Original Article

The analgesic efficacy of ultrasound-guided transversus abdominis plane block vs. local anesthetic infiltration technique in major gynecologic surgery: A randomized controlled trial

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Abstract

Background and Aim: Transversus abdominis plane (TAP) block and local anesthetic infiltration (LAI) technique are used as part of the multimodal analgesic regimen after abdominal surgery. Postoperative opioid consumption and analgesic efficacy was compared using TAP and LAI techniques in patients undergoing gynecologic surgery in a randomized, controlled clinical trial.

Material and Methods: Total of 135 patients scheduled for major gynecological surgeries were allocated into three groups: group T received bilateral TAP block with bupivacaine 0.25%; group I received LAI with 0.25% bupivacaine with epinephrine 5 μ/mL in the peritoneum and abdominal wall, and group C was control group. Anesthesia and postoperative analgesia were standardized. Outcome measures were cumulative and rescue tramadol consumption, numerical rating score (NRS) for pain and side effects in post-anesthesia care unit (PACU) at 4, 8, 12 hours postoperatively.

Results: Tramadol consumption, need for rescue analgesia, and NRS for pain between three groups at 4, 8, and 12 hours postoperatively had no statistically significant difference ($P < 0.05$). In PACU, median tramadol consumption used for rescue analgesia between group T (15 (15–30)) and group C (30 (15–45)) ($P = 0.035$), and between group T (15 (15-30)) and group I (30 (15-52)) was statistically significant ($P = 0.034$). In PACU, the percentage of patients having NRS >4 on movement in group C (72%) compared to group T (46.5%) and group I (46.5%) was significant ($P = 0.034$). No statistically significant difference was observed in the incidence of side effects among study groups ($P > 0.05$).

Conclusion: Except for the immediate postoperative period, neither TAP block nor LAI had added benefit to the multimodal analgesia regimen in patients undergoing gynecological surgeries.

Keywords: Low- and middle-income countries, multimodal analgesia, opioid availability, opioid consumption, opioid sparing strategies, postoperative pain management

Introduction

Major gynecological surgeries are abdominal procedures where reported incidence of pain ranges in intensity from moderate to severe.[1] Pain management after gynecological surgeries is specially challenging due to the complex innervation of the uterus, ovaries, and vagina.[2] Till date, opioid analgesics remain the drug of choice, particularly in low- and middle-income countries (LMIC). Although they provide good pain control, they are associated with adverse effects.[3–5] There is also a dearth of good quality opioids in these countries, as only 0.1 metric ton of morphine out of total 298.5 metric tons is distributed in LMIC.[3]

Combinations of various analgesics and/or regional analgesic techniques have been utilized to reduce opioid consumption and

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improve analgesia.[3,6] Transversus abdominis plane (TAP) block, a regional analgesia technique, has proven to be an effective and safe technique when used as a part of the multimodal analgesia for postoperative pain management in gynecological surgeries.[7–10] However, TAP block requires expertise and use of ultrasound (US) to optimize success rates and efficacy.

In contrast, a more traditional approach of local anesthetic infiltration (LAI) either into the abdominal wall or into the peritoneal cavity remains a favored postoperative pain relief method by surgeons.[11] Studies have shown mixed results regarding the efficacy of LAI in terms of reduction of postoperative opioid consumption in patients undergoing gynecological surgeries.[12–14]

A recent meta-analysis published in 2020 found comparable results between TAP block and LAI for short-term analgesia in the postoperative period after abdominal surgeries; however, TAP block was found to have a better long-lasting effect.[15] Out of 15 studies, only three targeted gynecological surgeries,[8,16,17] highlighting the scarcity of evidence regarding the efficacy of regional anesthetic techniques in gynecological surgeries. Therefore, the rationale for conducting the present study was to add to the limited available evidence on the role of TAP block and LAI in gynecological surgeries while trying to find the best opioid-sparing strategies in this group of patient populations.

The primary objective was to evaluate opioid-sparing effect of TAP block versus LAI when compared to control group after major gynecological surgeries. The secondary objectives were to assess the analgesic efficacy by observing the pain scores and safety or tolerability by observing the occurrence of side effects among three groups of patients.

