Enhancement of bupivacaine caudal analgesia using nalbuphine compared with fentanyl in children undergoing inguinal hernia repair

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Background
General anaesthesia in paediatrics is used usually accompanied with caudal block (CB) to allow for rapid and smooth recovery from anaesthesia and also for better control of pain associated with various surgical interventions especially those in the lower half of the body. However, CB using local anaesthetics alone provides short duration of analgesia. Therefore, various additives are being tested for providing longer duration of pain control. Opioids are one of the most beneficial additives to local anaesthetics in CB. Some researchers studied the analgesic efficacy of adding fentanyl or nalbuphine to different local anaesthetics in separate studies. In this trial, we wished to compare effects of adding fentanyl or nalbuphine to the local anaesthetic (bupivacaine: 0.125%) in single-shot CB.

Participants and methods
A total of 60 children scheduled for hernia repair operations under general anaesthesia combined with combined anaesthesia were divided into three groups: group C received caudal bupivacaine plus normal saline, group N received caudal bupivacaine plus nalbuphine and group F received caudal bupivacaine plus fentanyl. Anaesthesia was maintained with sevoflurane. Intraoperative standard monitoring was denoted every 15 min till the end of surgery which was allowed to start 15 min after caudal injection. Postoperatively, haemodynamics, pain score, adverse effects, sedation and agitation state were assessed.

Results
There were significant differences in postoperative pain score and sedation as group N had prolonged analgesia and prolonged sedation time than group F and group C with comparable incidence of adverse effects.

Conclusion
Adding nalbuphine 0.2 mg/kg to bupivacaine 0.125% provides better postoperative pain control than adding fentanyl 1 μg/kg to bupivacaine in the same concentration with comparable incidence of adverse effects.

Keywords:
bupivacaine, caudal analgesia, children, fentanyl, nalbuphine

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Introduction

Caudal epidural injection with local anaesthetic is a popular regional anaesthetic technique used in infants and children [1]. Various additives to the local anaesthetic solution have been employed in an attempt to prolong the duration of a single caudal epidural injection. Opioids are commonly used as adjuncts for caudal blockade (CB) and have been shown to consistently increase the duration of analgesia [2]. Fentanyl is a potent rapid-acting, completely synthetic mu receptor-stimulating opioid [3]. It was the first of the fentanyl family of opioids that somewhat later included sufentanil, alfentanil and remifentanil for human patients and carfentanil and thiofentanil approved for wild animals [4]. It has minimal cardiovascular effects, does not result in increases in plasma histamine, is relatively short acting and is easy and is inexpensive to synthesise and prepare for the marketplace [5]. Nalbuphine is a synthetic opioid agonist–antagonist analgesic derivative of the phenanthrene group, and its structure is similar to those of naloxone and oxymorphone. It acts as an agonist of kappa opioid receptors (KORs) and mu-opioid receptors (MORs), thus providing analgesia as well as sedation, and it protects against receptor blockade-dependent respiratory failure. Nalbuphine exhibits a ceiling effect; in other words, once its maximum plasma concentration has been reached, incremental doses do not potentiate its analgesic effects or increase the risk of respiratory failure [6]. Unacceptable adverse effects, including nausea, vomiting, pruritus and the risk of

respiratory depression, have limited the use of opioid additives in children undergoing day-case surgery [7]. The main goal of CB is to provide postoperative pain relief, and it is accepted that the block is performed in anaesthetized children [8].

Materials and methods

This was a double-blinded prospective randomized clinical trial that was performed in Assiut university paediatric hospital between August 2016 and September 2017. Our study was conducted after obtaining approval from Assiut University Hospital Ethical Committee and informed written consent from children' guardians. This study included 60 ASA status I paediatric patients, aged between 2 and 6 years old, who were scheduled for elective inguinal hernia repair.

Exclusion criteria included guardians' refusal and patients with congenital anomalies at the lower spine or meninges, increased intracranial pressure, skin infection at the site of injection, bleeding diathesis, known allergy to any drug used in this study, bilateral or recurrent inguinal hernia, cardiopulmonary disease and other congenital anomalies.

