Ketamine Versus Neostigmine as an Adjuvant To Bupivacaine In Caudal Block For Pediatric Patients Undergoing inguinal hernia repair

Mohamed Mosaad
Resident of anesthesia at Zagazig General Hospital, El Sharkia, Egypt, mosaad84m@gmail.com

Lobna Taha El Dorgham
Professor of Anesthesia, Intensive Care and Pain Management Faculty of Medicine - Zagazig University

Hala Ibrahim Zanfaly
Professor of Anesthesia, Intensive Care and Pain Management Faculty of Medicine - Zagazig University

Marwa Mahmoud Zakzouk
Lecturer of Anesthesia, Intensive Care and Pain Management Faculty of Medicine - Zagazig University

Abstract

Background Postoperative pain is one of the most common problems in surgical patients that can influence their physical and mental health. So, effective pain management is an essential component of postoperative care. Therefore pediatric surgeons, anesthetists and pharmacologists had been in a continuous search to locate a safe and effective analgesic for children. The purpose of the study was to Comparison between the analgesic effect of adding neostigmine or ketamine to bupivacaine in caudal block for pediatric patients undergoing lower abdominal surgeries. Materials and Methods: Comparative Prospective randomized double blind controlled clinical study. A total of 45 pediatric patients in age 1 - 3 years ASA I-II, scheduled for lower abdominal surgeries were equally divided into three groups (15 patients each): the study was carried out at the department of anesthesia in Zagazig University Hospitals. Group (C) 15 patients received GA and CEB using 0.25% bupivacaine 1ml/kg only. Group (K) 15 patients received GA and CEB using 0.25% bupivacaine 1 ml/kg plus 0.5 mg/kg ketamine. Group (N): 15 patients received GA and CEB using 0.25% bupivacaine 1ml/kg plus neostigmine 2µg/kg. HR, MAP and Spo2 were recorded before (baseline) and then every 10 min till end of operation and at 1, 2, 4, 6, 8, 12 hr. postoperatively. Pain scores were evaluated by the "Face, Leg, Activity, Cry, Console ability 'FLACC' pain scale. Time of 1st analgesic rescue and Total doses of rescue analgesic that administered in the postoperative period (12 hr) were recorded. Results: The results showed no significant difference between the studied groups as regarding different MAP, HR readings during the operation at before induction, 20 min, 50 min, 60 min and 70 min after induction. While there were highly significant difference between them as regarding intra-operative MAP and HR which was found to be significantly higher among group C compared to K and N groups at 10, 30 and 40 min after induction ($^{*}p < 0.001$). As regard SpO_2, the result of the current study is there was no significant difference between the studied groups. there were highly significant differences between the studied groups as regarding first time for rescue analgesia and the amount fentanyl intra operative needed

of paracetamol postoperatively to be significantly higher among C group compared to other groups. As regard pain assessment a significant increase in FLACC scale of group C compared with that of group K and group N ($p < 0.001$) at 1 H, 2 H, 4 H, 6 H and 8 H. Conclusion: the addition of 2μg/kg neostigmine, or 0.5 mg/kg ketamine as an adjuvant to 1 ml/kg of 0.25% caudal bupivacaine could lengthen the duration of postoperative analgesia in children undergoing lower abdominal surgeries without increasing the incidence of side effects. However, neostigmine offered a significant advantage over ketamine in this regard.

Keywords: *Neostigmine, ketamine, Bupivacaine, Caudal Block, Lower Abdominal Surgeries*.

INTRODUCTION

Postoperative pain is one of the most common problems in surgical patients that can influence their physical and mental health. So, effective pain management is an essential component of postoperative care [1]. Surgery is extremely stressful for any child, and the pain associated with tissue damage is an adverse experience. The perception of pain by children during the postoperative period has been demonstrated to be associated with an increased incidence of perioperative complications, longer hospitalization and slower wound healing. If poorly treated, pain can cause changes in the pain perception threshold or emotional disorders in later life [2].