Material and Methods

This prospective double-blinded, randomized study was conducted in a tertiary care hospital. Approval was obtained from the Ethical Review Committee (ERC no: 2019-1191-3325) on 19 April 2019.

After getting the ERC and University research grant approvals, registration of this clinical trial was done at http://clinicaltrials.gov (NCT04037878) in July 2019. Recruitment of patients was started from August 2019 to June 2020.

Patients scheduled for elective surgeries and meeting the inclusion criteria received information about the trial at the gynecology clinic. Inclusion criteria included patients belonging to the American Society of Anesthesiologists (ASA) class I to III, belonging to the age group 30–65 years, having weight ranging from 50–90 kg, and scheduled for gynecological surgeries via Pfannenstiel incision of abdominal wall. Surgeries that were included in the study were the following: myomectomy, total abdominal hysterectomy, and ovarian cystectomy/oophorectomy. Patients were excluded from the study if they refused to participate, had history of bleeding disorders, drug allergy, abdominal skin infections, or were on blood thinners. Patients fulfilling the inclusion criteria were asked to sign the consent form either in the clinic or at the time of hospital admission. Patients were enrolled in the study on the day of surgery and explained the use of patient control intravenous analgesia (PCIA) pump and numerical rating score (NRS) for pain.

Computer generated randomization sequence (http://www.randomization.com) was used for randomization using balanced permutation blocks of 15, by clinical trial unit at AKUH. Sealed opaque envelopes with the randomization number were used for allocation of patients to either of the three groups: peritoneal/abdominal wall infiltration group (group I), TAP block group (group T), or control (group C). There were 45 patients randomly allocated to each group giving a total sample of 135 patients. Patients and postoperative assessment teams were blinded to the treatment groups.

Patients were not provided with preoperative sedatives or analgesics. General anesthesia was given to all study participants with intravenous tramadol 1 mg/kg (Searle Pharmaceuticals Limited, Karachi, Pakistan), intravenous propofol 2 mg/kg (Dongkook Pharmaceutical Company Limited, South Korea), and intravenous atracurium 0.5 mg/kg (Brookes Pharma Limited, Karachi, Pakistan). Maintenance of anesthesia was provided with 0.4 oxygen/0.6 air with isoflurane (Piramal Critical Care, Inc. Bethlehem, Pennsylvania, USA) maintained at minimum alveolar concentration (MAC) of 1% to 1.2%. Intraoperatively any increase of heart rate and blood pressure to more than 20% of baseline was treated with additional doses of 10–20 mg intravenous tramadol. Intraoperative monitoring was done at 10-minute intervals and was recorded on the intraoperative chart. One copy of it was kept by the investigators for record keeping.

In group T, study participants received ultrasound (US)-guided TAP block after induction of anesthesia by one of the two identified anesthesiologists. The US machine used was Mindray M7 and US probe used was a 7L4s probe, 38-mm linear array with a frequency of 13 to 16 MHz (both from Bio-Medical Electronics Company Limited, Shenzhen, China). US-guided mid-axillary lateral approach was used for performing TAP block. The technique, as described

by Hebbard *et al.*,[18] involved positioning the probe in the axial plane of mid-axillary line, midway between the costal margin and the iliac crest. TAP block under real-time ultrasound guidance was performed using Stimuplex A insulated short bevel needle with length of 150 mm and gauge of 20 mm (B. Braun Melsungen, Germany). When the tip of the needle was visualized to lie between the internal oblique and the transversus abdominis muscles, aspiration was performed to rule out intravascular placement and 1 to 2 ml of 0.9% saline was injected to confirm correct location of the needle. After confirming the correct needle position, 20 ml of 0.25% bupivacaine was injected to obtain an echo lucent lens-shaped space between internal oblique and the transversus abdominis muscles. A similar technique was applied on the other side to obtain a bilateral block which was followed 20 minutes later by surgical incision.

