Caudal Bupivacaine-Neostigmine Effect on Postoperative Pain Relief in Children

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ABSTRACT

Objective: To assess the effect of different neostigmine doses added to caudal bupivacaine on postoperative pain relief in assigned pediatric herniotomy surgery.

Methods: Our randomized, double-blinded and prospective investigation included 134 patients, aged 7-14 years, classed I - II physical status class by the American Society of anesthesiologists (ASA), of both genders and scheduled for herniotomy. Children were randomly assigned into four groups to receive a caudal administration of 0.25% plain bupivacaine 0.5ml/kg (group I, n= 33). For the following three groups, bupivacaine was mixed with neostigmine in the following manner: 1.5mcg/kg neostigmine (group II, n= 34), 3mcg/kg neostigmine (group III, n= 33) and 6mcg/kg neostigmine (group IV, n= 34), with a total caudal volume of 1ml/kg administered in all groups after induction of general anesthesia. Postoperative use of rescue analgesics using paracetamol during the first postoperative 24 hours was recorded. Postoperative pain was evaluated using the numerical pain rating scale with a score from zero to 10. The Chi-square and Students t test were used to test statistical significance where $P < 0.05$ was considered significant.

Results: Mean duration of postoperative analgesia was 4.7 hours, 16.35 hours, 16.8 hours and 16.65 hours in groups I, II, III and IV, respectively, ($p<.05$). Mean postoperative paracetamol consumption was 41.9mg/kg in group I, 12.8mg/kg,14.1 mg/kg and 11.4mg/kg in groups II, III and IV, respectively ($P<0.05$), during the first 24 postoperative hours.

Conclusions: Administration of caudal neostigmine combined with bupivacaine significantly prolongs the duration of postoperative pain relief with decreased requirement for rescue analgesics.

Key words: Bupivacaine, Caudal, Neostigmine, Herniotomy, Pain.

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Introduction

Surgery is usually followed by different degrees of pain. Postoperative pain is a major issue for the anesthesiologist in pediatrics anesthesia practice. The society of pediatric anesthesia regarded the postoperative pain relief as an essential right.[1] Many types of minor procedures may induce severe pain in children. The aim of postoperative pain management is to decrease pain and in the same time to be economical. Effective pain control indicates an uneventful postoperative period and quick discharge. Postoperative pain control should be included in the anesthetic planning. Over years, different regional anesthetic interventions have been included in postoperative pain relief as they

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provide suitable postoperative analgesia and decrease the needs for general anesthesia intraoperatively. Preoperative caudal (epidural, extradural) analgesia reduces the stress response of anesthesia and surgery.[1] In our study, we administered neostigmine mixed with bupivacaine to extend the period of pain relief by a single administration caudal block injection. Caudal blockade is useful in lower, anoperineal and infraumbilical (abdominal) interventions in children for providing pain relief intra- and postoperatively. Caudal analgesia is the most popular and frequently used regional anesthesia technique for postoperative analgesia in children. The quality and level of the block depends on the dose, volume and drug concentration. Although it is a versatile block, one of its limitations as a single injection technique is the relatively short duration of postoperative pain relief.

Pain causes negative metabolic, neuroendocrine and cardio-respiratory effect. Although optimum postoperative pain relief in adults is fully investigated, this has taken only a second priority in children. New studies have modified the techniques for postoperative children's pain management.

Caudal block is considered the most common regional anesthetic procedure used in pediatrics. Preoperative caudal analgesia decreases the stress effect of anesthesia and surgery. Caudal block reduces postoperative opiates administrations.[1] Bupivacaine is a local anesthetic most frequently administered in regional anesthesia for pain relief after surgery. Caudal administration of bupivacaine only has a short duration of action (4-8 hrs).[2] Many caudal agents including epinephrine, morphine , clonidine, ketamine, midazolam , tramadol , fentanyl , butorphanol and neostigmine were used.[3] These have been administered mixed with caudal bupivacaine to prolong the period of pain relief. Neostigmine has been administered with local anesthetics in caudal analgesia for genitourinary and urological surgical interventions.[4]

The aim of this investigation was to assess the impact of caudal neostigmine in dose of 1.5, 3 and 6mcg/kg mixed with bupivacaine on the postoperative pain relief profile in child patients scheduled for herniotomy surgery.