Caudal block is one of the technical advancements that is regularly used in children. This block is safe, effective and easy with less side effects. It is the most common block technique used in lower abdominal or lower extremity infant surgeries. In this method, local anesthetics such as bupivacaine have been injected into the caudal canal providing block in the sacral and lumbar nerve roots [3].

Post-operative pain management had always been a major concern of parents as well as pediatric anesthetists. Contrary to the ancient nation that children don't feel pain, many studies have focused on the importance of good pain management in children [4]. Therefore pediatric surgeons, anesthetists and pharmacologists had been in a continuous search to locate a safe and effective analgesic for children. Interest of combining regional and general anesthesia (GA) to offer pain free in the intra and post-operative periods has been increased [5].

Many anesthetic agents have been used for caudal analgesia in pediatric patients, with lignocaine and bupivacaine being most common [6]. The relative short duration of analgesia after single -shot caudal injection even with the use of long acting local anesthetic such as bupivacaine is the main disadvantages of caudal anesthesia[7]. Prolongation of caudal analgesia using a "single-shot" technique has been achieved by the addition of various adjuvants , such as ketamine , clonidine [8] and opioid [9].

Patients and Methods

Comparative Prospective randomized double blind controlled clinical study. A total of 45 pediatric patients scheduled for lower abdominal surgeries were equally divided into three groups (15 patients each):

- Group (C): 15 patients received general anesthesia (GA) and caudal epidural block (CEB) using 0.25% bupivacaine 1ml/kg only.
- Group (K): 15 patients received GA and CEB using 0.25% bupivacaine 1 ml/kg plus 0.5 mg/kg ketamine .
- Group (N): 15 patients received GA and CEB using 0.25% bupivacaine 1ml/kg plus neostigmine 2μg/kg .

The study was carried out at the department of anesthesia in Zagazig University Hospitals after approval by institutional review board committee at Faculty of Medicine Zagazig University.

2. Sample size:

The sample size was calculated using open Epi/Info according to the following duration of analgesia, in bupivacaine neostigmine group it was 20.4 ± 14 h [10] and in bupivacaine ketamine group was 10 ± 4.3 h [11] and case to control ratio 2:1 so at power of study 80% and CI 95%, the sample size was calculated to be 45 cases, 15 in each group.

Inclusion criteria:

1. Parents accepting the procedure by written consent.

2. Age: 1 - 3 years.

3. Sex: both boys and girls.

4. Physical state: American Society of Anesthesiologists (ASA) class I and II.

5. Type of operation: lower abdominal surgeries.

6. Duration of surgery: about an hour and half.

Exclusion criteria:

1. Parent refusal.

2. Local infection and anatomical abnormalities at the site of caudal block and contraindication for regional anesthesia.

3. History of allergy to local anesthetics and other drugs used.

4. Coagulation disorders.

5. Pre-existing neurological or spinal diseases.

6. Patient with coexisting medical diseases.

7. History of developmental delay or mental retardation, which could make observational pain intensity assessment difficult.

8. Raised intracranial pressure.

9. Emergency surgery.

Parameters of the study were included:

1. Preoperative:

During preoperative visit, patient's age, weight, baseline vital parameters were recorded. Detailed history, physical examination was done. Routine laboratory investigations such as complete blood count (CBC), bleeding time, Prothrombine Time (PT), Partial Thromboplastine Time (PTT) and clotting time were carried out. All patients kept fasting as per institutional protocol 2 hr for clear liquid and 6 hr for semisolid and solid food, premedication was done by atropine IM 0.01-0.02 mg/kg.

Before surgery and before operation written and informed consent were taken from the parents.

2. Intraoperative:

On arrival to the operating room, all patients were connected to the monitor including (ECG), non-invasive blood pressure (NIBP), pulse oximetry for measuring the peripheral oxygen saturation (SpO_2) and capnogram to maintain End tidal carbon dioxide ($Etco_2$) 30-35 mmHg.

