A Comparative Study Between Combined Ketorolac Bupivacaine and Bupivacaine Alone for Transversus Abdominis Plane Block in Children Undergoing Lower Abdominal Surgeries: A Prospective Double-Blind Randomized Clinical Trial

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Abstract

Background: Recently, sonographic guided transversus abdominis plane (TAP) block was used in pediatrics to control postoperative pain. Our study aimed to compare the time of the first rescue analgesia between sonographic TAP block with and without ketorolac for postoperative analgesia in pediatric lower abdominal surgeries.

Patients and Methods: Ipsilateral ultrasound-guided TAP block was done in ninety children who underwent elective lower abdominal operations. Patients were split into two equal groups (45 patients each): Ketorolac Group (KG) and Control Group (CG). The time of the 1st rescue analgesic dose, post-recovery 24-hour ketorolac dose, the postoperative pain score, the patients who required no rescue analgesia, adverse events, and hemodynamic effects intraoperatively and along the postoperative 24 hours, as well as parental satisfaction, were collected and analyzed.

Results: The time for the first rescue analgesic dose was significantly longer in KG, and there was also significantly lower total ketorolac consumption in KG throughout the postoperative 24 hours. A significantly greater number of patients required no rescue analgesia in KG. There was a statistically significant reduction in pain scores in KG. There was also a significantly lower incidence of postoperative adverse events and more significant parent satisfaction in KG.

Conclusion: Combined ketorolac and bupivacaine in a sonographic TAP block for lower abdominal surgeries in children increased the analgesic efficacy with a longer time for first rescue analgesia, less total analgesic consumption, more patients requiring no rescue analgesia, lower pain scores, fewer adverse effects, and better parent satisfaction compared to bupivacaine alone

Keywords: Children; Ultrasound TAP block; Ketorolac.

Introduction:

Sonographic guided transversus abdominis plane (TAP) block is a regional procedure for analgesia in adult patients and has been used recently in pediatrics to control postoperative pain [1-3]. There are several additives to maximize efficacy and offer the best analgesia of a local anesthetic with TAP block [4]. Ketorolac is a non-steroidal anti-inflammatory drug used as an adjuvant with local anesthetic in TAP block [5-7]. The aim of the was to compare the effect of adding ketorolac to TAP block for postoperative analgesia in pediatric lower abdominal surgeries.

Patients and Methods:

In this prospective, observational, double-blind, randomized, comparative clinical trial, ninety children with ASA

physical status I–II, aged from six to twelve years and scheduled to have elective lower abdominal surgeries such as orchiopexy, hydrocele, hypospadias, and inguinal hernia were enrolled in the study from January 2024 to June 2024. Patients and their parents signed informed consent, approval from the Medical Research Ethics Committee of Sohag University's Faculty of Medicine under IRB Registration Number: 00013006 and the Clinical Trial register number (NCT06267820) on ClinicalTrial.gov were obtained. The criteria for exclusion were as follows: refusal of parents, emergency procedures, bilateral surgery, and sensitivity to bupivacaine and/or ketorolac.

Upon entering the operating room, all children received the same general anesthesia technique with the same anesthetist, and standard monitoring was applied, which included capnography, noninvasive blood pressure, an electrocardiogram, and pulse oximetry. General anesthesia was initiated using a dosage of propofol (2 mg/kg) and atracurium (0.5 mg/kg) as a muscle relaxant, intubated by suitable endotracheal tube and to maintain the patient's anesthesia, isoflurane (MAC 1.5 percent) was administered. Patients did not receive any preoperative or intraoperative analgesic drugs. A computerized system was used to randomly assign the patients into two groups, the Ketorolac Group (KG) and the Control Group (CG) (n = 45 for each). Before surgical incision and under aseptic conditions, an anesthesiologist with expertise in regional anesthesia performed a unilateral sonographic TAP block on the ipsilateral side of surgery. The **Ketorolac Group (KG)** received 0.5 ml/kg of 0.25% plain bupivacaine in conjunction with 0.5 mg/kg of ketorolac, while the **Control Group (CG)** received 0.5 ml/kg of 0.25% plain bupivacaine both diluted with normal saline 0.9% to 40 ml. At the end of surgery, isoflurane was stopped, neuromuscular blockade was reversed with atropine (0.02 mg/kg) and neostigmine (0.03 mg/kg), tracheal extubation was performed, and patients were moved to the post-anesthesia care unit (PACU).

