough pre-anaesthetic check-up was carried out and the baseline investigations were reviewed and recorded. All patients were instructed not to consume any solid food after midnight, but clear fluids were permitted up to two hours prior to the scheduled time of operation. All patients received tablet Alprazolam 0.5mg orally on the night before and another 0.5mg of the same drug in the morning of surgery to allay fear, anxiety and apprehension. The anaesthetic regimen and surgical procedure were standardized for all patients. After wheeling patients into the operating room, the standard monitors were attached. By using a computer generated random number table, the patients either granisetron or ramosetron for laparoscopic gynaecological surgery each day were chosen randomly. 40 patients were allotted in each group. Group A received i.v. Granisetron (2.5mg). Group B received i.v. Ramosetron (0.3mg). The study medications were prepared in identical 5ml syringe and diluted to 5 ml volume and administered intravenously over 30 seconds at the end of the surgery. In the operating room an intravenous cannula (18G) was inserted and provided with balanced salt solution at a rate which is titrated according to requirement. Standard monitors were attached and baseline parameters were duly noted. All the patients were pre-medicated with Midazolam (0.07mg/kg) intravenously (i.v.) 5 minutes before induction of anesthesia. Next the patients were given with i.v. fentanyl citrate (2µg/kg) and glycopyrrolate (0.01mg/kg). Ventilation was assisted with face mask (100% O_2) for 3 minutes. Anesthesia was induced with i.v. thiopentone (5mg/kg) followed by i.v. administration of succinylcholine (2mg/kg) to facilitate laryngoscopy and intubation. After intubation with a proper size cuffed endotracheal tube anaesthesia was maintained with nitrous oxide 66% and oxygen 33% on IPPV and titrated administration of halothane (0.5-2%) and intermittent non-depolarizing muscle relaxants i.v. Atracurium (0.05mg/kg) was used as and when necessary. Minute ventilation and respiratory rate was adjusted in such a way to keep $ETCO_2$ around 35mm of Hg. After intubation all patients were given a nasogastric tube placement in order to ensure baseline emptying of air and gastric contents from stomach, which was withdrawn subsequently. 75mg of diclofenac sodium was administered intramuscularly before surgical draping in order to prolong and improve analgesia in the peri-operative period. During operation, the abdomen was insufflated with carbon dioxide, maintaining an intra abdominal pressure (IAP) limit of 15mmHg. The following parameters were continuously monitored intra operatively – pulse rate, systolic and diastolic blood pressure and mean arterial pressure, E.C.G. in lead II, SpO_2, $ETCO_2$. Intravenous Ringer's lactate was used for intra operative and immediate fluid management for first 4 hours. Intravenously Granisetron and Ramosetron were administered at the completion of surgery during

skin closure. Residual neuromuscular blockade was reversed with i.v neostigmine (0.05mg/kg) and i.v. glycopyrrolate (0.01mg/kg). Extubation was done after clinical assessment of complete reversal. Patients were shifted to the recovery area where standard recovery criteria were fulfilled.

All patients were closely monitored in the post-anaesthesia care unit for the first 0-4 postoperative hours and thereafter in the ward for 4- 48 hours. All of them received supplemental oxygen (6L/min) by face mask in the postoperative period for first 2 hours. Number of episodes and severity of postoperative nausea and vomiting in both the study groups was assessed at 0-4 hours, 4-24 hours, and 24-48 hours intervals.