Children were randomly assigned to three groups: group C (control group) (n = 20) received bupivacaine 0.125% 1 ml/kg plus 2 ml normal saline. Group N (nalbuphine group) (n = 20) received bupivacaine 0.125% 1 ml/kg plus nalbuphine 0.2 mg/kg in 2 ml solution. Group F (fentanyl group) (n = 20) received bupivacaine 0.125% 1 ml/kg plus fentanyl 1 μg/kg in 2-ml solution. The total volume did not exceed 20 ml for each group. Randomization was done by using computer-generated randomization table. All routine investigations were checked preoperatively, and the results were available at the time of surgery. Premedication in the form of 0.5 mg/kg oral midazolam was given orally half an hour before induction of anaesthesia. Intraoperative standard monitoring (ECG, noninvasive blood pressure, pulse oximeter, temperature and end tidal CO_2) was considered. All children were adequately hydrated by using ringer solution according to rule of 4: 2: 1, and all operations were performed in the morning as the first case in the schedule.

Anaesthesia

The anaesthetic management of all cases was the same in the three groups; we used the volatile induction and maintenance of anaesthesia method using sevoflurane in oxygen. Anaesthesia was induced with sevoflurane 8% in oxygen 100% by face mask. After induction, venous access is established and laryngeal mask airway of appropriate size is inserted after the eyelash reflex of the child disappeared. Single-dose CB using a 22G needle (22 G Teflon Venous Cannula by Abbott Laboratories Lake Bluff, Illinois, United States) was given using the aforementioned drugs according to the group. Anaesthesia was maintained with sevoflurane, and intraoperative monitoring of vital signs (pulse, blood pressure, respiratory rate, end tidal CO_2) was denoted every 15 min till the end of surgery. Surgery was allowed to start 15 min after caudal injection. During surgery, inadequate analgesia was defined as increase in heart rate (HR) and systolic arterial blood pressure readings of more than 20% from values taken just before skin incision. When that occurred, it was treated with a rescue dose of intravenous perfalgan (10–15 mg/kg), and such cases were excluded from the study.

No other anaesthetics, analgesics, sedatives or antiemetics were allowed during the operation. At the end of the operation, patients were awakened and transported to a postanaesthesia care unit.

Postoperative assessment

Postoperatively, quality of recovery, haemodynamic, pain score, sedation and agitation state were assessed. Postoperative pain was assessed by an experienced nurse who was unaware of the patient's allocation using FLACC pain scale (Face, Legs, Activity, Cry and Consolability) (Table 1) [9]. FLACC pain scale is a measurement used to assess pain in children between the ages of 2 months and 7 years or in individuals who are unable to communicate their pain. The scale is scored every 2 h for 24 h in a range of 0–10, with 0 representing no pain whereas 10 is the worst pain. The duration of analgesic action was taken as the time from CB till the first complaint of pain (pain score ≥4)]. A pain score of at least 4 resulted in the administration of rescue analgesia, that is, intravenous paracetamol 10–15 mg/kg (could be repeated twice) and then intravenous nalbuphine 100 μg/kg for intractable pain. Agitation state was assessed using Richmond Agitation-Sedation Scale score (Table 2) [10]. It is a medical scale used to measure the agitation or sedation level of a person. It was developed with efforts of different practitioners, represented by physicians, nurses and pharmacists. Adverse effects such as pruritus, flushing, vomiting, respiratory depression and urine retention, all were checked for, managed and documented.

Statistical analysis

The data were tested for normality using the Anderson–Darling test and for homogeneity variances before further statistical analysis. Categorical variables

Table 1 FLACC Behavioural Pain Assessment Scale

Criteria	Score 0	Score 1	Score 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, and uninterested	Frequent to constant quivering chin and clenched jaw
Legs	Normal position or relaxed	Uneasy, restless and tense	Kicking or legs drawn up
Activity	Lying quietly, normal position and moves easily	Squirming, shifting, back and forth, and tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs and frequent complaints
Consolability	Content and relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Score: 0, no pain; 1-3, mild pain; 4-7, moderate pain; 8-10, severe pain.