TAP Block Technique:

The patient laid down supine and under aseptic conditions with the ultrasonography machine (Sonosite M-turbo, USA) on the operator's opposite side. Halfway between the iliac crest and costal edge, the linear high-frequency transducer was positioned in a transverse plane along the abdomen in the mid-axillary line. This allowed the three muscular layers of the abdominal wall to be seen clearly. The needle was placed anteriorly and somewhat away from the probe to enter the transverse plane through the fascial layer behind the internal oblique muscle. After that, it was gradually moved to its final location. After negative aspiration, 0.5 ml/kg of 0.25 percent plain bupivacaine (with ketorolac 0.5 mg/kg in KG and alone with CG) was injected while the dispersion of the local anesthetic was closely monitored.

Measurements:

Before the start of the surgery and, subsequently, every five minutes until the surgery was completed, the patient's hemodynamic parameters, such as heart rate (HR) and mean arterial blood pressure (MAP), were recorded. Patients' demographic data and surgery characteristics in age, sex, type, and duration of surgery were reported. Postoperative pain scores in the form of NRS of 0 to 10 (where '0' represents 'no pain' and '10' indicates great suffering) [**[8]**] were recorded at the following times: on reaching the PACU, (0 time) and then after 1, 2, 6, 8, 12, 18, and 24 hours, NRS≤ 3 = needed no analgesia, NRS>3 needed rescue analgesia as IV ketorolac (0.5 mg/kg), the time required for the 1st rescue analgesic dose was recorded, the total amount of ketorolac required along 24 hours postoperatively, as well as the number of patients required no rescue analgesia were also reported. Adverse events associated with ketorolac and bupivacaine (such as nausea, vomiting, headaches, stomach pain, and flatulence) were reported and managed. Parent satisfaction was measured using a 5-point Likert scale, with

one representing very satisfied, two satisfied, three neither satisfied nor dissatisfied, four dissatisfied, and five very dissatisfied for each parent [[9]]. All data were collected, analyzed, and compared between both groups.

The Primary Outcome

To compare the time of the first rescue analgesia between sonographic TAP block with ketorolac and without ketorolac for postoperative analgesia in pediatric lower abdominal surgery.

The Secondary Outcomes

Were the total amount of ketorolac as postoperative rescue analgesia within the first 24 hours, reduction in pain scores, number of patients who required no rescue analgesia, side effects of ketorolac and bupivacaine, effects on patient hemodynamics, and parental satisfaction.

Statistical Analysis:

The data were analyzed using SPSS v. 27 for Analytical Statistics. The quantitative parametric data, mean and SD, were analyzed using the unpaired student t-test. The non-parametric quantitative data were analyzed using the Mann-Whitney test. The Fisher's exact or Chi-square test was employed when statistical analysis was required for qualitative data such as frequencies and percentages. The two-tailed P value was assumed to be less than 0.05 to determine statistical significance.

Sample Size Calculation:

Based on the numerical rating scale for pain assessment, a post-HOC power analysis was conducted using the G*Power 3.1 program with a 0.05 error margin and a 3.00 effect size. Ninety children were calculated, with forty-five in each group.

Results:

This clinical trial enrolled 110 patients; 8 did not meet the inclusion criteria, 12 patients refused to participate in the trial, and 90 patients completed the study, as shown in the Consort flow chart. (Figure 1) Concerning baseline characteristics such as demographic data (age and sex), type of surgery, and surgical duration time between both groups, there was no discernible significant statistical difference. (Table 1)