Methods

This prospective, double-blinded and randomized investigation enrolled 134 male and female children, ranging from 7 to 14 years, classed I-II physical status class (ASA) and assigned for herniotomy surgery of ½-1 hour duration at Queen Raniah Al-Abdullah Hospital for Children, at King Hussein Medical Center, Amman-Jordan. Patients were enrolled from Jan-Dec 2013 after obtaining approval from the ethics committee of the Royal Medical Services and an informed written parental consent.

Patients with contraindications to caudal block (bleeding diathesis, local or systemic sepsis, severe stenotic valvular heart disease and acute neurological disease, preexisting spinal diseases) and those who had analgesics consumption in the preceding week were ruled out from participation in the study.

General anesthesia was induced using inhalational (4MAC) of sevoflurane with oxygen 6L/min which later was reduced to 2L/min, followed by intravenous atracurium 0.5 mg/kg after which a suitable laryngeal mask airway was placed, with mixture of oxygen 6L/min, nitrous oxide 2L/min and 1MAC of sevoflurane was administered. Anesthesia was maintained using 2L/min of oxygen mixed with 1MAC of sevoflurane and intravenous atracurium 0.1mg/kg. No intraoperative intravenous analgesic was administered in any child. Caudal blockade was achieved with the patient in the left lateral position using a 23 gauge short beveled needle. The needle is inserted at the depression of the sacral hiatus at S5 flanked by the sacral cornua. The needle is inserted via the skin and sacrococcygeal ligament in a cephalad direction at 45 degree to the skin. When the membrane is penetrated, the needle hub is depressed to the natal cleft and the needle introduced 2-3mm along the sacral canal. The patients were divided in a random manner into one of four groups. Group I patients (n= 33) received 0.5 ml/kg of 0.25% caudal bupivacaine only, group II patients (n=34) received 0.5 ml/kg of 0.25% caudal bupivacaine in combination with 1.5mcg/kg neostigmine, group III patients (n=33) received 0.5ml/kg of 0.25% caudal bupivacaine in combination with 3mcg/kg neostigmine and

Table I: Numerical pain rating scale

Score	Description
0	No pain
1-3	Mild pain
4-6	Moderate pain
7-9	Severe pain
10	Worst pain

Table II: Patient Characteristics (n, mean+/-SD)

	GI	GII	GIII	GIV	P
n=	33	34	33	34	>0.05
Age(yr)					>0.05
7	1	0	1	0	
8	0	0	0	0	
9	0	0	0	0	
10	0	1	0	1	
11	0	0	0	0	
12	19	20	19	20	
13	10	10	10	10	
14	3	3	3	3	
ASA					
I	27	25	30	28	>0.05
II	6	9	3	6	
Weight(kg)	37.1	37.2	37.1	37.2	>0.05
Gender					
M	25	27	23	26	>0.05
F	8	7	10	8	
Herniotomy					
Unilateral					
RT	19	19	20	19	>0.05
LT	10	11	10	10	
Bilateral	4	4	4	4	
Duration(min)	44+/-5	42+/-4	43+/-4	46+/-3	>0.05

group IV patients (n=34) received 0.5ml/kg of 0.25% caudal bupivacaine in combination with 6mcg/kg neostigmine. Surgery started 10 minutes after the caudal injection. Heart rate, arterial pressure, SpO_2 and end tidal CO_2 were monitored until the end of the surgery.

In the recovery room, the resident, unaware of the caudal analgesic modality used, recorded the postoperative pain score using the "numerical pain rating scale" (Table I).[5] Score from zero to 10 where zero score indicates no pain,1-3 score indicates mild pain,4-6 score indicates moderate pain,7-9 score indicates severe pain and 10 score indicates the worst pain. Rectal paracetamol 15 mg/kg was administered for pain score ≥5 in the recovery room and oral paracetamol 20 mg/kg for pain score ≥5 in the surgical ward.

Pain scores, time to first postoperative rescue analgesic demand and number of rescue analgesic consumption were compared between all groups using analysis of variance (ANOVA). The chi-square and Students t tests were used to compare the gender ratio and ASA class.