Table 2 The Richmond Agitation-Sedation Scale

Scores	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube (s) or catheter (s) or has aggressive behaviour toward staff
+2	Agitated	Frequent nonpurposeful movement or patient-ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	Spontaneously pays attention to caregiver
-1	Drowsy	Not fully alert, but has sustained (more than 10 s) awakening, with eye contact, to voice
-2	Light sedation	Briefly (<10 s) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

were described by *n* (%) where continuous variables described by mean and SD. The χ^2-test and fisher exact test were used to compare between categorical variables, whereas comparison between continuous variables was done by *t*-test and independent-samples *t*-test analysis of variance. A two-tailed *P* value of less than 0.05 was considered statistically significant. We used Pearson's and Spearman's correlation to appear the association between variables. All analyses were performed with the IBM SPSS 20.0 software statistics version 22.0 (SPSS Software, Chicago, IL, USA).

Results

There was no statistically significant difference ($P > 0.05$) among the three groups regarding age, weight, sex, ASA classification or operation type (Table 3).

Regarding postoperative analgesia, on comparing of the FLACC pain score in control group and fentanyl group, there was statistically significant difference ($P < 0.05$) between two groups at times 4, 6, 8, 10, 12, 14, 16, 18 and 24 h, postoperatively. Comparing control group with nalbuphine group, there was a statistically significant difference ($P < 0.05$) between the two groups at all times of study postoperatively. Finally, comparing fentanyl group with nalbuphine group, we found that there was statistically significant difference ($P < 0.05$) between two groups at all times of study postoperatively (Table 4 and Fig. 1).

On comparing analgesic profile, we found that there was a statistically significant difference ($P < 0.05$) between control group and fentanyl group regarding total intravenous paracetamol consumption and number of requests for postoperative analgesia. However, on comparing control group and nalbuphine group, we found that there was a statistically significant difference ($P < 0.05$) between two groups regarding time to first analgesic request, total paracetamol consumption and number of requests for postoperative analgesia. Finally, in comparing nalbuphine group and fentanyl group, we found that there was a statistically significant difference between them regarding time to first analgesic request, total intravenous paracetamol consumption, and number of requests for postoperative analgesia (Table 5).

On comparison of postoperative sedation and agitation in fentanyl group with control group, we found that there was a statistically significant difference ($P < 0.05$) between them at times from 2, 4, 6, 8, 10, 14, 16 and 18 h, postoperatively.

On comparing nalbuphine group and control group, we found that there was a statistically significant difference ($P < 0.05$) at all times 2, 4, 6, 8, 10, 12, 14, 16, 18, 20 and 22 h, postoperatively. However, on comparing nalbuphine group with fentanyl group, we found that there was a statistically significant difference ($P < 0.05$) between them at times 2, 4, 6, 8, 10, 12, 18 and 20 h, postoperatively (Fig. 2).

Concerning postoperative adverse effects, none of the patients developed respiratory depression at all times of study. As for vomiting and itching, five out of 60 patient developed vomiting [one (5%) patient in control group and four (20%) patients in nalbuphine group], with no significant differences on comparison among the three studied groups. Four out of 60 patients

Table 3 Demographic data and patient characteristics

	Control [*n* (%)]	Fentanyl [*n* (%)]	Nalbuphine [*n* (%)]	P_1	P_2	P_3
Age (mean±SD) (years)	3.78±1.67	3.1+1.39	3.9±1.6	0.178	0.802	0.112
Weight (mean±SD)	15.53±4.97	13.43±3.82	14.4±3.82	0.123	0.405	0.470
Sex						
Male	19 (95)	17 (85)	19 (95)	0.598	1.000	0.598
Female	1 (5)	3 (15)	1 (5)			
ASA I	20 (100)	20 (100)	20 (100)	-	-	-
Diagnosis						
OIH	16 (80)	16 (80)	19 (95)	1.000	0.339	0.339
DPH	4 (20)	4 (20)	1 (5)			
Operation time (mean±SD) (min)	43.5±10.65	39.5±12.13	37.75±10.94	0.266	0.112	0.625
Anaesthesia time (mean±SD)	77.0±9.38	67.0±9.23	68.75±10.99	0.002*	0.011*	0.578