The severity of postoperative nausea and vomiting was assessed by the following score where 0 = complete response (no PONV, no rescue antiemetic required), 1= only nausea, 2 = nausea with retching,3 = vomiting ***Complete response*** of prophylactic antiemetic was defined as no symptoms related to emesis and no need for rescue antiemetic within the study period. ***Nausea*** was defined as a subjective unpleasant sensation associated with an extreme urge to vomit. ***Retching*** was defined as rhythmic, laboured, spasmodic respiratory movements against a closed glottis with contractions of the abdominal muscles without any expulsion of gastric contents. ***Vomiting*** was defined as the rapid and forceful evacuation of stomach contents up to and out of the mouth. ***Rescue antiemetic*** was administered to all those patients who vomited 2 or more times or complained of nausea and/or retching lasting for at least 15 minutes. The drug used as a rescue antiemetic was metoclopramide 10mg intravenously. Frequencies of rescue antiemetics in these 2 groups was assessed. Incidences of any other *adverse effects* were assessed.

All results were statistically analyzed. Plan for statistical analysis: All clinical dates were tabulated and presented as Mean ± Standard Deviation. Demographic parameters like age, bodyweight, and data like duration of anesthesia and surgery in between group A & B were compared using unpaired t test. Post-operative parameters like SpO_2, respiratory rate, and pulse rate, systolic and diastolic blood pressure and postoperative nausea and vomiting score were compared using the appropriate test. The number of patients showing complete response, the episodes and severity of post-operative nausea and vomiting and those requiring rescue medications in between groups A & B are recorded and compared using Chi-square test. A p-value <0.05 was considered statistically significant.

Observations:

Table 1: Demographic data

	Groups			
	Group A	Group B		
Parameter	**Mean ± Std. Deviation**	**Mean ± Std. Deviation**	**p value**	**Significance**
Age (years)	32.05 ± 8.4	32.6 ± 8.89	0.777	Not Significant
Body Weight (kgs)	54.2 ± 5.71	54.57 ± 6.1	0.772	Not Significant

In our study, both the groups were comparable with regards to age (years) and body weight(kg) (P>0.05)

Table 2: Duration of Anaesthesia and Surgery of 2 groups

	Group			
	Group A	Group B		
Parameter	**Mean ± Std. Deviation**	**Mean ± Std. Deviation**	**p value**	**Significance**
Duration of Anaesthesia (minutes)	95.37 ± 20.08	94.88 ± 18.31	0.908	Not Significant
Duration of Surgery (minutes)	77.62 ± 20.22	78 ± 18.6	0.931	Not Significant

The differences between the mean duration of anesthesia and surgery amongst patients of group A and B were negligible and found to be statistically insignificant (P>0.05)

Table 3: Incidence of Nausea in post operative period

	Group				
NAUSEA	**Group A**	**Group B**	**Total**	**p value**	**Significance**
0 to 4 Hours	6(15)	4(10)	10(12.5)	0.499	Not Significant
4 to 24 Hours	5(12.5)	4(10)	9(11.2)	0.723	Not Significant
24 to 48 Hours	11(27.5)	3(7.5)	14(17.5)	0.019	Significant
Total 48 Hours	16(40)	11(27.5)	27(33.8)	0.237	Not Significant

This table shows the comparison of the incidence of nausea, between the groups A and B during the post operative period (0-48 hours) where the incidence of nausea was significant only in the last 24 hours (P=0.019) but in the total span it was found to be non-significant (P=0.234).

Figure 1: Bar diagram showing the incidence of nausea in post operative period

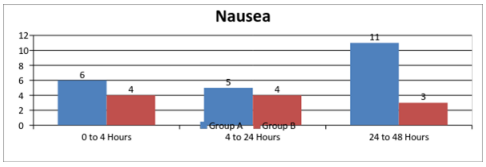

Table 4 : Incidence of vomiting in the post-operative period in 2 groups

	Group				
Vomiting	**Group A**	**Group B**	**Total**	**p value**	**Significance**
0 to 4 Hours	3(7.5)	2(5)	5(6.2)	0.644	Not Significant
4 to 24 Hours	3(7.5)	3(7.5)	6(7.5)	1.000	Not Significant
24 to 48 Hours	7(17.5)	2(5)	9(11.2)	0.077	Not Significant
Vomiting (48 hours)	11(27.5)	7(17.5)	18(22.5)	0.284	Not Significant