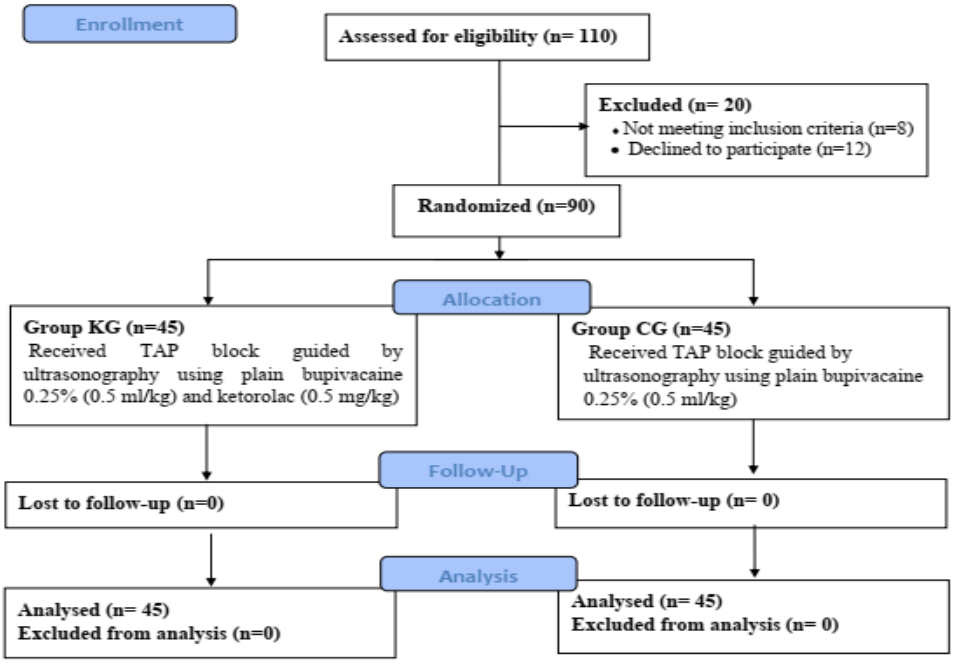

Figure 1: Consort flowchart of the studied groups

Table 1: Demographic data and surgical characteristics of both groups.

Variable	KG	CG	P value
Age (years)	8 ±1.9	7.9± 1.9	0.67
Gender (Male	41(91%)	43(95.5%)	
Female)	4 (9%)	2 (4.5%)	
Type of Operation:			
• Inguinal hernia	14 (31.12%)	15 (33.33%)	
• orchiopexy	10 (22.22%)	12 (26.67%)	
• hypospadias	9 (20 %)	7(15.55%)	
• Hydrocele	12 (26.66%)	11(24.45%)	
Duration of surgery (min.)	52.2±7.8	53.8±9.7	0.39

Results are given as mean ± SD, or number (%).

The time for the first rescue analgesic dose to be given was significantly longer in KG than CG, as the mean ± SD was 21.7 ± 1.9 and 12.4 ± 2.6 consequently (p-value = 0.0001). KG exhibited significantly reduced total ketorolac consumption than CG (7.3 ± 9.9 mg versus 34 ± 10.8 mg respectively), p-value = 0.0001, along 24 hours post-recovery. The number of patients who did not require rescue analgesia was significantly higher in KG compared to CG, 27 (60%) versus 3 (6.67%), p-value = 0.0001. There was a reduction in NRS in the first 8 hours with no significant difference between both groups (p-value > 0.05). Still, there was a statistically significant reduction in NRS at 12, 18, and 24 hours postoperative in KG than CG (p-value = 0.001). (Table 2)

Table 2: Time for rescue analgesia, the total amount of ketorolac, Postoperative NRS, and the number of patients who required no analgesia in the studied groups.

Variable	KG Mean ± SD median (min-max)	CG Mean ± SD median (min-max)	P value
Time of 1st rescue analgesia	21.7 ± 1.9	12.4 ± 2.6	0.0001
Total ketorolac consumption	7.3 ± 9.9 0 (0-30)	34 ± 10.8 30 (15- 60)	0.0001
NRS 0 h	1.5± 0.55 2 (1-3)	1.7 ± 0.73 2 (1-3)	0.26
NRS 1h	1.8 ± 0.42 2 (1-3)	2 ± 0.69 2 (1-3)	0.15
NRS 2h	1.9 ± 0.34 2 (1-2)	1.8 ± 0.39 2 (1-2)	0.57
NRS 6 h	2.1 ± 0.25 2 (2-3)	2.1 ± 0.36 2 (1-3)	0.73
NRS 8 h	2.2 ± 0.39 2 (2-3)	2.3 ± 0.46 2 (2-3)	0.22
NRS 12 h	2.1 ± 0.39 2 (2-3)	4 ± 0.62 4 (3-5)	0.001
NRS 18 h	2.1 ± 0.32 2 (2-3)	4 ± 0.62 4 (3-5)	0.001
NRS 24 h	3 ± 0.52 3 (3-4)	4.1 ± 0.58 4 (3-5)	0.001
Number of patients who required no analgesia	27 (60%)	3 (6.67%)	0.0001