P_1, comparison between control and fentanyl; P_2, comparison between control and nalbuphine; P_3, comparison between fentanyl and nalbuphine.*P<0.05, statistically significant difference in comparison with control.#P<0.05, statistically significant difference in comparison with fentanyl. OIH=Oblique inguinal hernia, DIH=Direct inguinal hernia

Table 4 Postoperative analgesia (FLACC Score)

	Control (mean±SD)	Fentanyl (mean±SD)	Nalbuphine (mean±SD)	P_1	P_2	P_3
T2	2.2±0.7	1.8±0.95	0.9±1.12	0.183	0.000*	0.004*
T4	3.05±0.76	1.65±0.93	0.45±0.6	0.000*	0.000*	0.000*
T6	3.6±0.94	1.85±0.67	0.45±0.6	0.000*	0.000*	0.000*
T8	2.5±0.69	1.6±1.1	0.45±0.51	0.001*	0.000*	0.000*
T10	2.95±0.69	2±1.12	0.45±0.51	0.001*	0.000*	0.000*
T12	2.75±1.16	1.65±1.53	0.5±0.69	0.005*	0.000*	0.003*
T14	2.8±0.83	1.55±1	0.35±0.59	0.000*	0.000*	0.000*
T16	2.8±1.2	1.85±1.39	0.35±0.81	0.012*	0.000*	0.000*
T18	2.5±0.89	1.8±1.36	0.35±0.75	0.036*	0.000*	0.000*
T20	2.7±1.03	2.25±1.33	0.85±0.93	0.206	0.000*	0.000*
T22	2.45±0.69	1.9±1.21	1±0.92	0.076	0.000*	0.004*
T24	2.85±1.14	2.1±1.29	0.95±0.89	0.038*	0.000*	0.002*

P_1, Comparison between control and fentanyl; P_2, Comparison between control and nalbuphine; P_3, Comparison between fentanyl and nalbuphine.*P<0.05, statistically significant difference.

Table 5 Postoperative analgesic profile

	Control (mean±SD)	Fentanyl (mean±SD)	Nalbuphine (mean±SD)	P_1	P_2	P_3
First analgesic request (h)	7.95±2.05	9.1±7.87	0±0	0.442	0.000*	0.000*
Total intravenous paracetamol consumption (mg/24 h)	628.5±289.39	236.5±248.91	0±0	0.000*	0.000*	0.001*
Number of request	2.7±0.8	1.15±1.04	0±0	0.000*	0.000*	0.000*
Total nalbuphine dose (μg/24 h)	0±0	0±0	0±0	-	-	-
Total nalbuphine frequency	0±0	0±0	0±0	-	-	-

P_1, comparison between control and fentanyl; P_2, comparison between control and nalbuphine; P_3, comparison between fentanyl and nalbuphine.*P<0.05, statistically significant difference.

developed itching [one (5%) patient in nalbuphine group and three (15%) patients in fentanyl group] but these changes of no statistical significance (Table 6).

Concerning intraoperative HR, there was a statistically significant difference (P < 0.05) between control group and nalbuphine group at times (after induction, after CB, skin incision, 15 min after CB, 30 min after CB and 45 min after CB). Moreover, there was a statistically significant difference (P < 0.05) between fentanyl group and nalbuphine group at the following times: after induction, after CB, 15 min after CB and 30 min after CB (Table 7).

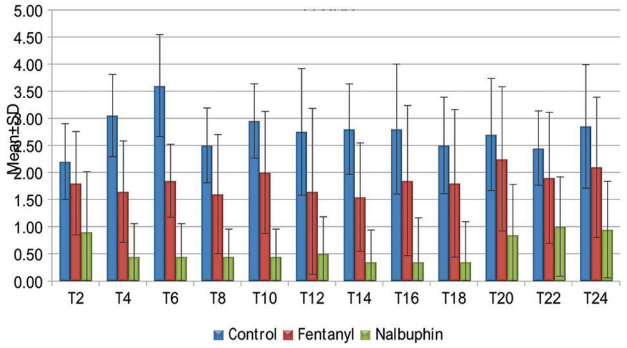
Regarding mean arterial blood pressure, there was a statistically significant difference (P < 0.05) between fentanyl group and nalbuphine group at 15 min and 45 and 60 min after CB (Table 8).