Table 5 shows the comparison of incidence of vomiting between the groups A and B in the post operative period where the difference between them was calculated to be non-significant in the entire 48 hours span(P=0.28)

Figure 2:Bar diagram showing of incidence of vomiting in the post operative period

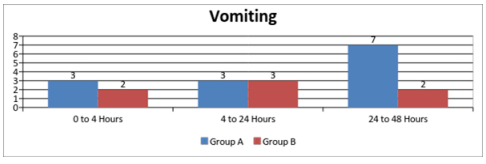

Table 5 : The complete response in the post operative period (48 hours) in 2 groups

	Group				
Complete Response	**Group A**	**Group B**	**Total**	**p value**	**Significance**
0 to 4 Hours	34(85)	36(90)	70(87.5)	0.499	Not Significant
4 to 24 Hours	35(87.5)	36(90)	71(88.8)	0.723	Not Significant
24 to 48 Hours	29(72.5)	37(92.5)	66(82.5)	0.019	Significant
Complete Response (48 Hours)	24(60)	29(72.5)	53(66.2)	0.237	Not Significant

This table compares the Complete Response to antiemetics among the patients of group A and B during the post operative period where the differences between the two groups was significant in last 24 hours but the differences in the total period of 48 pours was not statistically significant (p=0.237)

DISCUSSION

Postoperative nausea and vomiting (PONV) is a well-established entity, which has the potential to increase perioperative complications and morbidity. Kapur PA [1] has variously described PONV as the "big little problem", the "final therapeutic challenge" as well as the "big big problem" of ambulatory surgery.

Nowadays several gynaecologic procedures are done laparoscopically. PONV is a significant problem in these patients as they include multiple high risk factors for PONV such as female sex, non smokers, use of

volatile anaesthetics, use of N_2O, use of intra and post-operative use of opioids as well as duration of surgery more than 30 minutes.

5-HT_3 receptor antagonists are the preferred anti emetics because they are effective in prevention of PONV with fewer side effects. Granisetron which achieves its antiemetic property by acting on the 5-HT_3 receptors in the chemo-receptor trigger zone (CTZ)[5] has been found to be very effective by Wilson et al[6] for prevention of PONV. Moreover, Granisetron has been reported to be more efficacious and longer acting than Ondansetron by Dipasri et al[7] for prevention of nausea and vomiting in early postoperative period in patients undergoing day-care laparoscopic tubal ligation.

Ramosetron has been found to act through the same 5-HT_3 receptors and exhibited more potent and sustained antagonistic activities against 5-HT_3 receptors than the existing 5-HT_3 receptor antagonists[8]. It is also effective for the treatment of cisplatin-induced emesis. The exact mechanism of Ramosetron for prevention of PONV is unknown but may act at the area prostrema and nucleus tractus solitarius, which contain a large number of 5-HT_3 receptors. The affinities of 5-HT_3 receptor antagonist was compared to be Granisetron 1 vs. Ramosetron 41[9,10] and the elimination half-life was Granisetron 3.1±1.2 hrs versus Ramosetron 5.8±1.2 hrs[11.] In this present study, comparison and evaluation has been done ***between the efficacy of Granisetron and Ramosetron group*** for prevention of PONV following laparoscopic gynaecological surgery for a span of 48 hours.

The major deficiency in our study design was the failure to include a control group receiving placebo. It has been previously demonstrated that Granisetron is a better anti-emetic than placebo for preventing PONV in major gynecologic surgery. Aspinall and Goodman[12] have also suggested placebo controlled trial are unethical if active drugs are available because PONV are common and distressing symptoms against which there is an effective treatment. Therefore, a control group was not included in the study.