Then general anesthesia were induced using inhalation of 8 MAC sevoflurane in 100% oxygen with spontaneous ventilation, intravenous line was inserted (22 or 24 G cannula), secured then ringer lactate and glucose 5% 1:1 were infused at a rate of 4 ml/kg/h for 1st 10kg and 2 ml/kg/h for 2nd

10kg during and after the operation till oral fluid and feeding is started. Tracheal intubation by appropriate size of endotracheal tube (ETT) was facilitated by intravenous atracurium 0.5 mg/kg. Anesthesia was maintained by sevoflurane mean alveolar concentration MAC 0.8 with oxygen and maintenance of muscle relaxation by atracurium every 20 minutes when needed. Controlled mechanical ventilation was used to keep $EtCO_2$ between 30-35mmHg.

Patients were positioned in a lateral decubitus position. The sacral region was under complete aseptic condition with betadine and the sacral hiatus between the sacral conru was palpated. Then, a 23 G short needle was used to puncture the sacral surface at a 45 degree angle. When the sacro-coccygeal ligament seemed to be punctured, the needle was tilted more toward the skin surface and the needle was inserted 2-3 mm deeper. The proper placement of the needle was confirmed by 'swoosh' test in which a stethoscope was placed over the lower lumbar spine, corresponding to an area immediately above the end of the cannula. If the injection heard, this was recorded as a positive result that indicate proper placement of the needle. If the injection inaudible or equivocal, it was recorded as a negative test that indicate improper placement of the needle [11].

Inadvertent Dural puncture or intravascular placement was excluded by negative aspiration, both initially and after 2 ml of injection of the anesthetic drug. In addition, the volume of local anesthetic was injected slowly with continuous ECG monitoring.

Patients were numbered according to their orders at pre-anesthesia clinic and randomly allocated into three equal groups using enclosed envelope which were opened immediately before surgery by the anesthetist who will prepare the study solutions and not involved in further data handling.

Results

Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0). According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD , the following tests were used to test differences for significance;. difference and association of qualitative variable by Chi square test (X2) .

Table (1): Demographic data and clinical characters of the studied groups

	Group C	Group K	Group N	F	P
Age (months)	23.9±7.5	23.8±5.2	24.8±7.5	0.094	0.910
Weight (kg)	12.1±1.32	11.96±1.17	11.43±1.33	1.711	0.133
Gender N (%) Boy Girl	 7 (46.7%) 8 (53.3%)	 6 (40%) 9 (60%)	 8 (53.3%) 7 (46.7%)	0.535#	0.765

Mean ± SD N: Number ASA: American Sociaty of Anesthesia group C: control group group K: Ketamine group group N: Nostigmine group $p > 0.05$ was considered non significant.

The patient characteristics including age, weight, gender did not show any statistically significant difference between the three groups (p>0.05).

Table (2): Duration of anesthesia surgery, emergence time among studied groups

	Group C	Group K	Group N	F	P
Duration of anesthesia (minutes)	71.0 ± 13.3	74.3 ± 14.4	74.5 ± 15.2	0.280	0.758
Emergence time (minutes)	17.1 ± 2.2*	11 ± 1.1	10.7 ± 0.7	82.5	<0.001

As regard the duration of anesthesia comparing the duration of anesthesia among studied groups revealed that there were no significant differences found between the groups (p>0.001). However there was highly significant difference between them as regarding emergence time *p <0.001).