Discussion

Paediatric regional anaesthesia has attained wide use internationally because of its efficacy and safety [11]. Owing to short duration of analgesia, it is better to use additives to local anaesthetics to increase analgesic duration. Opioids are commonly used to enhance analgesic efficacy and to decrease adverse effects of using local anaesthetics alone in CB.

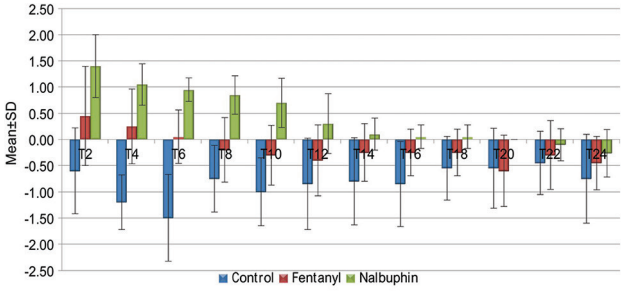
In our study, we found that nalbuphine provides longer duration of analgesia (24 h) with no exogenous analgesic

Figure 1



Postoperative analgesia (FLACC score).

Figure 2



Postoperative sedation (RASS score).

Table 6 Adverse effects

	Control [*n* (%)]	Fentanyl [*n* (%)]	Nalbuphine [*n* (%)]	P_1	P_2	P_3
Respratory depression						
Yes	-	-	-	-	-	-
No	20 (100)	20 (100)	20 (100)			
Urinary retention						
Yes	0 (0)	0 (0)	1 (5)	-	0.003*	0.003#
No	20 (100)	20 (100)	19 (95)			
Itching						
Yes	0 (0)	3 (15)	1 (5)	0.230	1.000	0.598
No	20 (100)	17 (85)	19 (95)			
Vomiting						
Yes	1 (5)	0 (0)	4 (20)	1.000	1.000	0.114
No	19 (95)	20 (100)	16 (80)			

P_1, comparison between control and fentanyl; P_2, comparison between control and nalbuphine; P_3, comparison between fentanyl and nalbuphine. *P<0.05, statistically significant difference in comparison with control. #P<0.05, statistically significant difference in comparison with fentanyl.

consumption when compared with fentanyl (analgesic duration; 9.1 ± 7.87 hours and analgesic consumption; 236.5 ± 248.91 mg/24 h) and bupivacaine alone (analgesic duration; 7.95 ± 2.05 h and analgesic consumption; 628.5 ± 289.39 mg/24 h). Moreover, nalbuphine causes sedation more than fentanyl.

Nalbuphine acts as an agonist of KORs and MORs, thus providing analgesia through two different mechanisms [6] (supraspinal analgesia by MORs and spinal analgesia and sedation by KORs), and it protects against receptor blockade-dependent respiratory failure. However, fentanyl [3] acts only as an agonist on MORs which is responsible for supraspinal analgesia only. In addition, nalbuphine caused vomiting more than fentanyl which may be attributed to stimulation of the medullary chemoreceptor trigger zone which is responsible for opioid-induced nausea and vomiting which does not explain the disappearance of vomiting in fentanyl group. This also may be owing to many other causes that may cause vomiting in the early postoperative period and that can explain occurrence of vomiting in control group. However, itching was more in fentanyl than nalbuphine group, and this can be explained by inhibition of pain neurons in the dorsal horn cell by opioids, which allows itch neurons to fire into the ascending tract without a real peripheral stimulus. However, we may need to study these drugs on much more paediatric population to make these results more accurate.

