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Comparative study of caudal bupivacaine versus bupivacaine with tramadol for postoperative analgesia in paediatric cancer patients

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Abstract ***Objective:*** Caudal epidural analgesia has become very common analgesic technique in paediatric surgery. Adding tramadol to bupivacaine for caudal injection prolongs duration of analgesia with minimal side effects. The aim of the study was to investigate the different effects of caudal bupivacaine versus bupivacaine with thamadol for postoperative analgesia in paediatric cancer patients. ***Methods:*** A prospective randomized controlled trial was conducted over 40 paediatric cancer patients who were recruited from Children Cancer Hospital of Egypt (57357 Hospital). Patients were randomized into 2 groups: bupivacaine group (group B, 20 patients) to receive single shot caudal block of 1 mL/kg 0.1875% bupivacaine; tramadol group (group T, 20 patients) prepared as group B with the addition of 1 mg/kg caudal tramadol. ***Results:*** The mean duration of analgesia was significantly longer among group T than group B [(24 ± 13.7) hours versus (7 ± 3.7) hours respectively with *P* = 0.001]. Group T showed a significantly lower mean FLACC score than group B (2.2 ± 0.9 versus 3.6 ± 0.6 with *P* = 0.002). The difference in FLACC score was comparable on arrival, and after 2 and 4 hours. At 8 and 12 hours the group B recorded significantly higher scores (*P* = 0.002 and 0.0001 respectively). There were no significant differences between the groups as regards sedation score [the median in both groups was 1 (0–1) with *P* value = o.8]. No one developed facial flush or pruritis. ***Conclusion:*** Caudal injection of low dose tramadol 1 mg/kg with bupivacaine 0.1875% is proved to be effective, long standing technique for postoperative analgesia in major paediatric cancer surgery and almost devoid of side effect.

Key words caudal bupivacaine; tramadol; paediatric analgesia

Among multiple methods aiming at pain control which is a basic human right, caudal epidural analgesia has become very common analgesic technique in paediatric surgery [1, 2]. Being simple, safe, and effective caudal block can be used for pain control during and after any infraumbilical surgery with high rate of success in paediatric patients [3]. Advantages of caudal block is not limited to intraoperative reduction of anaesthetics and good recovery profile but it extends to rapid discharge from recovery room, reduction of postoperative analgesic requirements and decrease of postoperative complications [4].

To increase the duration and potency of caudal analgesia, many drugs were added instead of using local anaesthetic alone [5]. The amide local anaesthetic (bupivacaine) which is the commonest caudally injected agents acts by inhibiting sodium channels (membrane stabilizer) but with short duration [6]. Addition of caudal opioids prolongs analgesia but with increased risk of developing respiratory depression, vomiting, flushing, and pruritis [3].

Although the affinity of tramadol to μ receptors is weak, the inhibition of monoamines reuptake (serotonin and noradrenaline) make it equivalent to pethidine with very weak respiratory depression [7]. Many studies combined tramadol with bupivacaine for caudal injection resulting in longer duration of analgesia with minimal side effects [8–11].

Up to our knowledge randomized controlled trial investigating this subject is still deficient in Egypt especially among paediatric cancer patients who undergo prolonged and extensive surgery. The aim of the study was to compare caudal analgesia using bupivacaine versus bupivacaine with tramadol for postoperative analgesia in paediatric cancer cases undergoing major abdominal surgery.

Patients and methods

Study design and subject

This study was conducted in Children Cancer Hospital, Cairo, Egypt (57357 Hospital) from February to June

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Table 1 FLACC score

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

2012. This study was a prospective randomized controlled trial. Any paediatric cancer patient with 5 years old or less who was eligible for the study during the period of work was recruited after obtaining approval by the hospital ethical committee and written consent from his or her parent.

We studied 40 cases ASA physical status I, II and III scheduled for abdominal surgery. Patients were excluded if there was a history of relevant drug allergy, elevated liver enzymes, hepatoblastoma, or conditions that contraindicate caudal block (local infection, coagulopathy, congenital anomaly, or mass involving the sacral area).

Randomization was done by sealed envelope into two groups: bupivacaine group (group B, 20 patients) to receive single shot caudal block of 1 mL/kg 0.1875% bupivacaine (prepared by equal volumes of 0.25% and 0.125%); tramadol group (group T, 20 patients) prepared as group B with the addition of 1 mg/kg caudal tramadol. The staff (resident and pain high nurse) providing postoperative care were blinded to group assignment. After inhalational induction with sevoflurane, all parients received general anaethesia (fentanyl 2 μg/kg, propofol 2–3 mg/kg, atracurium 0.5 mg/kg, and morphine 0.1 mg/kg intravenously) and maintained with isoflurane using standard monitoring.

The study was approved by the local ethical committee (57357 Hospital). Confidentiality of data was respected.