Table (3): Intra-operative MAP (mmHg) distribution among studied groups

Intraoperative MAP (mmHg)	Group C	Group K	Group N	F	P
Before induction MAP	84.26±2.12	82.93±1.66	84.0±2.23	1.825	0.174
10 min after induction	102.06±1.9	84.93±1.66	85.76±2.01	40.349	<0.001
20 min	85.53±2.41	83.93±1.66	85.0±2.23	32.364	0.124
30 min	90.26±1.98	84.98±1.66	84.66±2.01	41.531	<0.001
40 min	101.53±2.41	83.93±1.66	85.0±2.23	32.364	<0.001
50 min	85.55±2.75	84.93±1.66	84.88±2.28	3.226	0.068
60 min	85.06±2.89	84.85±2.95	84.65±2.87	2.188	0.129
70 min	85.03±2.33	84.97±2.71	84.55±2.01	0.207	0.814

Mean ± SD group C: control group group K: Ketamine group group N: Nostigmine group $p < 0.05$ was considered non significant. Min: minute MAP: mean arterial pressure

As regard MAP the mean and standard deviation values of intra-operative MAP (mmHg) before induction, 20 min, 50min, 60 min and 70 min after there were no significant differences between the groups. While there were highly significant difference between them at 10 min, 30 min and 40min.

Table (4): Intra-operative HR (beat/minute) distribution among studied groups

Intra operative HR (b/m)	Group C	Group K	Group N	F	P
Before induction HR	110.2±8.79	107.46±8.4	112.2±7.9	1.201	0.311
10 min after induction	133.2±8.79	109.33±7.6	113.2±8.1	36.811	<0.001
20 min	111.46±7.46	109.86±7.42	113.13±7.26	0.733	0.487
30 min	110.22±8.79	107.46±8.45	112.2±7.99	1.201	0.311
40 min	128.53±7.54	109.2±8.02	113.13±7.27	26.989	<0.001
50 min	112.53±7.54	111.33±7.41	114.13±7.33	0.546	0.583
60 min	110.53±9.27	108.66±8.11	112.2±7.89	0.668	0.518
70 min	112.46±9.12	108.90±7.11	112.3±8.39	1.347	0.271

Mean ± SD group C: control group group K: Ketamine group group N: Nostigmine group

p < 0.05 was considered non significant. Min: minute HR: heart rate

As regard HR the mean and standard deviation values of intra-operative HR (beat/minute) before induction, 20 min, 30 min, 50 min, 60 min and 70 min were no significant differences between the groups in intra-operative HR. while there were highly significant difference between them at 10 min and 40 min after induction (*p <0.001).

Table (5): Intra-operative SpO_2 (%) distribution among studied groups

Intra operative SpO_2 (%)	Group C	Group K	Group N	F	P
Before induction SpO_2	98.26±0.59	98.4±0.51	98.53±0.52	0.913	0.409
10 min after induction	98.44±0.61	98.58±0.55	98.68±0.49	0.253	0.778
20 min	98.45±0.55	98.48±0.53	98.53±0.52	0.516	0.601
30 min	98.63±0.45	98.46±0.66	98.59±0.52	1.138	0.330
40 min	98.36±0.59	98.48±0.51	98.58±0.59	0.605	0.551
50 min	98.28±0.52	98.51±0.56	98.55±0.51	1.1320	0.332
60 min	98.12±0.51	98.58±0.58	98.88±0.57	2.932	0.064
70 min	98.22±0.59	98.61±0.41	98.82±0.34	2.010	0.147

Mean ± SD group C: control group group K: Ketamine group group N: Nostigmine group

p < 0.05 was considered non significant. Min: minute SPO2: oxygen saturation

As regard SpO_2 there were no significant differences between the groups in intra-operative SpO_2 at different times.