In our study, the incidence of nausea in 0-4 hour and 4-24 hour interval for Granisetron group were 15% and 12.5% respectively, while the incidences for nausea in the same time interval for Ramosetron group were 10% and 10% respectively. It was seen that in the last 24 hrs of the study period of 48 hours, 27.5% patients of the Granisetron group and only 7.5% patients from the Ramosetron group, ***complained of nausea.*** The differences between the study groups were found to be statistically significant (p=0.019) only in the last 24 hours but if the total span of 48 hours is considered the differences between the two groups were found to be insignificant (p=0.237).

It was noted in the study that 7.5% of Granisetron group and 5% of Ramosetron group vomited in the 0-4 hour interval and incidence of vomiting in the next 4-24 hour interval was 7.5% for both groups and finally 17.5% (7 out of 40) patients of the Granisetron group and only 5% (2 out of 40) patients from the Ramosetron group, ***vomited*** at the end of the study period of last 24 hours**.** The differences were found to be statistically insignificant (p=0.077) in the span of 48 hrs.

The ***complete response was noted*** in 72.5% patients of the Granisetron group and the response was 92.5% in patients who received Ramosetron. Statistical analysis suggested the difference between the Granisetron and the Ramosetron group was found to be statistically significant (p=0.019) only in the last 24 hours but in total 48 hours post operative span this difference was not statistically significant. Our findings were corroborated by a study conducted by Won Suk Lee et al[13] where comparison of palanosetron, granisetron, ramosetron for prevention of postoperative nausea and vomiting after laparoscopic gynaecological surgery was conducted and they concluded that two drugs granisetron and ramosetron were found to be equally effective in 48 hours post operative time span.

Incidence of adverse effects like ***headache***, was reported by 2 patients in both the Granisetron group and Ramosetron group. ***Dizziness*** was reported by 2 in the Granisetron group, however only 1 patient from the Ramosetron, no one in 2 groups was found to be ***sedated***. One patient from each group had ***postoperative shivering***, whereas there was no incidence of any hypersensitivity reaction or extra pyramidal symptoms in any of the treatment groups. The differences of the adverse events between the study groups were found to be statistically non-significant (p>0.05). None of the side effects needed treatment. Thus, Ramosetron, like Granisetron, is devoid of clinically important side effects and the findings corroborated with the previous studies.

In conclusion, prophylactic therapy with Ramosetron is equally effective as prophylactic therapy with Granisetron for the prevention of PONV in laparoscopic gynecological surgery.

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ORIGINAL ARTICLE

THE EFFICACY OF CLONIDINE ADDED TO BUPIVACAINE AS COMPARED WITH BUPIVACAINE ALONE USED IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES

Suchismita Pal[1], Tulsi Nag[2]

HOW TO CITE THIS ARTICLE:
Suchismita Pal, Tulsi Nag. "The Efficacy of Clonidine added to Bupivacaine as Compared with Bupivacaine Alone used in Supraclavicular Brachial Plexus block for Upper Limb Surgeries". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 41, September 04; Page: 10384-10391, DOI: 10.14260/jemds/2014/3349

ABSTRACT: INTRODUCTION: Clonidine when added 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. **MATERIALS AND METHODS:** Sixty patients aged 18 to 60 years, scheduled for elective orthopedic operations in the upper limb, of ASA Grade I or II were included in the study. We conducted the study with 2 groups consisting of 30 patients each to compare the effects of Clonidine added to Bupivacaine with Bupivacaine alone in supraclavicular brachial plexus block. First group received 40 ml of Bupivacaine 0.25% plus 0.15mg (1ml) of Clonidine, second group had 40 ml of Bupivacaine 0.25% plus 1 ml 0.9% Saline respectively. The onset as well as duration of sensory and motor block along with monitoring of heart rate, NIBP, oxygen saturation were recorded. The level of sedation and side effects were also noted. **RESULTS:** In this study the addition of Clonidine to Bupivacaine resulted in faster onset (study group 15.2±1.44, control group 20.4±1.12, $p<0.001$) and longer duration of sensory block (study group 544±31.2, control group 302±34.4, $p=0.0363$) as well as analgesia (study group 561.2±30.96, control group 324.4±34.08, $p=0.0001$) without any adverse hemodynamic changes.