Results are shown as mean ± SD or median (min-max) or number (%); present, NRS; Numeric Rating Scale.

The incidence of postoperative adverse events differed significantly between both groups as about 93% of patients in KG showed no side effects at all, and 7% of patients showed side effects as two patients showed nausea and one patient showed vomiting compared to 40% of patients in CG showed no side effects at all and 60% of patients showed side effects as 12 patients showed nausea, 13 patients showed vomiting, two patients showed headache, four patients showed abdominal pain and two patients showed flatulence (p-value =0.001). Table 3

Table 3: Postoperative Adverse Events

Postoperative Adverse Events	**KG No (%)**	**CG No (%)**	**P value**
None	42 (93.33%)	18 (40 %)	0.001
Nausea	2 (4.44%	12 (26.66%)	
Vomiting	1(2.22%)	13 (28.8%)	
Headache	0 (0%)	2 (4.44%)	
Abdominal pain	0 (0%)	4 (8.88%)	
Flatulence	0 (0%)	2 (4.44%)	

Results were shown as numbers (N) and percentages (%).

The parent satisfaction scale was significantly different in KG than in CG, where 87% of parents were very satisfied, 13% were satisfied, none of parents were neither satisfied nor dissatisfied and none of parents were dissatisfied or very dissatisfied in KG compared to 7% of parents were very satisfied, 35% of parents were satisfied, 29% of parents were neither satisfied nor dissatisfied, 29 of parents were dissatisfied and none of parents were very dissatisfied in CG (p-value = 0.0001). (Table 4)

Table 4: Parent Satisfaction Scale (Likert Satisfaction Scale)

Variable	**KG No (%)**	**CG No (%)**	**P value**
Very satisfied	39 (86.6%)	3 (6.66%)	0.0001
Satisfied	6 (13.33%)	16 (35.55%)	
Neither satisfied nor dissatisfied	0(0%)	13(28.8%)	
Dissatisfied	0 (0%)	13 (28.8%)	
very dissatisfied	0 (0%)	0 (0%)	

Results were shown as numbers (n) and percentages (%).

Regarding hemodynamics, the mean values of HR in the preoperative (baseline), intraoperative, and 1st 8 hours postoperative were within normal limits with no statistically significant difference between KG and CG as mean ± SD were 108 ± 31, 96.9±2.9, 88.8±1.6 for KG and 07.4± 3.85, 98.3±6.3 and 89.6±5.1 for CG respectively with p-values > 0.05. After 8 hours and up to 24 hours postoperatively, the mean values of HR were within the normal range in both groups but significantly lower in KG than CG as mean ± SD 90.5±3.2 in KG and 101.1±4.9 in CG with p-value = 0.001.

Also, the mean values of MBP in the preoperative (baseline), intraoperative, and 1st 8 hours postoperative were within normal limits with no statistically significant difference between KG and CG as mean ± SD were 75.7±6, 81.6±5.9, 89.6±8.4 for KG and 73.3±6, 81.8±8.3 and 90±13.5 for CG respectively with p-values > 0.05. After 8 hours and up to 24 hours postoperatively, the mean values of MBP were within the normal range in both groups but significantly lower in KG than CG as mean ± SD 75.8±5.7 in KG and 72.7±7.5 in CG with p-values < 0.05. (Figures 2 and 3)

