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Analgesic Efficacy of Addition of Clonidine to Bupivacaine in Transversus Abdominis Plane Block for Postoperative Analgesia in Laparoscopic Appendicectomy

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Abstract

Background and Objectives: Transversus abdominis plane block is widely practised peripheral nerve block and has been shown to provide postoperative pain relief following various abdominal surgeries. Proper pain management is essential for optimizing clinical outcomes and early ambulation post operatively. Alpha-2 agonists are mixed with local anesthetic agents to extend the duration of spinal, extradural and peripheral nerve blocks. We compared addition of clonidine as an adjuvant to bupivacaine in transversus abdominis plane block with respect to duration of analgesia and total analgesic requirement in 24 hours.

Methods: Sixty ASA I and II patients scheduled for elective or emergency laparoscopic appendicectomy were divided into two equal groups in a randomized double-blinded fashion. Group B received bilateral USG guided TAP block with 15ml of 0.25% bupivacaine (total of 30ml). Group C received bilateral USG guided TAP block with 15ml of 0.25% bupivacaine + clonidine 1mcg/kg (total of 30ml + clonidine 2mcg/kg). Duration of analgesia and total analgesic requirement in 24 hours were studied. Hemodynamic parameters like pulse rate, systolic and diastolic BP and possible side effects were observed.

Results: Duration of analgesia in Group B and Group C was 11.18 ± 2.51 hrs and 19.73 ± 2.33 hrs respectively. Total analgesic requirement in 24-hours in Group B and Group C was 2.63 ± 0.67 and 1.20 ± 0.48 respectively.

Conclusion: Clonidine as an adjunct to bupivacaine in bilateral USG guided TAP block provides prolonged and sustained pain relief with reduced analgesic requirement and lesser side effects as compared to bupivacaine alone.

Keywords: TAP Block; Clonidine; Bupivacaine; VAS; Postoperative Analgesia.

Introduction

Laparoscopic appendicectomy is one of the most common surgical procedures and patients undergoing surgery suffer significant postoperative pain and require effective analgesia.[1] Proper pain management is essential for optimizing clinical outcomes and early ambulation post operatively. Post operative pain in acute appendicitis is mainly caused by surgical wound and viscero-peritoneal pain due to peritoneal insufflation.[2]

Transversus abdominis plane (TAP) block is one of the newer regional anesthetic technique that blocks the anterior abdominal wall neural afferents(T7-T11) and significantly reduces the pain associated with it.[3]

Local anesthetic agents are deposited in neuro-fascial plane between internal oblique

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and transversus abdominis muscle via needle inserted through the lumbar triangle of Petit under ultrasound guidance.[1,4]

The block was first described by Rafi in 2001.[5] The USG guided TAP block was described by Hebbard and colleagues[6] in 2007. The conventional TAP block is performed at so-called "Triangle of Petit" is bounded anteriorly by external oblique muscle (EOM), posteriorly by latissimus dorsi muscle and inferiorly by iliac crest, by advancing the needle for "double pop" or "pop" sensation of puncturing fascia to inject the local anaesthetic.[7,8]

Different adjuvants have been studied to improve the efficacy and to increase the duration of local anesthetic action in various nerve block techniques. Although opioids have been found to have effect on peripheral receptors, studies related to their effect as an additive to local anesthetic for TAP block are lacking.

Clonidine is an alpha agonist and an anti-hypertensive agent with properties of analgesia and sedation when given intravenous was used in this study as an adjuvant for prolonging the duration of TAP block, as it is cost effective and easily available.

Fatal complication like bowel puncture and hepatic injury have been reported while performing TAP Block.[9] These complications are now reduced by performing ultrasound guided TAP block, since precise location of needle and diffusion of local anesthetics can be directly observed by this technique.

The present study was planned to investigate whether addition of 1mcg/kg of Clonidine to 0.25% Bupivacaine in in bilateral USG guided TAP blockincreases the duration of postoperative analgesia in Laparoscopic appendicectomy as compared to 0.25% bupivacaine alone.

Material and Methods

This study was conducted in multi-speciality tertiary care teaching hospital associated with medical college. After approval by college ethical committee, study was conducted from April 2018 till August 2019.

Study design

This study was a prospective randomized double blind study.

Study population

A total of 60 patients of ASA I and ASA physical status undergoing elective or emergency laparoscopic appendicectomy were taken in the study. They were divided in two equal groups with 30 patients in each group by random chit method.