Procedure

After induction the block was done in the lateral position with both hips flexed using 22 gauge short spinal needle (3.8 cm) under full aseptic precaution by identifying the sacral hiatus (felt as groove or notch above the coccyx and between two bony prominences, the sacral cornuae). The needle must be placed exactly in the midline at 45 degree angle to the cronal plane and advanced till distinct pop was felt as the sacrococcygeal membrane was pierced then the angle was lowerd to 20 degree and the needle was advanced 2–3 mm. Appropriate volume was injected after being sure of absence of CSF or blood. After end of surgery, muscle relaxant was antagonized by neostigmine 50 μg/kg with atropine 20 μg/kg and extubated fully awake and the patient was transferred to the postoperative care unit (PACU) to receive paracetamol 10 mg/kg intravenous infusion and tramadol 1 mg/kg intravenous both every 8 hours but the first tramadol dose was given on parents' request or FLACC score > 3.

The collected data

The following data were collected:

(1) Intraoperative heart rate, systolic blood pressure, oxygen saturation, and isoflurane concentration at induction of anaesthesia then every 30 min thereafter till recovery.

(2) Type of tumour and duration of surgery.

(3) Pain score (FLACC score was shown in Table 1) [12] on arrival to PACU, after 2 and 4 hours, and every 4 hours thereafter till 1st tramadol dose was given, maximum 48 hours.

(4) Duration of analgesia from time of caudal injection till 1st intravenous tramadol dose.

(5) Any episode of respiratory depression (decreased respiratory rate), pruritis or facial flush.

(6) Sedation was assessed on arrival to PACU and after 4 hours based on eye opening (eyes open spontaneously = 0, eyes open to verbal stimulation = 1, eyes opens in response to physical stimulation = 2) [13].

Statistical analysis

Data was coded and entered on SPSS version 15 for further analysis. Descriptive statistics in the form of percent and proportion for categorical data and mean with standered deviation (SD) or median with 25 percentiles and 75 percentiles were done for numerical data after checking distribution normality. Chi square, *t* test, and Mann-Whitney test were used appropriately. *P* value less than 0.05 was considered statistically significant.

Results

This study recruited 40 patients who were assigned into 2 groups: group T (tramadol group) and group B (bupivacaine group) with 20 patients each. Both groups were comparable as regards age, sex, body weight as well as the

Table 2 General characteristics of the studied groups (*n*)

Characteristics	Group T (*n* = 20)	Group B (*n* = 20)	*P* value
Age (median and inter quartile range; year)	2 (1–3.1)	2.5 (1–4)	0.8*
Sex [*n* (%)]			
Male	14 (70)	10 (50)	0.6#
Female	6 (30)	10 (50)	
Weight (mean ± SD; kg)	11.9 ± 3.3	12 ± 4.7	0.9**
Type of tumor [*n* (%)]			
Wilm's tumor	13 (65)	10 (50)	0.7#
Neuroblastoma	6 (30)	10 (50)	
Pelvic rhabdomyosarcoma	1 (5)	0 (0)	

* Mann-Whitney test was used because age was not normally distributed; # chi square test; ** Student's *t*-test

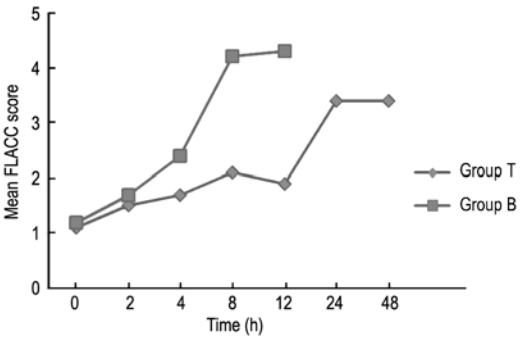

Fig. 1 Mean FLACC score during follow up period among studied groups

type of the tumor (Table 2).

Although the mean heart rate, mean systolic blood pressure, and mean isoflurane concentration in group T were less than those of group B, yet the results were not statistically significant (P = 0.9, 0.2 and 0.9 respectively; Table 3).

The mean duration of analgesia was significantly longer among group T than group B [(24 ± 13.7) hours versus (7 ± 3.7) hours respectively with P = 0.001]. The minimum analgesic duration in group T was 8 hours versus 2 hours in group B. On the other hand the maximum analgesic duration was > 48 hours in group T versus 12 hours only in group B.

Group T showed a significantly lower mean FLACC score than group B (2.2 ± 0.9 versus 3.6 ± 0.6 with P = 0.002). The difference in FLACC score was comparable on arrival, and after 2 and 4 hours. At 8 and 12 hours the group B recorded significantly higher scores (P = 0.002 and 0.0001 respectively). The results were illustrated in Fig. 1.