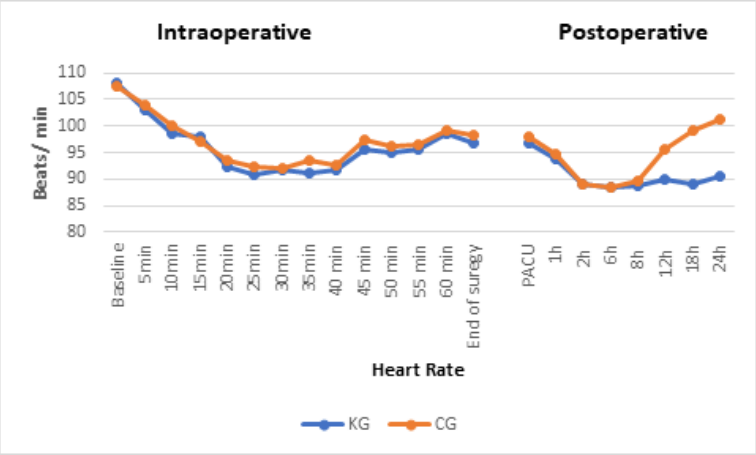

Figure 2: Intraoperative and Postoperative Mean HR in Both Groups

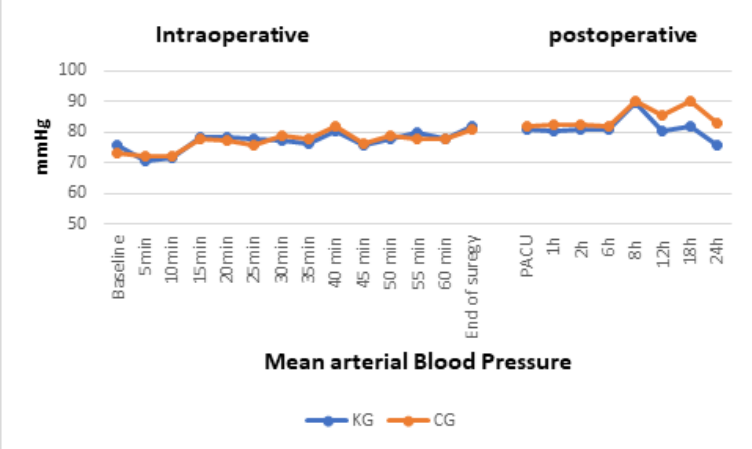

Figure 3: Intraoperative and Postoperative MAP in Both Groups

Discussion:

Ketorolac and local anesthetic combination were used in many studies in adult patients in sonographic TAP block for postoperative analgesia in abdominal and lower abdominal operations. This particular study is the first to examine the analgesic effects of the combination of local anesthetic (bupivacaine) and ketorolac in sonographic TAP block in pediatric patients who underwent lower abdominal operations **(Unique Study),** so we compare our results with sonographic TAP block of combined bupivacaine with ketorolac in adult patients and with other adjuvants added to bupivacaine in sonographic TAP block in pediatric patients. The variations in results among the following studies might be due to different adjuvants used, variable surgical procedures, different age groups, and different numbers of patients in each study. Also, some studies used intraoperative and postoperative fixed dose analgesics in addition to rescue analgesia; some did bilateral TAP block while others did unilateral block, and lastly, they were single-center studies.

In the present study, children who underwent lower abdominal surgeries received ipsilateral sonographic TAP block before skin incision with both ketorolac and bupivacaine (KG) had significantly more time for the first analgesic request than the controlled bupivacaine group (CG) ($p < 0.0001$). In line with this result **Jiang *et al.*** [**[10]**] research, who studied the effect of the combination of ketorolac and bupivacaine (Ketorolac Bupivacaine Group) compared to bupivacaine alone (Bupivacaine Group) in bilateral sonographic TAP block in adult women who underwent laparoscopic gynecologic surgery and concluded that Ketorolac Bupivacaine Group had a longer time for the first analgesic drug to be given than Bupivacaine Group. The extended effects of analgesia were due to the inhibiting of prostaglandin synthesis by