Group B (n=30) received bilateral USG guided TAP block with 15ml of 0.25% bupivacaine (total of 30 ml).

Group C (n=30) received bilateral USG guided TAP block with 15ml of 0.25% bupivacaine + clonidine 1 mcg/kg (total of 30 ml + clonidine 2 mcg/kg).

Inclusion Criteria

Patients belonging to ASA grade I and grade between the age groups 18-60 years weighing > 50 kg scheduled for elective/emergency laparoscopic appendicectomy.

Exclusion Criteria

- Patient not willing.
- Patients with history of chronic pain condition with analgesic usage on regular basis.
- Patients with known allergy to drugs used in the study .
- Patients who are mentally handicapped.
- Patients with localized infection at site of block.

Methodology of Study

All patients were evaluated preoperatively as per the proforma and were familiarized with Visual analogue scale (VAS) score.Written informed consent was obtained after explaining the procedure and NPO guidelines were followed in both the groups. Intravenous line was setup in ward. The patient and the investigator were kept unaware of the group allocated and standard protocol of GA was followed in both the groups as follows:

Preoperative

Inj. Glycopyrrolate 0.2 mg IV in preoperative room as premedication. Patient was then taken in Operation theatre. Multiparameter monitor (NIBP, SPO_2, ECG and HR) was attached. Premedication was done with Inj. Midazolam 1 mg IV and Inj. Fentanyl 1mcg/kg IV in both the groups. Pre oxygenation with 100% O_2 was done for 3 minutes. Induction was done with Inj. Thiopentone Sodium

5 mg/kg IV slowly. Intubation was done under effect of Inj. Succinylcholine 2 mg/kg IV under direct laryngoscopy with cuffed endotracheal tube of appropriate size.Intravenous fluid was started according to Holiday and Segar formula. (<10kg=100kcal/kg/day,10–20kg=1000kcal+50 calorie for each kg over 10kg, >20kg=1500kcal+20 calorie for each kg over 20kg.)

Maintenance

Was done on O_2 + air + Sevoflurane with intermittent Inj. Vecuronium 0.08mg/kg IV and intermittent positive pressure ventilation with closed circuit.After completion of the surgical procedure, bilateral USG guided TAP block was given as mentioned with 23 G spinal needle, before reversal of Neuromuscular blockade.At the end of procedure, reversal was done with Inj. Neostigmine 0.04mg/kg I.V. + Inj. Glycopyrrolate 0.01mg/kg IV.Extubation was done after fulfilment of extubation criteria.

Postoperative

The patients was assessed at interval of 30 min for first hour, 1 hourly till 6th hour then 6 hourly till 24hours.Pain severity was measured using VAS score(1-none,2-mild,3-moderate, 4-severe) patients was given analgesia on VAS score >4 . Inj. Dynapar 75mg IV in 100ml Normal saline was used as rescue analgesia.Sedation was evaluated using a four-point ordinal scale. Other associated side effects such as dryness of mouth, hypotension(SBP<20%of baseline),and bradycardia(HR<60/min) were observed.

Ordinal scale for sedation[3]

Grade	Ordinal scale
1	wide awake and alert
2	awake but drowsy responding to verbal stimulus
3	arousable, responding to physical stimulus
4	not arousable, not responding to physical stimulus

A note of the total analgesic need for the first 24hours was recorded after the USG guided TAP block. The TAP block was considered to be fail if rescue analgesia was needed within 2 hrs of block.

Statistical analysis[10,11,12]

The inter-group comparison of categorical variables is performed using Chi-square test / Fisher's exact probability test. The statistical significance of inter-group difference of mean of continuous variables is tested using independent sample 't' test or unpaired 't' test. The underlying normality assumption is tested before subjecting the study variables to 't' test. The entire data is entered and cleaned in MS Excel before it's statistical analysis. All the results are shown in tabular as well as graphical format to visualize the statistically significant difference more clearly.

The p-values less than 0.05 were considered to be statistically significant. All the hypotheses were formulated using two tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS ver. 16.0, IBM Corporation; NY, USA) for MS Windows.

Results

Sixty patients posted for elective/emergency laparoscopic appendicectomy were assessed for suitability to enroll in the study. Two patients were excluded from the study as analgesic was given in immediate postoperative period. Patients fulfilling the inclusion criteria were randomly assigned to one of the two groups. Standard protocol were followed in all groups.