In group I, patients received 50 ml of 0.25% bupivacaine with epinephrine 5 microgram/mL. Before wound closure, 30 mL of the solution was administered by the operating surgeon into the divided edges of visceral and parietal peritoneum and rectus aponeurosis edges and 20 ml in all layers of abdominal wall. In group C, patients received standard anesthesia and analgesia, but no additional regional technique.

Intravenous (IV) ondansetron 4 mg and paracetamol 15 mg/kg was administered 30 minutes before the completion of surgery. Diclofenac 100 mg suppository was given in the operating room at the end of the surgery. After patients were shifted to the post-anesthesia care unit (PACU), a postoperative analgesic regimen which was standardized for every patient was commenced. This regimen consisted of PCIA using tramadol, regular rectal diclofenac 100 mg every 12 hours and IV paracetamol 1000 mg every 6 hours. PCIA machine was set for delivering a demand bolus dose of 15 mg with 8 minutes lock out period. Rescue analgesia of tramadol at a dose of 1 mg/kg was administered if NRS was >4 after getting three demand boluses from PCIA pump.

The primary outcome in the study was tramadol consumption (cumulative and rescue) in the PACU and in the ward at 4, 8, and 12 hours postoperatively. Secondary outcome measures were NRS at rest and movement, satisfaction of patient with pain management, patients' preference to have similar analgesic regimen in future and incidence of side effects like excessive sedation, nausea and vomiting.

Postoperative monitoring included estimation of cumulative tramadol consumption, percentage of patients requiring rescue analgesia, total consumption of tramadol as rescue analgesia, NRS for pain, incidence of side effects like excessive sedation, nausea and vomiting. Patients were assessed in the PACU and at 4, 8, and 12 hours postoperatively. A team from acute pain management service (APMS) blinded to the group allocation was responsible for pain assessment and provision of rescue analgesia for NRS ≥4. Myles and Wengritzky[19] scale was used for assessing postoperative nausea and vomiting (PONV): scores were 0 for none, 1 for one episode, 2 for two episodes, and 3 for three or more episodes. Scoring for nausea included 0 for none, 1 for sometimes, 2 for often, and 3 for all the time. Numerical responses were added and a score of ≥5 was defined as clinically important. Patients were provided with rescue antiemetic according to the protocol used in the hospital. The APMS team assessed sedation using a scale of 0 to 3 where score 0 denoted patients alert and awake, 1 denoted patient quietly awake, 2 denoted patient asleep but arousable, and 3 denoted patient in deep sleep. Satisfaction of patient with pain management was evaluated by using a Likert scale of 7 points, starting from scale 1 for strongly disagree to scale 7 for strongly agree. Patients were also asked for the preference of similar analgesic regimen for the future.

The primary clinical endpoint of this study was tramadol consumption within 12 hours. Secondary outcome measured included NRS scores and side effects associated with tramadol consumption. For sample size calculation, we assumed that a clinically important reduction in 12-hour tramadol consumption would be a 35% absolute reduction. Based on a study by Mrunalini P *et al.*[20] in which at 12 hours, mean tramadol requirement was 36 mg with a standard deviation of 16.93 mg in the control group, a sample size of 41 patients in each group was required to achieve 80% power with a two-tailed and 5% type I error. To minimize any effect of data loss, we were elected to recruit 45 patients in each group with 10% drop out.

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS-19, Chicago IL). Kolmogorov–Smirnov and histogram were used for normality test for continuous variables. Point estimation were reported in term of mean ± SD and median (IQR, 25–75 percentile) for numeric observation. Continuous parametric and non-parametric data were analyzed by ANOVA and Kruskal–Wallis one-way ANOVA respectively for mean pain score and tramadol consumption. Box and whisker plot and multiple bar diagrams are presented. Categorical variables were reported as proportion and percentage. Categorical variables, sedation, vomiting and nausea (at rest and on movement with different point time) were analyzed using Chi-squared or Fisher's exact test. $P \leq 0.05$ was considered significant but for multiple comparisons, adjusted level of significance was set at 0.017 for each comparison.