ketorolac. Also, they extended the absorption of ketorolac through the abdomen muscles in KG, which explains the differences between ketorolac and non-ketorolac groups. Also, in the **Abdelwahab *et al.*** [11] trial, which compared the efficacy of adding dexamethasone as an adjuvant to bupivacaine (dexamethasone bupivacaine group) with bupivacaine alone (bupivacaine group) in bilateral sonographic TAP block in pediatric major abdominal surgery, the time to first request analgesia was prolonged in dexamethasone bupivacaine group than bupivacaine group, in agreement with the current work. In line with our research, **Fatma A. Abdelaal et al.** [12] study on 80 pediatric patients scheduled for laparoscopic orchiopexy, divided equally into two groups with bilateral sonographic TAP block, adding dexmedetomidine to bupivacaine (Group A) and bupivacaine alone (Group B) for analgesia postoperatively; they concluded that, the mean time to first analgesic request was prolonged in Group A than Group B ($p<0.001$).

This study had no significant differences in the baseline characteristics, as demographic data (age and sex), type of surgery, and surgical duration time align with all previously mentioned studies [10-12].

In the current study, the total rescue analgesic dose of ketorolac throughout 24 hours postoperatively was less in KG versus CG with a statistically significant p-value ($p < 0.0001$), which is consistent with **Jiang *et al.*** trial [10], which concluded that the total rescue analgesic dose (sufentanil) was lower in ketorolac bupivacaine group than bupivacaine group. In agreement with us, **Abdelwahab *et al.*** [11] reported that less acetaminophen was taken over 36 hours post-recovery in the dexamethasone bupivacaine group than in the bupivacaine group. **Fatma A. Abdelaal et al.** [12] study also reported less postoperative total opioid requirements for Group A than Group B, in agreement with our study.

In our trial, NRS was low in both groups in the first 8 hours postoperatively, with no statistical significance ($p > 0.05$). Still, it was significantly lower after that up to 24 hours postoperatively in KG than CG ($p < 0.001$). Also, the number of patients who required no rescue analgesia was 27 patients (60%) for KG compared to 3 patients (6.6%) for CG ($p <0.0001$). In the **Jiang *et al.*** study [10], the NRS was significantly lower in the Ketorolac Bupivacaine Group than in the Bupivacaine Group only at 1, 2, 4, 6, and 24 hours, which is not in line with our results. Still, they did not mention the number of patients who required no analgesia. Also, **Abdelwahab *et al.*** [11] reported a significant reduction in pain score at 8, 10, and 12 hours postoperatively in the dexamethasone bupivacaine group compared to the bupivacaine group, which is not similar to our results. Also, they did not mention the number of patients who required no analgesia. The postoperative pain-free time after sonographic TAP block in our study and other studies could be explained by the duration of action of LA used in both groups and the prolonged effects of the analgesics used in adjuvant groups.

Regarding hemodynamics in the preoperative (baseline), intraoperative, and 1st 8 hours post-recovery, there was comparable stable hemodynamics with no statistically significant difference between both groups (p-value > 0.07), but after that time up to 24 hours, the mean values of HR and MAP were lower in KG than CG, which was statistically significant ($p < 0.05$). In contrast, the study of **Jiang *et al.*** [10] and **Abdelwahab *et al.*** [11] reported no significant difference in hemodynamics.

In this work, the **adverse events** decreased significantly in KG than in CG ($p < 0.001$). There were variable results in the previous studies, such as the **Jiang *et al.*** study [10], which concluded that there was no significant difference between the Ketorolac Bupivacaine group and the Bupivacaine group concerning nausea and vomiting. However, they used a 4 mg ondansetron injection preoperatively in all groups.

Importantly, in our reports, there was a statistically significant improvement in family satisfaction in KG compared to CG ($p < 0.0001$), and this is supported by **Jiang**

et al. [10] research, the only similar study which reported that parent satisfaction concluded that Ketorolac Bupivacaine Group showed greater parent satisfaction with analgesia than Bupivacaine Group.

Conclusion:

Combined ketorolac and bupivacaine in sonographic TAP block for children who underwent lower abdominal surgeries increased the analgesic efficacy in the form of longer time for first rescue analgesia, less total analgesic consumption; more patients required no rescue analgesia, lower pain scores, fewer adverse effects, and better parents' satisfaction compared to bupivacaine alone.

Recommendations:

Multicentric studies with a large sample size are recommended.

Limitations: No limitations

Funding: Nil.

Conflict of Interests: Nil.

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