Table 1: Patient characteristics.

Variable	Group B Mean± SD	Group C Mean± SD	P value
Age (years)	28.53 ± 7.62	28.53 ± 9.58	0.999NS
Weight (kg)	62.40 ± 9.12	65.00 ± 7.17	0.224NS
Gender (M/F)	17/13	16/14	0.795NS
ASA grade(I/□)	24/6	25/5	0.999NS
Duration of surgery (hours)	2.875 ± 0.278	2.868 ± 0.253	0.459NS

(P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.)

Both groups were comparable in terms of age, gender, weight, ASA grading and duration of surgery. (Table 1) (P> 0.001)

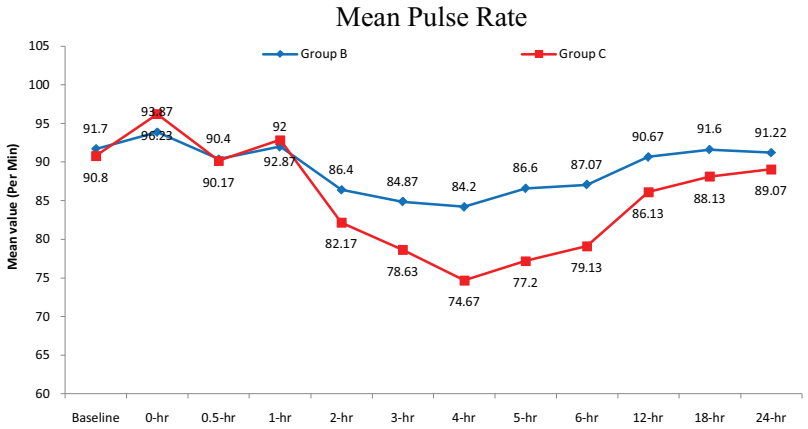
Table 2: Baseline parameters.

Variable	Group B Mean± SD	Group C Mean± SD	P value
VAS	3.0	3.0	0.470^{NS}
Pulse (per min)	91.70	90.80	0.062^{NS}
Systolic BP (mmHg)	123.33	122.47	0.450^{NS}
Diastolic BP (mmHg)	79.07	76.33	0.054^{NS}
Respiratory rate (per min)	16.07	16.13	0.656^{NS}
Spo2(%)	98.70	98.53	0.470^{NS}

(P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.)

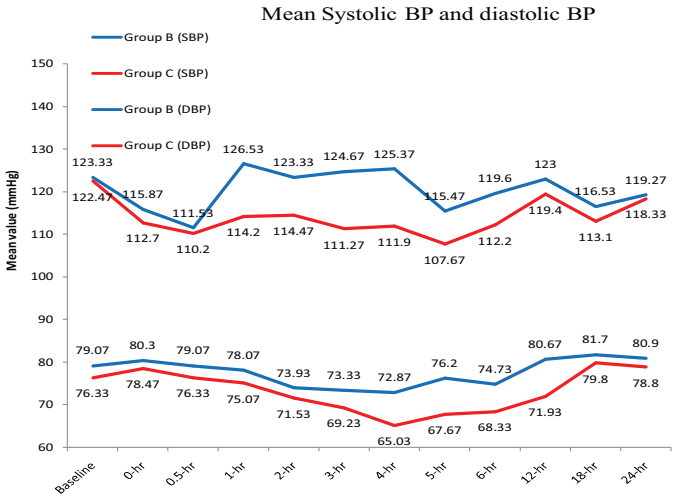
The baseline parameters like pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate, SPO2 and mean VAS were also comparable in both the groups (Table 2).

Graph 1: Mean pulse rate.



Distribution of mean pulse rate at 2-hr, 3-hr, 4-hr, 5-hr and 6-hr postoperatively among the cases studied was significantly higher in Group B compared to Group C (P-value<0.05 for all).(Graph 1).