Results

There were no significant differences between the four groups in terms of patient demographics (age, gender, weight, ASA class and duration of surgery) (Table II).

Caudal administration of bupivacaine with the addition of neostigmine (groups II, III and IV) had superior analgesia in comparison with the plain bupivacaine group (group I). Postoperative duration to first paracetamol demand (the duration of postoperative analgesia) was 4.7 h+/-1.9h in group I but it was 16.35h+/-4.5h,16.8h+/-5.15h and 16.65h+/-4.4h in groups II, III and IV, respectively (P<0.05) (Table III).

Significantly more patients of plain bupivacaine group (I) received postoperative rescue analgesics (oral paracetamol syrup) than of the bupivacaine-neostigmine groups (II, III and IV)

Table III: Postoperative pain relief profile (mean+/-SD).

	GI			P	GII			P
Duration of analgesia(h)	4.7+/-1.9	GII	16.35+/-4.5	<0.05	16.35+/-4.5	GIII	16.8+/-5.15	>0.05
		GIII	16.8+/-5.15	<0.05		GIV	16.65+/-4.4	>0.05
		GIV	16.65+/-4.4	<0.05				
Total paracetamol consumption (mg)	663.3+/-219.2	GII	213.7+/-156.9	<0.05	213.7+/-156.9	GIII	235.9+/-159.3	>0.05
		GIII	235.9+/-159.3	<0.05		GIV	196.3+/-145.4	<0.05
		GIV	196.3+/-145.4	<0.05				
Mean paracetamol consumption(mg/kg)	41.9	GII	12.8	<0.05	12.8	GIII	14.1	>0.05
		GIII	14.1	<0.05		GIV	11.4	>0.05
		GIV	11.4	<0.05				

Table IV: Postoperative 0 pain score (%)

	GI			P	GII			P
0h	100	GII	100	>0.05	100	GIII	100	>0.05
		GIII	100	>0.05		GIV	100	>0.05
		GIV	100	>0.05				
1h	100	GII	100	>0.05	100	GIII	100	>0.05
		GIII	100	>0.05		GIV	100	>0.05
		GIV	100	>0.05				
2h	84.8	GII	100	>0.05	100	GIII	100	>0.05
		GIII	100	>0.05		GIV	100	>0.05
		GIV	100	>0.05				
4h	57.6	GII	100	<0.05	100	GIII	100	>0.05
		GIII	100	<0.05		GIV	100	>0.05
		GIV	100	<0.05				
6h	9.1	GII	94.1	<0.05	94.1	GIII	100	>0.05
		GIII	100	<0.05		GIV	100	>0.05
		GIV	100	<0.05				
8h	0	GII	88.2	<0.05	88.2	GIII	93.9	>0.05
		GIII	93.9	<0.05		GIV	94.1	>0.05
		GIV	94.1	<0.05				
12h	0	GII	58.8	<0.05	58.8	GIII	69.7	>0.05
		GIII	69.7	<0.05		GIV	79.4	<0.05
		GIV	79.4	<0.05				
16h	0	GII	50	<0.05	50	GIII	48.5	>0.05
		GIII	48.5	<0.05		GIV	50	>0.05
		GIV	50	<0.05				
20h	0	GII	29.4	<0.05	29.4	GIII	33.3	>0.05
		GIII	33.3	<0.05		GIV	29.4	>0.05
		GIV	29.4	<0.05				
24h	0	GII	29.4	<0.05	29.4	GIII	27.3	>0.05
		GIII	27.3	<0.05		GIV	29.4	>0.05
		GIV	29.4	<0.05				

to attain optimum pain relief in the first 24 postoperative hours ($p<0.05$) (Table III). Total postoperative paracetamol consumption was 663.3mg+/-219.2mg with a mean of 41.9mg/kg in group I but it was 213.7mg+/-156.9mg with a mean of 12.8mg/kg in group II,235.9mg+/-159.3mg with a mean of 14.1mg/kg in group III and 196.3mg+/-145.4mg with a mean of 11.4mg/kg in group IV.