Table (6): Post-operative MAP (mmHg) distribution among studied groups

Post operative MAP (mmHg)	Group C	Group K	Group N	F	P
1h	85.57±3.25	84.87±2.88	84.68±3.25	2.082	0.138
2h	84.66±3.21	84.35±2.55	84.28±1.85	1.831	0.172
4h	96.16±2.88	84.97±1.86	84.56±2.01	123.4373	<0.001
6h	95.73±2.73	83.93±2.97	83.84±2.89	85.4650	<0.001
8h	85.55±2.75	84.98±1.88	84.85±3.28	1.992	0.158
12h	84.56±2.99	84.15±3.94	84.65±2.87	2.533	0.099

Mean ± SD group C: control group group K: Ketamine group group N: Nostigmine group

p < 0.05 was considered non significant. h: hour MAP: mean arterial pressure

As regard operative MAP (mmHg) at 1st. 2nd, 8th and 12th hour there were no significant differences between the groups in post-operative MAP. While there were significantly higher among group C compared to K and N group at 4th, 6th hour postoperative.

Table (7): Post-operative HR (beat/minute) distribution among studied groups

Post operative HR (b/m)	Group C	Group K	Group N	F	P
1h	110.66±8.23	110.4±8.34	114.13±7.69	1.129	0.333
2h	111.22±9.21	107.46±8.45	112.12±7.99	0.786	0.462
4h	129.46±7.46	109.96±7.55	112.99±7.88	28.3561	<0.001
6h	125.53±7.54	112.58±7.74	114.13±7.65	12.8393	<0.001
8h	110.53±9.27	108.66±8.13	112.37±7.82	0.113	0.894
12h	111.53±7.89	111.68±8.88	111.11±7.79	0.223	0.801

Mean ± SD group C: control group group K: Ketamine group group N: Nostigmine group p < 0.05 was considered non significant. h: hour HR:heart rate

As regard post-operative HR (beat/minute) at 1st, 2nd, 8th and 12th hour there were no significant differences between the groups in post-operative HR. while there were significant differences between the groups at 4th and 6th H post-operative.

Table (8): Post-operative SpO_2 (%) distribution among studied groups

Post operative SpO_2 (%)	Group C	Group K	Group N	F	P
1h	98.43±0.49	98.61±0.63	98.85±0.64	2.613	0.085
2h	98.56±0.58	98.59±0.51	98.83±0.51	0.253	0.778
4h	98.26±0.62	98.51±0.59	98.68±0.41	2.532	0.092
6h	98.62±0.48	98.49±0.61	98.59±0.53	0.584	0.562
8h	98.39±0.58	98.46±0.66	98.88±0.63	1.082	0.348
12h	98.45±0.53	98.53±0.58	98.81±0.55	2.600	0.086

Mean ± SD group C: control group group K: Ketamine group group N: Nostigmine group

$p < 0.05$ was considered non significant. h : hour SPO2: oxygen saturation

As regard post-operative SpO_2 (%)revealed there were no significant differences between the groups in intra-operative SpO_2 at different times

Table (9): Total intra operative fentanyl consumption (µg/kg) and total postoperative (IV) paracetamol consumption (mg/kg).

	Group C Mean ± SD	Group K Mean ± SD	Group N Mean ± SD	F	P
Total intra operative fentanyl consumption (µg/kg)	7.86 ± 5.79	1.4 ± 3.73	0.73 ± 2.84	12.56	<0.001
1st Time for post operative analgesia (h)	5.73±1.03	10.66±1.32	11.66±0.81	90.762	0.00**
Post-operative (IV) paracetamol consumption (mg/kg)	17.0±3.16	8.66±2.55	5.66±1.098	34.140	0.00**

Group C: control group group K: Ketamine group group N: Nostigmine group

$p < 0.001$ was considered non significant. Mean ± SD: mean and standard deviation

As regard the total intra operative fentanyl consumption (µg/kg) was found to be significantly higher among C group compared to the other groups. Also there were highly significant differences between the studied groups as regarding first time for rescue analgesia and the amount of post-operative (IV) paracetamol consumption (mg/kg). It was found that first time for rescue analgesia was significantly longer in group N. Also, the total amount of paracetamol needed postoperatively was the significant lowest among N compared to other groups.