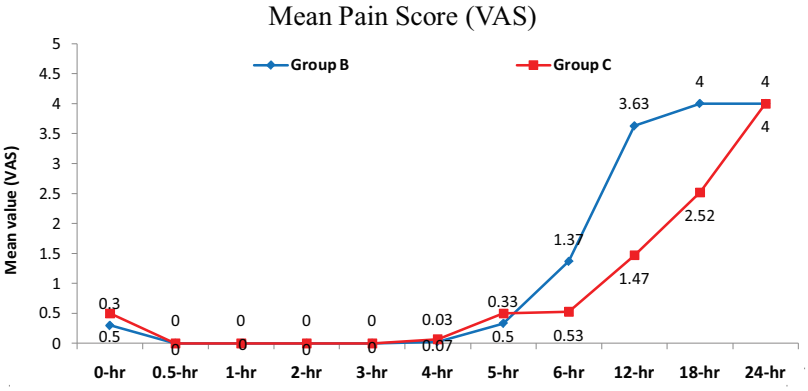
Graph 2: Mean systolic BP and diastolic BP.



Distribution of mean systolic BP at 1-hr, 2-hr, 3-hr, 4-hr, 5-hr, 6-hrand 12-hr postoperativelyamong the cases studied was significantly higher in Group B compared to Group C (P-value<0.05 for all).

Distribution of mean diastolic BP at 3-hr, 4-hr, 5-hr, 6-hr and 12-hr postoperatively among the cases studied was significantly higher in Group B compared to Group C (P-value<0.05 for all). (Graph 2).

Graph 3: Mean pain score.



The baseline VAS was comparable in both groups. VAS score in both groups did not differ upto 5-hr. In 6-hr there was comparable difference in VAS between both groups after which group B required rescue analgesia . Group C had better VAS upto 12-hr and 18-hr, after which rescue analgesia was given. At 24-hr VAS did not differ between both the groups (Graph 3).

Table 3: Duration of analgesia.

No. of hrs of analgesia (Hrs)	Group B (n=30)		Group C (n=30)		P-value
	Mean	SD	Mean	SD	
No. of hrs of analgesia (Hrs)	11.18	2.51	19.73	2.33	0.001***

Values are mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant. ***P-value<0.001.

The mean ± SD of No. of hrs of analgesia among the cases studied in Group B and Group C was 11.18 ± 2.51 hrs and 19.73 ± 2.33 hrs respectively. (P-value<0.001) (Table 3).

Table 4: Total analgesic doses.

Total analgesic doses in 24-hrs	Group B (n=30)		Group C (n=30)		P-value
	Mean	SD	Mean	SD	
Total analgesic doses in 24-hrs	2.63	0.67	1.20	0.48	0.001***

Values are mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant. ***P-value<0.001.

The mean ± SD of Total analgesic doses in 24-hrs among the cases studied in Group B and Group C was 2.63 ± 0.67 and 1.20 ± 0.48 respectively. (P-value<0.001) (Table 4).

Discussion

The advances in surgical techniques and the development of newer anesthetics techniques have enabled the current rapid growth of outpatient surgical procedures. With recent development of technology and endoscopic surgical intervention, the patient satisfaction and outcomes have been better.

Acute appendicitis is one of the most common causes of acute abdomen. Appendicectomy remains the "gold standard" in management of acute appendicitis. Minimally invasive laparoscopic intervention is preferred. Pain due to surgery is lesser compared to open surgical method.

Pain interferes with recovery and rehabilitation. Adequate pain relief is an important aspect of post operative care. This is important not only for psychological well being of patient, but also decreases the stress response to surgery and favors a better outcome. It facilitates rehabilitation and accelerates recovery from surgery.

Different post-operative pain relief modalities like enteral, parenteral analgesics, regional blocks i.e central neuraxial block and peripheral nerve blocks are available, having their own advantages and disadvantages.

Transversus Abdominis Plane block has been used as a multimodal strategy to optimize post operative pain outcomes. Many additives are added like opioids, dexamethasone, dexmeditomedine, clonidine etc. to prolong the duration of peripheral nerve blocks.

Many previous investigations have reported the analgesic benefit of TAP block in patients undergoing lower abdominal surgeries including laparoscopic appendicectomy, but very few used clonidine as an additive to local anesthetic.

This study was formulated with an aim to compare the efficacy of clonidine as an additive to 0.25% bupivacaine in transversus abdominis plane block for postoperative pain relief.

The demographic profile of patients in our study was comparable in relation to age, gender, ASA grade, mean body weight and mean duration of surgery (Table 1).