KEYWORDS: Brachial plexus block, bupivacaine, clonidine.

INTRODUCTION: Acute postoperative pain is the result of a complex physiological reaction to tissue injury. The dorsal horn of the spinal cord is the site of termination of primary afferents and there is complex interaction between such afferent fibers, intrinsic spinal neurons, descending pain modulating fibers, and various associated neurotransmitters such as serotonin, norepinephrine, acetylcholine, adenosine, and glutamate in the dorsal horn.[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 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 Alpha-2 adrenergic agonist with some Alpha-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]

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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]

A number of these studies have focused on the effect of clonidine as adjuvant to either lignocaine[8] or mepivacaine.[7] further; these studies were done using clonidine 150 mcg, a moderately high dose with its attendant risk of adverse drug reactions. We have also compared this moderately high dose of clonidine versus placebo as adjuvant to bupivacaine for brachial plexus block, by supraclavicular approach, for orthopedic procedures of moderate duration in our population.

MATERIAL AND METHODS: The study was conducted in Ramakrishna Mission Seva Pratisthan, Vivekananda Institute of Medical Sciences. Written informed consent was obtained from all patients and the study was approved by the Institutional Ethics Committee.

Sixty patients aged 18 to 60 years, scheduled for elective orthopedic operations in the upper limb, under supraclavicular brachial plexus block, were included in this study. They were of American Society of Anesthesiologists (ASA) Grade I or II physical status. The procedures were of moderate duration and included implant removal, both bone plating, fixation of lower third of humerus and olecranon fixation.

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 study was designed as a prospective, randomized, double-blind, placebo-controlled trial. Participants were allocated to two equal groups of 30 each using a computer generated random number list. Group A (study group) patients received 40 ml of 0.25% bupivacaine and 0.15mg (1ml) clonidine, while group B (control group) received 40 ml of 0.25% bupivacaine and 1 ml of 0.9% sodium chloride through a supraclavicular approach for brachial plexus block. The allocation sequence was generated by the author entrusted with statistical analysis.

The anesthesiologist administering the injections and observing the effects received serially numbered sealed envelopes indicating the A or B codes for the anesthetic mixture to be administered. The A and B syringes were loaded with drug by another author not involved in administering the injections and in further evaluation of the patients. All observations (hemodynamic variables, oxygen saturation, level of sedation, time required to achieve surgical block in the operation theater and the time to rescue analgesic in the post-anesthesia care unit) were also recorded in a blinded manner.

Once a patient was brought into the operation theatre, standard monitoring was set up, including noninvasive arterial blood pressure, heart rate, and pulse oximetry. An 18-gauge IV cannula was inserted in the forearm and an infusion started with lactated Ringer's solution. The surgical procedure was performed by using a standard arm tourniquet inflated to 70 mmHg higher than systolic blood pressure. Hemodynamic variables were measured 10 min before block placement and every 15 min thereafter till the end of surgery.

Nerve blocks were performed, with the aid of a nerve stimulator, by using a 22G short-beveled, insulated (Teflon-coated) 50 mm long stimulating needle. Stimulation frequency was set at 2 Hz, while the intensity of stimulating current was initially set to deliver 1 mA and gradually decreased to < 0.5 mA. Negative aspiration was performed while injecting the drug solution to avoid any intravascular placement.

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The onset of sensory and motor blocks on the operated limb were evaluated every 5 min after the completion of anaesthetic injection by one of the authors who were unaware of the drug combination administered. Sensory block was assessed by pinprick discrimination (with 22G hypodermic needle) and motor block was evaluated by asking the patient to move the forearm against resistance and to flex the forearm. A pinprick sensation on the contralateral arm was scored as 100 points. Patients were requested to compare pinpricks in the primary innervation areas of the respective nerves in the anesthetized arm with the contralateral arm as reference.