Mohamed *et al.* [12] studied the efficacy of caudal nalbuphine in postoperative pain control. They compared nalbuphine plus bupivacaine (BN group) versus bupivacaine alone (B group) in single-shot CB. Patient's pain intensities were evaluated by Pain Discomfort Scale for the first 24 h postoperatively. They found that duration of analgesia was longer in BN group, and time-to-first analgesic request was 10.1 ± 1.5 h in BN group versus 6.2 ± 1.4 h in B group. Regarding sedation scores, they used an objective score based on eye opening, and they found that in BN group there was more sedation scores at 30 min and 1 h postoperatively. Their results were in consistence with the results of the current study in postoperative pain reduction, and no respiratory depression was observed. In contrast with our study, no adverse effects have been reported in their study. This can be explained by their use of smaller dose of nalbuphine (0.1 mg/kg) than our study (0.2 mg/kg) and higher concentration of bupivacaine (0.25%) (vs. 0.125% in our study), which may be responsible for the occurrence of adverse effects and the difference in haemodynamics in our study than their study.

Salama [13] also studied the effect of adding nalbuphine to local anaesthetic in single-shot CB. He compared levobupivacaine alone (L group) versus levobupivacaine plus nalbuphine (LN group). In line with our study, they found that FLACC pain scores were significantly less in LN group compared with L group after the second hour and in the next time intervals. The first time for postoperative analgesic requirement was significantly longer in LN group (384 ± 23.1 min) compared with L group (202.20 ± 23.42 min) (P > 0.001). The total dose of postoperative supplementary analgesia (intravenous

Table 7 Intraoperative heart rate (beats/min)

	Control (mean±SD)	Fentanyl (mean±SD)	Nalbuphine (mean±SD)	P_1	P_2	P_3
Basal	135.85±7.47	136.7±11.42	133.15±20.83	0.852	0.555	0.438
After induction	128.25±10.61	128.45±13.56	118.3±16.05	0.963	0.024*	0.022*
After caudal block	122.35±12.82	123.1±15.66	111.35±17.42	0.878	0.028*	0.019*
Skin incision	122.45±13.5	121±15.83	111.5±17.65	0.772	0.032*	0.062
15 min after caudal block	122.9±12.94	121.35±14.71	112.65±13.28	0.721	0.021*	0.049*
30 min after caudal block	119.9±15.38	120.35±16.04	109.25±14.21	0.926	0.031*	0.025*
45 min after caudal block	120±12.78	118.63±16.5	110.3±16.02	0.779	0.048*	0.092
60 min after caudal block	117.13±16.08	117.33±20.98	111.2±16.9	0.978	0.411	0.455
75 min after caudal block	103±20.23	114.33±18.48	124±3.74	0.370	0.094	0.441

P_1, comparison between control and fentanyl; P_2, comparison between control and nalbuphine; P_3, comparison between fentanyl and nalbuphine.*P<0.05, statistically significant difference.

Table 8 Intraoperative mean arterial blood pressure (mmHg)

	Control (mean±SD)	Fentanyl (mean±SD)	Nalbuphine (mean±SD)	P_1	P_2	P_3
Basal	69.1±6.15	70.7±8.5	70.65±6.03	0.472	0.486	0.982
After induction	67.4±6.39	69.1±8.69	67.4±6.23	0.458	1.000	0.458
After caudal block	66.85±7.17	67.15±8.82	64.3±6.55	0.901	0.291	0.239
Skin incision	66.9±6.02	66.3±8.57	64±6.74	0.793	0.207	0.316
15 min after caudal block	66.65±6.26	67.79±7.89	63.3±6.2	0.603	0.125	0.044*
30 min after caudal block	66.15±7.12	67.15±9.34	62.85±5.16	0.671	0.164	0.072
45 min after caudal block	66.1±7.05	67.53±8.34	62.35±5.15	0.524	0.093	0.024*
60 min after caudal block	65.63±6.13	70.2±7.81	62.2±4.1	0.076	0.179	0.007*
75 min after caudal block	67.75±4.5	76.33±2.31	67.5±8.23	0.091	0.953	0.084

P_1, comparison between control and fentanyl; P_2, comparison between control and nalbuphine; P_3, comparison between fentanyl and nalbuphine.*P<0.05, statistically significant difference.

paracetamol infusion) in the first 12 h was significantly lower in LN group (200.5 ± 65.5 mg) in comparison with L group (355.25 ± 69.9 mg). In contrast to our study, they found that no serious adverse effects were recorded in the first 12 h in all patients. No postoperative sedation, hallucination, nausea, vomiting, allergy or significant HR and blood pressure changes were reported. Such difference between the two studies may be explained by the different effects of levobupivacaine which is less toxic to the central nervous system and is also less likely to cause myocardial depression and fatal arrhythmias than bupivacaine [14]. In addition, this can be explained by their use of lower concentration of levobupivacaine in group LN (0.125 vs. 0.25%), whereas we used the same concentration of bupivacaine in both groups.