The intergroup comparison of mean pulse rate, SBP, DBP were comparable between two groups. Distribution of mean pulse rate was significantly lower in Group C varying between 70-90 beats/ min, but none showed bradycardia of < 60beats/ min requiring intervention (Graph 1). Similarly mean systolic blood pressure and mean diastolic blood pressure showed significant difference from 1-hr to 12-hr and 3-hr to 12-hr respectively, which was lower in group C (Graph 2). Mean pulse rate, SBP and DBP did not show significance at 18-hr and 24-hr as group B was receiving Diclofenac injection. Similar observations were made by B Manju Sruthi et al[13] in 2019, they concluded that there is dose dependent variation in vitals. Higher doses of clonidine showed dose dependent adverse effects like hypotension and bradycardia.

The baseline VAS was comparable in both groups. VAS score in both groups did not differ upto 5-hr. In 6-hr there was comparable difference in VAS between both groups after which group B required rescue analgesia . Group C had better VAS upto 12-hr and 18-hr, after which rescue analgesia was given. At 24-hr VAS did not differ between both the groups. (Graph 3).

The mean duration of analgesia in group B was 11.18 ± 2.51 hrs while in group C it was 19.73 ± 2.33 hrs (Table 3). Similar observations were made by Ranjusinghet al[3] in 2016, they observed that addition of clonidine in bilateral TAP block for post operative analgesia in caesarean section significantly increased duration of analgesia. They observed that duration of analgesia was longer in clonidine group (17.8±3.7 hours) compared to bupivacaine alone group (7.3±1.2 hours). Similar observations were made by Deshpande JP et al[14] in 2017 ,Mehmet Aziretet al15 in 2018 and Kayla Krajicket al[16] in 2019, they observed that TAP block provided lower VAS and better analgesia.

The total analgesic consumption was comparable in both the groups (Table 4). The total requirement of Diclofenac in group B was 2.63 ± 0.67 mg (197.25 mg) and group C was 1.20± 0.48 mg (90 mg). There was almost 50% reduction in analgesic consumption in group C. Similar observation were seen by Ranjusinghet al[3] in 2016 , they observed that the mean consumption of diclofenac in group with bupivacaine alone was 150 mg and group with clonidine was 65.5mg in 24 hours. Also Zanghiet al[17] in 2015 observed that TAP Block with bupivacaine and clonidine after laparoscopic cholecystectomy resultedin effective pain control and decreased post operative analgesic requirements.

There were nocomparable adverse effects. In group B ,three candidates had nausea/vomiting and in group C four showed similar effects. It can be attributed to patient and surgery related factors like peritoneal handling and fasting period.

Other known side effects of clonidine like bradycardia, hypotension and dry mouth requiring intervention was not observed. Similarly, Zanghiet al[17] in 2015 observed no clonidine related side effects like hypotension, bradycardia and sedation when clonidine was given as adjunct in TAP block for postoperative analgesia after laparoscopic cholecystectomy.

Studies conducted by Rakesh Dhupia et al[18] in 2017 and B Manju Sruthi et al[13] in 2019 observed dose dependent increase in side effects when two different doses of clonidine were compared in TAP block. They compared addition of 150 mcg and 300 mcg and 75 mcg and 150 mcg respectively. The lower dose of clonidine i.e 1 mcg/kg produced effective analgesia without adverse effects .

Contrary to our study, Bollaget al[19] in 2012 observed wound hyperalgesia and long term pain descriptions after cesarean delivery in women receiving an USG guided bilateral TAP block with 0.375% bupivacaine with 75mcg clonidine on each side. They concluded that performing a TAP block with or without clonidine does not appear to offer any benefits in chronic pain description after 12 months. But it provided significant reduction in hyperalgesia index in 48 hrs and reduction in analgesic consumption in clonidine group.

Thus in our study it was observed that the TAP block with bupivacaine and clonidine as an additive provided better postoperative analgesia and lesser total requirement of analgesic in 24 hours when compared with bupivacaine alone with no incidence of significant side effects in either groups.

We recommend that additional studies using ultrasonography and different drug combinations and doses of local anesthetics for TAP block can be done.

Conclusion

Clonidine as an adjunct to bupivacaine in bilateral USG guided TAP block provides prolonged and sustained pain relief with reduced analgesic requirement and lesser side effects as compared to bupivacaine alone.

Limitations

1. The first limitation of our study was small sample size.
2. Second limitation was that we used intermittent Dynapar as rescue analgesic, the use of Patient controlled analgesia (PCA) Pump in the postoperative period would have given better idea in assessing analgesic requirement more precisely.
3. The results of our study may vary as compared to other studies due to variable ethnic population as pain tolerance may vary.

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