Results

A total of 146 patients scheduled for major abdominal gynecological surgeries were assessed for eligibility from August 2019 to June 2020. Of these, 135 patients consented to participation and were randomized into three study groups of 45 each. Subsequently, five patients were excluded due to change in surgical incision from transverse to mid-line, drug allergy or protocol violation, leaving 43 patients in both group C and group I, and 44 patients in group T [Figure 1]. Personal characteristics of patients in three groups were comparable with regards to age, BMI, and ASA physical status. However, mean weight of patients in group T was significantly higher as compared to group I and group C. Mean duration of surgery was comparable among the three study groups [Table 1].

Median cumulative tramadol consumption between three groups at different time points were comparable with no statistically significant difference among three study groups ($P < 0.05$) [Figure 2]. However, during PACU's stay, a statistically significant difference was found in the median tramadol consumption used for rescue analgesia between groups T and C ($P = 0.035$) and between groups T and I (P-value = 0.034) [Table 2]. The tramadol consumption for rescue analgesia in ward for all time intervals for next 12 hours was comparable among the three study groups.

Comparison of percentage of patients requiring rescue analgesia among three groups at different time intervals is shown in Figure 3. A statistically higher percentage of patients in group C demanded rescue analgesia compared to group T and group I ($P = 0.041$). Number of patients demanding rescue analgesia in ward for all time intervals for next 12 hours was comparable among the three study groups.

Comparison of median NRS and number of patients (%) having NRS >3 at rest and movement among three groups at different times is shown in Table 3. A statistically significant difference was observed in the percentage of patients having moderate to severe pain (NRS >3) upon movement in group C compared to group T and group I ($P = 0.034$). Overall pain score at rest and during movement were comparable among three groups in the ward at 4, 8 and 12 hours postoperatively [Table 3].

No statistically significant difference was observed in the satisfaction score ($P = 0.614$) and preference or desire for similar type of postoperative analgesia regimen for future surgery ($P = 0.589$) between patients of the three study groups. In group T, satisfaction with pain management and preference to have the similar postoperative pain management regimen was observed in 97% of patients. Similarly, satisfaction with pain management was observed in 97% of patients from group-I and 95% patients from group C. The preference to have similar postoperative analgesia for future surgery was recorded in 93% of patients in group C and 95.5% in group I, which was comparable to group T.

All three groups were comparable in the incidence of postoperative side effects and complications. No statistically significant difference was observed in the sedation score and postoperative nausea and vomiting (PONV) score among three groups at all time interval in the postoperative period ($P > 0.05$).

Discussion

The present randomized, controlled trial found no significant difference between the total postoperative opioid consumption, NRS and opioid-related side effects between the three study groups. However, significantly higher number of patients in control group had NRS >4 on movement and required rescue analgesia in PACU, suggesting better pain control by both regional interventions compared to controls in the early postoperative phase. In addition, tramadol consumption for rescue analgesia in PACU was statistically lower in patients

Table 1: Patient's characteristics and duration of surgery (*n*=130)

Variables	Group T *n*=43	Group I *n*=44	Group C *n*=43	*P*
Age, Years, mean (sd.)	40.16 (7.57)	37.95 (8.23)	41.98 (7.87)	0.063
Weight, kg, mean (sd.)	70.69 (15.85)	63.79 (10.85)	68.90 (12.75)	0.046
Height, cm, mean (sd.)	157.78 (6.74)	155.86 (6.09)	157.65 (5.55)	0.269
BMI, kg/m^2, mean (sd.)	28.49 (6.08)	26.13 (4.12)	27.59 (6.12)	0.134
Duration of surgery, hours, median [IQR]	130 [115-180]	120 [106-172]	135 [120-180]	0.348
ASA Status, n (%)				
I	8 (18.6)	16 (36.4)	11 (25.6)	0.287
II	33 (76.7)	24 (54.5)	28 (65.1)	
III	2 (4.7)	4 (9.1)	4 (9.3)	