Postoperative pain evaluation started at zero hour in the recovery room where the percentage of patients with zero score, on numerical pain rating scale, was 100% in all the four groups ($P>0.05$) (Table IV). This percentage of 100%

continued at one hour in the recovery room in all groups. This percentage began to change at two hours in the surgical ward when it began to decrease in group I to become 84.8% (n=28) but the percentage continued to be 100% in the other groups until four hours in the surgical ward. At six hours, this percentage changed in group II to become 94.1% but remained 100% in groups III and IV.

Discussion

Continuous investigations regarding optimization of postoperative pain is being the concern of anesthesiologists in different types of surgery and in different patient ages. Caudal extradural anesthesia is used frequently in pediatric surgery. Caudal block is simple and safe procedure. We have administered increasing doses of neostigmine (1.5mcg /kg.3 and 6mcg/kg) mixed with bupivacaine to prolong the duration of pain relief. We showed that caudal neostigmine mixed with 0.25% caudal bupivacaine improve post-operative pain relief in children undergoing herniotomy surgery. Caudal neostigmine acts directly at spinal cord after passing to CSF or acts at wound area by anti-nociceptive mechanism after systemic absorption.[3] Caudal with general anesthesia is used for many pediatric surgical interventions. Our results with neostigmine increasing doses (1.5mcg/kg, 3 and 6mcg/kg) explain a spinal cord rather than an anti-nociceptive action.

Spinal neostigmine containing methyl and propylparabens is not correlated with neurotoxicity.[6] Our investigation has no long term follow-up, and this is one of our study limitations. Neostigmine blocks the activity of both true and pseudo-cholinesterase and increasing accumulation of acetylcholine at sites of pain relief.[6] Caudal extradural neostigmine with or without local anesthetics has been used to prolong the duration of pain relief.[4] Caudal injection of 1 mcg/kg neostigmine combined with bupivacaine has no benefits over bupivacaine alone. Caudal neostigmine 2 μg/kg induced postoperative pain relief equal to caudal bupivacaine alone.[3] Administration of neostigmine with bupivacaine prolonged postoperative pain relief.[4]

Although caudal neostigmine was shown to produce a dose dependent analgesia,[7] caudal neostigmine (2, 3 and 4 mcg/kg) with bupivacaine attained a dose independent pain relief action (16-17 hrs) in children in comparison to bupivacaine alone (5 hrs).[8] Our investigation shows a dose dependent pain relief action of caudal neostigmine. Caudal or spinal neostigmine is not an accepted pain relief technique. As there are debating results in terms of various doses of caudal neostigmine, we suggest more investigation to specify the least potent caudal neostigmine dose with pain relief characteristics in children. In our investigation, we found that the postoperative analgesic potency of caudal neostigmine increases with increasing its dose but the differences between the three doses are not so significant, therefore, we recommend the use of the smallest dose which is 1.5 mcg/kg as to avoid any potential adverse effects of caudal neostigmine. Kaushal *et al*. recommended the use of 5mcg/kg of caudal neostigmine for prolonged duration of postoperative pain relief.[9] It is mandatory to remark that Bhardwaj *et al*. concluded in his study that the addition of 2-4 mcg/kg of neostigmine to 1.875 mg/kg of caudal bupivacaine did not result in prolongation of duration of analgesia after hypospadias surgery in children and caudal bupivacaine alone in a volume of 0.75ml/kg was enough to provide optimum analgesia for 24h in more than 1/3 of patients.[10] Keely reported that patients who received 0.5mg/kg of 0.25% bupivacaine with 2mcg/kg neostigmine caudally, had prolonged postoperative pain relief during hypospadias surger.[11] Tobin *et al*. showed that by using caudal neostigmine 1.5mcg/kg mixed with bupivacaine 0.25 obtained prolonged time to first analgesic demand with decrease in postoperative analgesic needs.[12]

Limitations of the Study

The study group was small and limited to one type of surgical procedure. In the future, having a larger study group and using caudal neostigmine in lower abdominal surgeries other than hernia would be beneficial.

Conclusion

Administration of neostigmine mixed with bupivacaine extended the duration of surgical pain relief after caudal administration. Caudal neostigmine with bupivacaine induced a dose-

independent pain relief impact (16 hrs) in comparison to bupivacaine only (4 hrs). We recommend the use of neostigmine mixed with bupivacaine for surgeries lasting more than two hours.

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