The scale ranged from 100 points (full sensation) to 0 points (no sensation). Brachial plexus block was considered successful by Vester-Andersen's criteria [10] when at least two out of four nerve territories (radial, ulnar, median, and musculo cutaneous) were effectively blocked. Onset of sensory block was defined as a reduction of sensibility to 30% or less while onset of motor block was defined as reduction of muscle power to grade 3 or less.

The time to surgical blockade was defined as the time from the end of anesthetic injection to loss of pinprick sensation along the distribution of the ulnar and radial nerves along with inability to circumrotate the thumb of the concerned limb. When surgical anesthesia was not achieved in a patient even after 30 min from the anesthetic injection, the case was considered as failed block and the operation was then performed under general anesthesia.

Following operation, all patients were observed in post-anesthesia care unit and received rescue analgesic as soon as they complained of any pain. This consisted of inj. tramadol 100 mg IV, repeated if necessary. Patients were given clear instruction to ask for a rescue analgesic as soon as they sensed discomfort caused by pain on the operated hand. The time from the end of anesthetic injection in the operated hand till the first request for postoperative rescue analgesic was recorded in each patient.

The primary outcome measure was duration of analgesia. This was estimated as the time interval from placement of the block till first injection of rescue analgesic. Secondary outcome measures were onset and duration of sensory and motor blockade and any suspected adverse drug reactions.

Noninvasive arterial blood pressure, heart rate and oxygen saturation monitoring was done throughout the procedure. The degree of sedation was evaluated by using the University of Michigan Sedation Scale (UMSS)[11] of 0 to 4[0=awake and alert; 1 = minimally sedated/sleepy, appropriate response to conversion and/or sound; 2 = moderately sedated, somnolent/sleepy, easily aroused with tactile stimulation and/or simple verbal command; 3 = deeply sedated/deep sleep, aroused only with significant stimulation and 4 = could not be aroused].

All patients were clinically assessed during discharge from the orthopedic ward and again after 3 weeks (at the first routine postoperative examination) for occurrence of any neurological complications.

All 30 patients in the two groups were considered for adverse event analysis. However, subjects who failed blocks were excluded from effectiveness assessment.

Duration of analgesia was taken as the outcome measure of interest for the purpose of sample size calculation. It was estimated that 23 subjects would be required per group in order to detect a difference of 30 min in this parameter between the two groups, with 90% power and 5% probability of Type 1 error. This calculation assumed a pooled standard deviation of 30 min for the duration of analgesia.

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Data are summarized as mean ± standard deviation or as percentages. Statistical analysis was performed by MS Excel 2010 software. Comparison of categorical variables between the two groups was by Chi-square test. Numerical variables were normally distributed and were compared by Student's unpaired' test. All analyses were two-tailed and $P < 0.05$ was considered statistically significant.

RESULTS: We recruited 30 subjects per group, more than the calculated sample size. The age, sex distribution, body weight and the duration of surgery in the two groups were found to be comparable (table1).

Table 2 shows onset and duration of sensory and motor blocks and post-operative requirement of rescue analgesia. It was found that the onsets of both sensory and motor blocks were significantly shorter in group A and durations of sensory block were also significantly greater in this group receiving clonidine. Requirement of rescue analgesia was delayed. The mean time from block placement to the first request for pain medication i.e. duration of analgesia was 561±30.96 min in the clonidine group but 324.4±34.08 min in the other group. This difference was highly significant ($p<0.001$) statistically as well as clinically.

Regarding time to onset of surgical block, this was also faster by 6 minutes in the clonidine adjuvant group A.

No statistically significant difference was observed in heart rate, blood pressure, and oxygen saturation between the two groups at any time.

The sedation score between clonidine and the control group was comparable throughout the study period. All the patients were alert (sedation score 1) in both the groups at all times of observation.