Data are presented as mean (SD) for normal and n (%) for categorial data

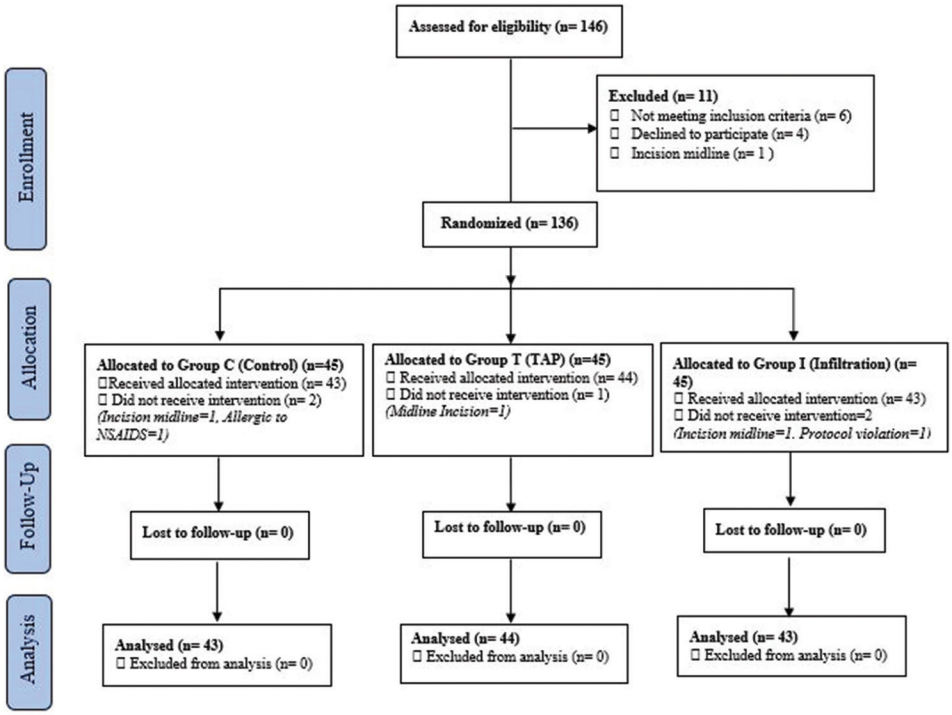

Figure 1: CONSORT 2010 Flow Diagram

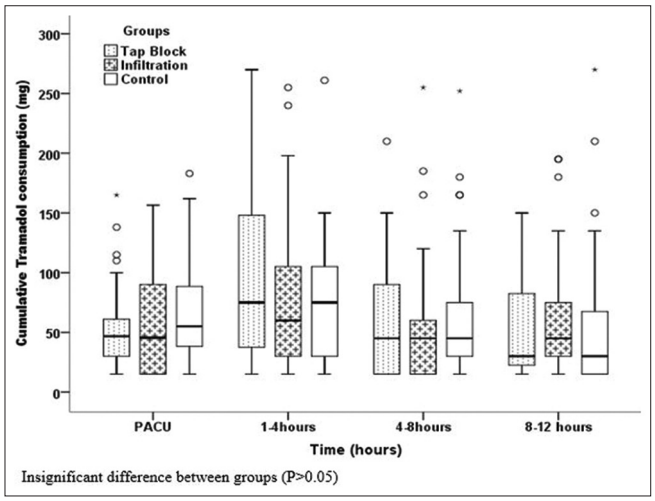

Figure 2: Comparison of median cumulative tramadol consumption between transversus abdominus plane (T) block group, infiltration (I) group, and control (C) group during the postoperative period in post-anesthesia care unit (PACU), 1–4 hours, 4–8 hours, and 8–12 hours

receiving TAP block, suggesting superiority of TAP block in the immediate postoperative period.