In group T, 72.4% of patients didn't require intravenous tramadol up to 12 hours postoperatively, and 35.7% did not require rescue analgesia up to 24 hours, while in group B, all patients required rescue analgesia within 12 hours.

Three patients (15%) did not receive intravenous tramadol at all, while the patient who had pelvic exenteration received his 1st analgesic dose after 36 hours.

There were no significant differences between the groups as regards sedation score [the median in both groups was 1 (0–1) with P value = 0.8]. No one developed facial flush or pruritis.

Discussion

Decreasing postoperative pain, analgesic drugs, and ultimately side effects are part of quality control especially in paediatric patients by performing caudal block before surgical stimulation [6].

Early requirement of postoperative analgesia is the main drawback of using local anaesthetic (bupivacaine) as a single agent in caudal block [4].

Multiple studies compared the addition of different drugs (adrenaline, clonidine, ketamine or various opioids) to local anaesthetic to prolong and potentiate analgesia but they reported less duration of analgesia than our figure in addition to the side effects especially respiratory depression which is more obvious with the use of opioids [14–16].

On the other hand, many studies compared the effectiveness of adding tramadol to bupivacaine and proved longer duration of analgesia and less side effects. While bupivacaine provides analgesia in the early postoperative period, the analgesic effect of caudal tramadol extends for

Table 3 The intra- and post-operative clinical data of the studied groups

Clinical data	Group T (*n* = 20)	Group B (*n* = 20)	*P* value
Mean heart rate (mean ± SD; beat/min)	117.8 ± 12.4	118.3 ± 9.5	0.9*
Mean systolic blood pressure (mean ± SD; mmHg)	93.1 ± 8.3	99.5 ± 7.3	0.2*
Mean surgical duration (mean ± SD; hour)	2.9 ± 0.4	3.2 ± 0.6	0.6*
Mean isoflurane concentration (mean ± SD)	0.7 ± 0.1	0.8 ± 0.1	0.9*
Analgesic duration [median (25th percentile–75th percentile); hour]	23 (13–33)	7.5 (3.25–10.25)	0.01#
FLACC score [median (25th percentile–75th percentile)]	2 (1.5–2.5)	3.7 (3.3–4.3)	0.02#

* Student's *t*-test; # Mann-Whitney test was used because analgesic duration and FLACC score were not normally distributed

longer postoperative period [17].

In our study, we used low doses of tramadol and bupivacaine. According to NYSORA 2009 the optimum concentration of bupivacaine is 0.125%–0.175% for caudal use in paediatric. Compared with the 0.25% preparation, low concentration provides a similar duration of postoperative analgesia (4 to 8 hours) but with less motor blockade [18]. The mean duration of analgesia in group T was more than triple that of group B which is highly significant. According to Murthy [19], installation of tramadol in the epidural space appears to act only as a depot for immediate and delayed systemic absorption. Our results far exceeds the results reported by Senel and colleagues [(13 ± 2.2) hours] [8], Shrestha, Bhattarai (8 h) [10], and Ozkan *et al* (8.5 ± 2.8) [4]. Nearly two thirds and one third of group T did not receive intravenous tramadol in the first 12 and 24 hours respectively, while all patients in group B received intravenous tramadol in the first 12 hours. This result exceeds the findings of Majid and Mohammed [6] who found that fifty two percent of their patients in tramadol group did not require analgesics in the first 12 hours. This may be due to routine use of intravenous paracetmal postoperatively in our study. In addition the difference in duration of analgesia between different studies depends on age, type of surgery, pain scoring system, dosage and volume of the administrated medications [4].

Although self report methods for pain assessment is superior to behavioral methods as regard pain assessment, in our study we used the FLACC score owing to young age group. In the early post operative period, the FLACC score was comparable in both groups but at 8 and 12 hours, the score differed significantly being lower in group T. This result is in agreement with the studies of Majid and Mohammed [6], Batra *et al* [20], and Ozkan *et al* [4].

Fifteen percent of patients in group T did not receive intravenous tramadol at all. One patient who undergone pelvic exenteration received his first intravenous tramadol after 36 hours. We considered the previous two points as a great success of the combination.

All patients had urinary catheter and nasogastric tube so we could not comment on urine retention or vomiting. No one in both groups developed respiratory depression, pruritis, or facial flushing. Similar finding was reported by Khan and Memon [3].

Limitation of the study

Pain was assessed by behavioral method rather than the more expressive self report method due to inclusion of young age group.

Conclusion

Caudal injection of low dose tramadol 1 mg/kg with bupivacaine 0.1875% is proved to be effective and long standing technique for postoperative analgesia in major paediatric cancer surgery and almost devoid of side effect.

Recommendation

We recommend the routine use of caudal bupivacaine tramadol combination for infraumbilical surgery in paediatric patients provided that there is no contraindication.

Conflicts of interest

The authors have no conflicts of interest to declare.

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