Adverse effect was observed in any of the groups.

	GROUP A	GROUP B
SEX (F/M)	12/18	14/16
AGE (years)	38.8±11.3878	38.6±11.975
HEIGHT (cms)	161.8±7.967	161±5.965
WEIGHT (kgs)	59.8±7.087	57±7.0466

TABLE 1. COMPARISON OF THE DEMOGRAPHIC DATA

	Onset of sensory block (min)	Onset of motor lock (min)	Duration of sensory block (min)	Duration of motor block (min)	Duration of analgesia (min)
Bupivacaine and clonidine (GROUP A)	15.2±1.44	17.2±1.44	544±31.2	464±39.2	561.2±30.96
Bupivacaine only (GROUP B)	20.4±1.12	22.4±1.12	302±34.4	260±32	324.4±34.08

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	p<0.001	p<.001	p=0.0363	p=0.2946	p=0.0001

Table 2. COMPARISON OF ONSET OF SENSORY AND MOTOR BLOCK, DURATION OF SENSORY, MOTOR, ANALGESIA BETWEEN GROUP A AND B

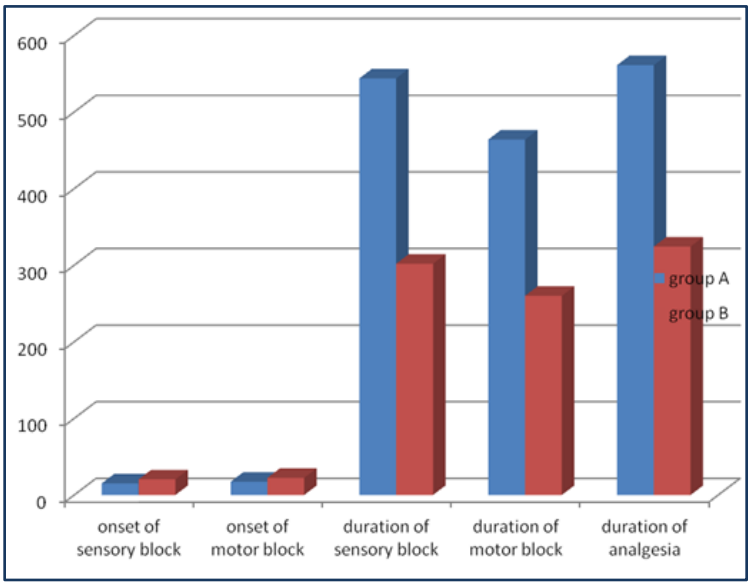

Fig.1 : Bar diagram representing table 2

diastolic BLOOD PRESSURE	(mm of Hg)										
	BASELINE	15min	30min	45min	60min	75min	90min	105min	120min	240min	480min
group A	80.06667	73.73333	76.43333	77.8	75.76667	79.6	78.2	78.8	77.5	78.5	76.7
groupB	78.93333	72.43333	74.93333	75.06667	74.23333	76.6	76.1	75.73333	76.23333	77.03333	74.86667

Table 3: Comparison of diastolic blood pressure between 2 groups

SYSTOLIC BLOOD PRESSURE (mm of Hg)											
	BASELINE	15min	30min	45min	60min	75min	90min	105min	120min	240min	480min
group A	130.5667	128.0333	129.2333	127.9	129.6	128.2	129.5667	130.7	130.3667	130.2333	129.9667
group B	130.5667	128.0333	129.2333	129.7667	132.8667	132.7333	129.5667	130.7	130.3667	130.2333	129.9667

Table 4: Comparison of systolic blood pressure between 2 groups

HEART RATE											
TIME	BASELINE	15	30	45	60	75	90	105	120	4 HRS	8HRS
group A	77.6	73.8	74.6	75.2	74.6	73.6	75.2	76.8	77.2	79	80.03333
group B	77.6	75.4	73	73.2	74.2	74.6	75.4	75.6	78	80.8	81.83333