The present study found no significant difference in total opioid consumption and incidence of opioid related side effects between TAP block and LAI groups. This finding is consistent with the meta-analysis conducted by Yu *et al.*,[21] suggesting both techniques have similar postoperative analgesic roles in terms of morphine consumption and opioid-related side effects. Our results, however, contrast with the findings of Gasanova *et al.*[22] who reported reduced opioid consumption and superior pain relief in infiltration group compared to the TAP group. Although our studies follow a similar methodology, the difference in the use of liposomal bupivacaine in infiltration group vs bupivacaine HCL in the TAP group in Gasanova *et al.*[22] may have resulted in the superior outcomes in the infiltration group in their study. Liposomal bupivacaine has not yet been approved for perineural administration and thus cannot be used for TAP block. Therefore, to maintain uniformity among the groups in our study, bupivacaine HCL was used in both groups, which could have led to no difference in the outcome.

Previous studies have shown reduced 24 hours postoperative morphine in the TAP block and LAI compared to the control group.[23,24] However we observed this effect only in the early postoperative phase in PACU, where patients in the control group required significantly higher levels of opioids when compared to regional technique groups. Previous trials on acute pain have shown that adequate pain control (assay sensitivity) with analgesia may only be achieved when patients are experiencing moderate to severe pain.[25,26] This explains why in our study, the analgesic effect of TAP block or infiltration/peritoneal instillation of local anesthetic was most evident in the immediate postoperative period in PACU, when patients may have had moderate or higher pain. The use of balanced multimodal analgesia in the current study for all three groups, consisting of a combination of paracetamol, NSAIDs

Table 2: Comparison rescue tramadol consumption among groups

Measurement Time	Group T *n*=43	Group I *n*=44	Group C *n*=43	(GT-GC) Difference in Median (CI)	*P*	(GI-GC) Difference in Median (CI)	*P*	(GT-GI) Difference in Median (CI)	*P*
Rescue Tramadol consumption (mg)									
PACU	15 [15-30]	30 [15-52]	30 [15-45]	-15 (-28.9 to -1.07)	0.035	0 (-13.8-13.8)	0.99	-15 (-13.8 to -1.15)	0.034
1-4 hours	60 [30-135]	60 [30-105]	60 [30-105]	0 (-36.9 to 36.13)	0.99	0 (-35.9 to 35.9)	0.99	0 (-35.9 to 35.9)	0.999
4-8 hours	45 [15-75]	30 [15-60]	45 [30-75]	0 (-24.9 to 24.9)	0.99	-15 (-39.8 to 9.82)	0.234	15 (-0.98 to 39.8)	0.234
8-12 hours	30 [0-45]	30 [15-60]	30 [15-60]	0 (-19.5 to 19.4)	0.99	0 (-19.3 to 19.3)	0.99	0 (-19.3 to 19.3)	0.99

Data are presented as median [25–75 percentile]. Median difference (95% CI); Adjusted significant criteria, P=0.05/12=0.00416, Kruskal-Wallis test

Table 3: Comparison of numerical rating score (NRS) for pain and number (%) of patients having pain score>3 at rest and movement among groups at different times

Variables	Group T *n*=43	Group I *n*=44	Group C *n*=43	*P*
At PACU				
NRS at rest, median [IQR]	1 [0-4]	2 [0-3.7]	2.5 [0-4]	0.257
Number (%) of patients with NRS >3 at rest	11 (25.6)	11 (25)	13 (30.2)	0.835
NRS at movement, median [IQR]	3 [2-5]	3 [2-5]	4 [2-5]	0.185
Number (%) of patients with NRS >3 at movement	20 (46.5)	22 (50)	30 (72.1)	0.034
At 4 hours				
NRS at rest, median [IQR]	1 [0-2]	0 [0-2]	1 [0-2]	0.962
Number (%) of patients with NRS >3 at rest	0	0	0	
NRS at movement, median [IQR]	2 [2-3]	2 [2-3]	2 [2-3]	0.395
Number (%) of patients with NRS >3 at movement	4 (9.3)	4 (9.1)	5 (11.6)	0.909
At 8 hours				
NRS at rest, median [IQR]	0 [0-1]	0 [0-1]	0 [0-1]	0.939
Number (%) of patients with NRS >3 at rest	0	0	0	
NRS at movement, median [IQR]	2 [2-2]	2 [2-3]	2 [2-2]	0.322
Number (%) of patients with NRS >3 at movement	2 (4.7)	6 (13.6)	0 (0)	0.027
At 12 hours				
NRS at rest, median [IQR]	0 [0-1]	0 [0-0]	0 [0-0]	0.098
Number (%) of patients with NRS >3 at rest	1 (2.3)	0 (0)	0 (0)	0.361
NRS at movement, median [IQR]	2 [2-2]	2 [2-2]	2 [2-2]	0.903
Number (%) of patients with NRS >3	3 (7)	2 (4.5)	1 (2.3)	0.589