Table (10): FLACC distribution among studied groups

FLACC	Group C	Group K	Group N	Kruskal-Wallis H	P
	Median (IQR)	Median (IQR)	Median (IQR)		
FLACC_30min	0 (1-0)	0 (1-0)	0 (0-0)	0.235	0.889
FLACC_1h	1 (2-1)	0 (1-0)	0 (1-0)	21.077	<0.001
FLACC_2h	2 (3-2)	0 (1-0)	0 (1-0)	30.023	<0.001
FLACC_4h	5 (5-4)	0 (1-0)	0 (1-0)	31.723	<0.001
FLACC_6h	8 (9-6)	0 (1-0)	0 (1-0)	29.042	<0.001
FLACC_8h	3 (4-3)	2 (2-1)	1 (1-0)	26.646	<0.001
FLACC_12h	3 (3-2)	4 (4-3)	3 (4- 2)	4.114	0.128

group C: control group group K: Ketamine group group N: Nostigmine group

$p < 0.05$ was considered non significant. FLACC: face, leg, activity, cry, console ability

min: minutes h: hour IQR: inter quartile range **: Highly significant difference ($p<0.001$).

As regard FLACC scale there was a significant difference between the studied groups at 1 H, 2 H, 4 H, 6 H and 8 H. There was a significant increase in FLACC scale of group C compared with that of group K and group N ($p < 0.001$). While there was a no significant difference at 30 min and 12h as regarding FLACC.

Table (11): Post-operative complication distribution among studied groups

			Group			X^2	P
			Group C	Group K	Group N		
Vomiting	No	N	14	11	8		
		%	93.3%	73.3%	53.3%		
	Yes	N	1	4	7	6.13	0.047*
		%	6.7%	26.7%	46.7%		
Pruritus	No	N	15	14	11		
		%	100.0%	93.3%	73.3%		
	Yes	N	0	1	4	5.85	0.054
		%	0.0%	6.7%	26.7%		
Bradycardia	No	N	13	14	13		
		%	86.7%	93.3%	86.7%		
	Yes	N	2	1	2	0.45	0.79
		%	13.3%	6.7%	13.3%		

group C: control group group K: Ketamine group group N: Nostigmine group

$p < 0.05$ was considered non significant. N: number

As regard post-operative complication among studied groups the vomiting was found to be significantly higher among N group followed by K group. Comparing the pruritus and bradycardia revealed that there were no significant differences found between the groups.

DISCUSSION

Postoperative pain relief is great concern to anesthesiologists in various types of surgery in patients of all age group [13]. Caudal block is a simple and safe method that is used frequently in pediatric surgery. Caudal blockade is considered the most popular regional anesthetic procedure used in children, and it is an applicable method for providing postoperative analgesia after lower abdominal surgeries. It can reduce the amount of inhaled and intravenous anesthetic requirement, attenuate the stress response of anesthesia and surgery, and provide excellent immediate postoperative analgesia [14].

Caudal bupivacaine is frequently used for perioperative pain relief after surgery in children [13]. Although it is the local anesthetic with the longest duration of action that is currently available, however, it provides short duration of action (2-4 h) after a single injection [15]. Many agents including different opioids, epinephrine, ketamine, midazolam, neostigmine, and α2 agonists have been added to caudal bupivacaine when used as a single-shot' technique to lengthen the period of analgesia[15].

In our study, there was statistically non significant difference regarding the patient characteristics between the three groups (p>0.05). Sawan et al [13] (agreed with our study \) also found statistically insignificant difference the patient characteristics including age, weight and ASA grade did not show any statistically significant difference between the two groups. In another study Omar et al [16] reported that according to patient's demographic data (age in years and sex), duration of surgery and Total volume (ml) given in caudal block, there was no significant difference among the three groups (pvalue >0.05).