Table 5: Comparison of heart rate between group A & B

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SPO2											
	BASELINE	15min	30min	45min	60min	75min	90min	105min	120min	240min	480min
group A	97.36667	98.86667	98.83333	98.86667	98.76667	98.96667	98.9	98.83333	98.9	97.4	97.6
group B	98.2	98.8	99	98.9	98.8	98.76667	98.8	99	98.8	98.2	98

Table 6: Comparison of saturation of oxygen between group A &B

DISCUSSION: The result of the present randomized controlled trial clearly suggests that clonidine, as adjuvant to 0.25% bupivacaine for supraclavicular brachial plexus block, prolongs the duration of analgesia as well as motor block. Onset times of blocks were also shown to be shortened though the study was not powered to measure these effects.

These findings are at variance with 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. [12] 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. More explanations may be forthcoming when the mechanism of adjuvant action of clonidine in this setting is elucidated.

Bernard and Macarie,[8] evaluating the effects of adding 30-300 μg clonidine to lignocaine for axillary brachial plexus anesthesia, reported that the addition hastened the onset of the block and improved the efficacy of surgical anesthesia. There are reported differences in the effects of administration of low-dose clonidine on time of onset and efficacy of nerve block, which may be explained by differences in the type of nerve block, exact mixture injected, and technique used to perform the block (single injection versus multiple injections). In fact, a multiple-injection technique was used, which is known to improve both onset time and quality of nerve block, [13] and this could have reduced the differences in onset time between the two groups.

In a dose-finding study evaluating the minimum effective dose of clonidine required to prolong duration of analgesia after axillary brachial plexus block, Singelyn et al[7] suggested that 0.5 μg/kg clonidine should be used. At this dose, significant prolongation of analgesia was achieved without undue sedation, hypotension, or bradycardia. It has been widely demonstrated in different studies that subcutaneous or intramuscular injection of clonidine is not as effective as perineural administration[14] suggesting that the local anesthetic-prolonging effect of clonidine is probably mediated locally at the neuron.[15]

This may also explain the variation in response in different types of peripheral nerve blocks, probably related to the rate and extent to which the injected anesthetic solutions penetrate into the nerve.[10] Even though injecting clonidine as the sole analgesic into the brachial plexus sheath does not provide clinically relevant analgesia,[16] it has been demonstrated to inhibit the action potential of A and C fibers in de-sheathed sciatic nerves.[9] Many authors favor the hypothesis that clonidine exerts its local anesthetic-prolonging effect directly on the nerve fiber, as a result of complex interaction between clonidine and axonal ion channels or receptors.[5,10,14] Peripheral antinociception induced by clonidine has also been related to 2-adrenoceptor-mediated local release of enkephalin-like substances.[17]

We selected a 150 µg dose of clonidine keeping in mind the hemodynamic adversities that might be produced. It was found that this dose provided satisfactory prolongation of the duration of analgesia without producing significant hemodynamic compromise in the patients. But we need a dose finding study to come up with the ideal dose of clonidine as adjuvant to 0.25% bupivacaine for supraclavicular brachial plexus block.

In conclusion, clonidine added to bupivacaine is an attractive option for improving the quality and duration of supraclaicular brachial plexus block in upper limb surgeries.

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AUTHORS:

1. Suchismita Pal
2. Tulsi Nag

PARTICULARS OF CONTRIBUTORS:

1. Resident Medical Officer (R.M.O) Cum clinical Tutor, Department of Anaesthesiology, Institute of Post Graduate Medical Education & Research (I.P.G.M.E & R), Kolkata.
2. Professor, Department of Anaesthesiology, Vivekananda Institute of Medical Sciences, Kolkata.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Suchismita Pal,
3A, Christopher Road,
Kolkata - 700014.
Email: piu.suchismita.pal@gmail.com

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