Salama *et al.* [15] compared nalbuphine, dexmedetomidine and bupivacaine alone in three separate group in single-shot CB. They found that dexmedetomidine and nalbuphine are additives used safely in caudal epidural analgesia/anaesthesia in children to improve and prolong the analgesic profile of caudal analgesia. In consistence with our study, they found that the postoperative FLACC pain scores were significantly less in BD group and to a lesser extent in BN group than in B group (P < 0.001). The first time for postoperative analgesic requirement was significantly longer in BD group (16.89 ± 0.74 h) and to a lesser extent in BN group (6.70 ± 0.38 h) than the B (control) group (4.84 ± 0.70 h) (P < 0.001). The total dose of postoperative supplementary analgesia (intravenous paracetamol) in the first 24 h was significantly lower in BD group (128.75 ± 32.72 mg) and to a lesser extent in BN group (263.25 ± 69.99 mg) than in the control group (276.25 ± 94.41 mg) (P < 0.001). Regarding sedation, patients in BD and BN groups were more sedated in the first 6 h than in control group. In contrast to our study, they found that no adverse effects were recorded in the first 24 h in all patients. No postoperative hallucination, nausea, vomiting, allergy or significant HR and blood pressure changes were reported.

Gaitini *et al.* [16] studied the effect of adding fentanyl to bupivacaine, compared with bupivacaine alone on the stress response (on the plasma level of catecholamines) and postoperative analgesia using the modified Children's Hospital of Eastern Ontario Pain Score (mCHEOPS) score. Their patients were randomly assigned to two groups (group A = bupivacaine alone and group B = bupivacaine and fentanyl). In contrast to our study, they found that pain score (using mCHEOPS) was similar in both groups. No statistically significant differences between the two groups were found regarding either the time of the first intravenous fentanyl administration or the number of patients who required fentanyl. There were also no significant differences between the two groups regarding the time of the first dose and the number

of patients who received paracetamol in the ward. In line with our study, nausea and/or vomiting were experienced by three patients in group A and four patients in group B; they were treated effectively with intravenous metoclopramide. No child demonstrated respiratory frequency of less than 12 breaths/min. Nasal pruritus occurred in one patient in group A and two patients in group B.

Ahuja *et al*. [17] studied the efficacy of caudal fentanyl versus ketamine on postoperative pain and neuroendocrine stress response in children undergoing infraumbilical and perineal surgery. In line with our study, they achieved good pain relief with very low visual analogue scale scores in all the three groups in immediate postoperative period. However, in children who received bupivacaine alone, we found that rescue analgesia was required at a much earlier time, ~4 h, as compared with 8 h in ketamine and 6 h in fentanyl group. Mean time for requirement of rescue analgesia in bupivacaine group was 4.10 ± 0.5 h, whereas it was 5.95 ± 0.63 in fentanyl group and 8.23 ± 0.57 in ketamine group. Time for rescue analgesia was highest in ketamine group, indicating longer duration of postoperative analgesia with ketamine as compared with fentanyl and bupivacaine group. They did not agree with our study regarding adverse effects such as motor weakness, urinary retention or pruritis, which was not found in any group.

Limitations and recommendations

A larger group of patients can be further studied for occurrence of opioid-induced adverse effects to give more accurate and conclusive results concerning this point.

Conclusion

The current study showed that single-shot CB adding nalbuphine 0.2 mg/kg to bupivacaine 0.125% provides better postoperative pain control than adding fentanyl 1 mg to bupivacaine in the same concentration with comparable incidence of adverse effects.

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Conflicts of interest

There are no conflicts of interest.

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