As regard analgesic duration duration there was no significant difference as regard anesthesia time. (Median ± SD) was 71.0 ± 13.3, and 74.5 ± 15.2 (minutes) in group C and group N respectively. In agreement with Ataro and Bernard [17] compared the analgesic duration (Median ± SD) was 8.7 ± 5.3 hrs in Group BN and 5.8 ± 2.3 hrs in Group-B (p=0.003). Although highly significant prolongation of analgesia time, the duration in combination group was slightly shorter than the one reported in a previous study with 2 mic/kg dose of neostigmine. Also Taheri et al [18] reported that the duration of absolute analgesia was significantly prolonged in group BT compared to group BN (17.30 ± 8.24 h vs. 13.98 ± 10.03 h, P < 0.05. Kumar et al [19] reported that there were no differences among groups in HR, and MAP during the study period. The duration of surgery and duration of general anesthesia were also similar.

In this study the Emergence time (minutes) (Median ± SD) was 17.1 ± 2.2,and 10.7±0.7 in group C and group N respectively. There was highly significant difference between them as regarding emergency time which was found to be significantly lower among N group compared to C group. In agreement with Sinha and Sood [20] reported that recovery characteristics and complications were recorded. The emergence time (minutes) was 11±3.2 in NC, 14.5±1.5 in group B, and 24±2.5 in group BK, (P<0.05). Emergence time and duration of pain relief were significantly higher in the NC group (P<0.05). Duration of analgesia and emergence time were significantly more in group BK than groups B and NC.

As regard MAP and HR, the result of the current study is there was no significant difference between the studied groups as regarding different MAP, HR readings during the operation at before induction, after induction 20 min, 50 min, 60 min and 70 min. While there were highly significant difference between them as regarding intra-operative MAP and HR which was found to be significantly higher among group C compared to N group at 10, 30 and 40 min after induction ($^{*}p < 0.001$).

As regard MAP and HR the result of the current study is there was no significant difference between the studied groups as regarding different MAP, HR readings postoperative at 1h, 2h, 8h and 12h. While there were highly significant difference between them as regarding postoperative MAP and HR which was found to be significantly higher among group C compared to N group at 6th and 4th hour postoperative ($^{*}p < 0.001$).

As regard SpO_2, the result of the current study is there was no significant difference between the studied groups as regarding different SpO_2 readings during and after the operation. This was in agreement with Abdulatif and El-Sanabary [21] who reported better perioperative hemodynamics with the use of the caudal bupivacaine/ neostigmine mixture rather than bupivacaine or neostigmine alone. Intraoperative heart rate was significantly increased in the caudal neostigmine group compared with the bupivacaine/neostigmine and the bupivacaine groups.

The result of the current study is there was non-significant difference between the studied groups as regarding different MAP, HR, SPO_2 readings after the operation at 1 hour, 2hour, 4hour, 6hour, 8hour and 12hour.

Omar et al [16] reported that HR, MAP and SpO_2 were recorded at baseline (before induction) and 15, 30, 60 min after induction of anesthesia and 5, 30, 60 & 120 min after recovery (postoperative). Heart rate and mean arterial blood pressure were statistically non-significant difference in the three groups but it was statistically significant difference between the pre-operative heart rate and mean arterial blood pressures and at 25min in group I. There was no a statistically significant difference in SpO_2 between the three groups. Also Sawan et al [13] reported the heart rate (HR), there was statistically significant lower HR at 2, 4 and 6 hours postoperatively in group I (II/IH group) , while no significant at other times. Regarding systolic blood pressure, group I (II/IH group) showed statistically significant lower readings at 4 and 6 hours postoperatively. while the difference was insignificant at other times .while there was no significant difference regarding diastolic blood pressure between the 2 groups .Also, there was no statistically significant difference between the two groups regarding oxygen saturation(SpO_2) and end-tidal CO_2(Et co_2).