Data are presented as median [IQR] for non-normal and n (%) for categorial data. Kruskal-Wallis test and Chi-squared test according to assumptions of test

with opioid PCIA, may have also played a symbiotic role in controlling pain to less than moderate level once patients were shifted to the ward. Thus, the low pain levels in all three groups could explain the lack of benefits either of the regional techniques with the control group in terms of opioid consumption and pain scores.[27,28]

The current study found lower tramadol consumption for rescue analgesia in the TAP block patients in PACU compared to both LAI and control group, suggesting superiority of TAP block in the immediate postoperative period. In contrast, Yu *et al.*[21] found no difference in the pain scores in the early post operative phase between TAP and infiltration group. However, they did report a significantly lower pain score in the TAP group at 24 hours postoperatively while also highlighting the fact that the statistical significance was by a narrow margin, thus doubting the clinical significance. In our study we assessed pain scores till 12 hours postoperatively and hence this limits us from deducing if TAP block may have a slightly better long-lasting role in controlling pain postoperatively. However, one study investigating the role of TAP block in reducing tramadol consumption among patients undergoing laparoscopic gynecological surgeries found significant reduction only in the early postoperative time of 0–6 hours.[29]

The exact component of multimodal regimen would differ depending on the patient, settings, surgical procedure, and resources available. The strength of the study is that it can guide the readers, especially from LMIC, for provision of

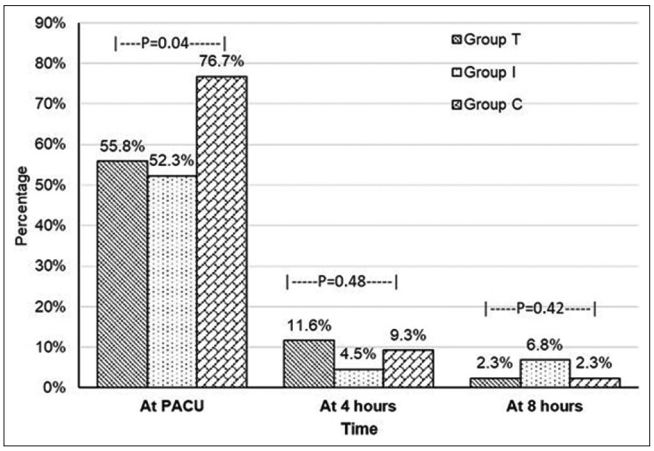

Figure 3: Comparison of percentage of patients requiring rescue analgesia among three groups at different time intervals

multimodal analgesia when faced with a shortage of good quality opioids.

This study has few limitations: we observed postoperative opioid consumption and pain scores 12 hours after surgery, which could have prevented us from observing long-lasting roles of TAP block. We also did not administer sham block in patients in the control group due to concerns from our ethics review board for subjecting patients to placebo interventions.

Conclusion

In conclusion, this study revealed no significant difference in the analgesic effects of either TAP block or LAI in patients undergoing major gynecological surgeries when added to multimodal analgesia regimen. Regional techniques had beneficial roles in providing pain relief in the immediate postoperative period as compared to controls. A multimodal analgesic technique with simple LAI can provide adequate postoperative analgesia in a health care setting where logistic and expertise of TAP block and/or good quality opioids are not available.

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Data availability Statement

The data that support the findings of this study are available from the corresponding author, upon request.

Patient consent Statement

Written informed consent was obtained from all the patients.

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Conflicts of interest

There are no conflicts of interest.

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