In this work there were highly significant differences between the studied groups as regarding first time for rescue analgesia and the amount of paracetamol and fentanyl needed postoperatively. It was found that total intra operative fentanyl consumption (µg/kg) was found to be significantly higher among C group (7.86 ± 5.79) compared to N group (0.73 ± 2.84). Also, the total intra operative fentanyl consumption (µg/kg) needed intraoperatively was the significant lower in N group compared to K and C groups. There were highly significant differences between the studied groups as regarding first time for rescue analgesia and the amount of post-operative (IV) paracetamol consumption (mg/kg). It was found that first time for rescue analgesia was

significantly longer among N (11.66±0.81) group compared to C group respectively.

Also, the total amount of paracetamol needed postoperatively was the significant lowest among N (5.66±1.098) group compared to C group (17.0±3.16) mg respectively

In the line with current study Abdulatif and El-Sanabary [21] the recovery to first rescue analgesic times were (mean ± sd) 22.8 ± 2.9 h, 8.1 ± 5.9 h, and 5.2 ± 2.1 h in the bupivacaine/neostigmine, bupivacaine, and neostigmine groups, respectively ($P < 0.001$). In addition, the bupivacaine and neostigmine groups received more doses of paracetamol than the bupivacaine/neostigmine group to maintain adequate analgesia in the first 24 postoperative h. Postoperative vomiting occurred in 25%, 10%, and 30% in the caudal bupivacaine/neostigmine, bupivacaine, and neostigmine groups, respectively ($P < 0.01$).

Sawan et al [13] reported that first call for analgesia in hours was 5.2+/- 1.5 in group I (II/IH group), and 4+/-1.3 in group II (caudal group) which is statistically difference. By comparing the analgesic consumption ,group I (II/IH group) showed less doses of analgesics needed and the total amount of analgesics used also was statistically lower in group I (II/IH group).

As regard pain assessment, this study assessed the pain by FLACC scale which was significantly increased within the same group at different measurement times in the three groups. There was a significant increase in FLACC scale of group C compared with that of group N ($p < 0.001$) at 1 H, 2 H, 4 H, 6 H and 8 H. While there was a non- significant difference at 0.5 H and H as regarding FLACC. This is in agreement with Omar et al [16] the FLACC pain score was significantly lower in dexmedetomidine group than bupivacaine only group. The FLACC pain score was significantly lower in neostigmine group than bupivacaine only group. There was no a statistically significant difference between group I & group II at 1hr, 2hr, 6hr, 12hr, 24hr (p-value <0.05). Sawan et al [13] reported that there was statistically significant difference between the two groups regarding pain score (ChIPPS) at four hour and at six hours post – operatively ($p<0.05$), as the number of patients has lower ChIPPS score was more in group I (II/IH group) but the difference was insignificant at other times.

In line with the results of the current study, co-administration of 2 μg/kg neostigmine and 1 ml/kg of caudal bupivacaine of 0.25% in children who endured hypospadias surgery extended the duration of the postoperative analgesia significantly and reduced the need for oral paracetamol [22].

As regard to post-operative complication the vomiting was found to be significantly higher among N group, followed by K group (46.7% versus 26.7% respectively). However, only 6.7% of patients in C group experienced vomiting.. This agreement with Abdulatif and El-Sanabary [21] Vomiting occurred in the recovery room in 5 (25%), 2 (10%), and 6 (30%) patients in the caudal bupivacaine/neostigmine, bupivacaine, and neostigmine groups, respectively ($P < 0.01$) Taheri et al [19] reported Adverse effects excluding the vomiting were not observed in any patients. Postoperative vomiting was detected in 9 (30%) and 7 (23.3%) patients in group BN and group BT, respectively duration.

Conclusion

The results of this study made us to conclude that the addition of 2μg/kg neostigmine, or 0.5 mg/kg ketamine as an adjuvant to 1 ml/kg of 0.25% caudal bupivacaine could lengthen the

duration of postoperative analgesia in children undergoing lower abdominal surgeries without increasing the incidence of side effects. However, neostigmine offered a significant advantage over ketamine in this regard.

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