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Research Article

Fentanyl, dexmedetomidine, dexamethasone as adjuvant to local anesthetics in caudal analgesia in pediatrics: A comparative study

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KEYWORDS

Fentanyl;
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Abstract *Background:* Caudal analgesia is a good, reliable and easy method to provide intraoperative and postoperative analgesia in the infraumbilical surgery in pediatrics. Many additives were used in combination with local anesthetics in caudal block to prolong the postoperative analgesia (fentanyl, dexmedetomidine and dexamethasone).

Aim of the study: This study aimed to compare the intraoperative hemodynamics, postoperative analgesia, postoperative sedation and postoperative side effects of fentanyl, dexmedetomidine and dexamethasone as adjuvant to bupivacaine in caudal analgesia in pediatrics.

Methods: 120 pediatric patients (3–10 years old) scheduled for lower abdominal surgeries under general anesthesia allocated to 4 groups. Group I (control), in this group the patients received 0.5 ml of a equal mixture of bupivacaine 0.25% and lidocaine 1% diluted in saline (in a dose of 0.5 ml/kg) caudally. In Group II (fentanyl group), the patients received the same mixture of Group I + fentanyl (1 μg/kg) caudally. In Group III (dexmedetomidine group), the patients received the same mixture of Group I + dexmedetomidine (1 μg/kg) caudally. In Group IV (dexamethasone group), the patients received the same mixture of Group I + dexamethasone (0.1 mg/kg) caudally.

Results: The demographics and hemodynamics were comparable among the studied groups. The dexmedetomidine group and dexamethasone group were less in pain score, prolong the duration of analgesia and less in number of patients required analgesia compared to control and fentanyl groups. More sedation was present in the fentanyl and dexmedetomidine groups. The fentanyl group showed significant increase in the adverse effect incidence.

Conclusion: Both caudal dexmedetomidine and caudal dexamethasone added to local anesthetics are good alternatives in prolongation of postoperative analgesia compared to caudal local anesthetic alone or added to caudal fentanyl. Also they showed less side effects compared to caudal fentanyl.

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1. Introduction

Caudal analgesia is a good, reliable and easy method to provide intraoperative and postoperative analgesia in the infraumbilical surgery in pediatrics. But the single shot caudal analgesia is short in duration so the use of catheter injection may be used to prolong the analgesia time but it is associated with infection [1,2].

Many additives were used in combination with local anesthetics in caudal block to prolong the postoperative analgesia [3].

Fentanyl has been widely used as analgesic adjuvant to epidural analgesia and it acts on substantia gelatinosa on the dorsal horn of spinal cord by blocking fibers carrying nociceptive impulses both pre- and postsynaptically. But it has undesirable side effects as respiratory depression, itching and vomiting [4,5].

Dexmedetomidine is α_2 adrenergic receptor agonist which has sedative and analgesic effects. When it is combined with local anesthetics caudally, it prolongs the postoperative analgesia [6,7].

Administration of dexamethasone in the epidural space can reduce postoperative pain and analgesic requirements [8,9].

2. Aim of the study

This study aimed to compare the intraoperative hemodynamics, postoperative analgesia, postoperative sedation and postoperative side effects of fentanyl, dexmedetomidine and dexamethasone as adjuvant to local anesthetics in caudal analgesia in pediatrics.

3. Patients and methods

This study was approved by the local Clinical Research Ethics Committee of Menoufiya hospital and written informed consent was obtained from the parents of patients before the surgery. 120 boys with the American Society of Anesthesiologists (ASA) physical status I–II, aged 3–10 years scheduled for lower abdominal surgeries were included in this study.

Clinical examination and routine investigation were done to all the patients.

The exclusion criteria included the following: patients with contraindication to caudal anesthesia, cardiovascular diseases, drug allergy, and clotting disorders, or those whose families did not approve inclusion in the study.

In the operating room, the standard monitors including pulse oximetry, ECG, noninvasive blood pressure were present. 22-gauge cannula was inserted into an available peripheral vein.

All patients underwent general anesthesia that was conducted by the face mask sevoflurane and endotracheal intubation was facilitated by atracurium 0.5 mg/kg and controlled ventilation till regular spontaneous ventilation was achieved. The patients tilted on the side (lateral position) and caudal anesthesia was performed under complete aseptic condition by using loss of resistance technique. The correct caudal needle placement is identified by injecting 3 mL of saline rapidly through the caudal needle while palpating the skin overlying the sacrum. If no midline swelling was detected, the needle is probably correctly positioned. In contrast if no midline swelling was detected during saline injection, the needle was incorrectly positioned and redirected again. Then the patients were enrolled randomly by sealed envelope into 4 groups (30 patients for each) and the anesthesiologist was blinded for each solution.

Group I (control group), in this group the patients received 0.5 ml/kg of a equal mixture of bupivacaine 0.25% and lidocaine 1% diluted in saline caudally.
Group II (fentanyl group), in this group the patients received the same mixture of Group I + fentanyl (1 μg/kg) caudally.
Group III (dexmedetomidine group), in this group the patients received the same mixture of Group I + dexmedetomidine (1 μg/kg) caudally.
Group IV (dexamethasone group), in this group the patients received the same mixture of Group I + dexamethasone (0.1 mg/kg) caudally.

After 15 min from the caudal block, the surgical procedure started and the block considered failed if the heart rate (HR) or mean arterial blood pressure (MAP) was 15% from the base line. The block failed patient excluded from the study and i.v. fentanyl (1 μg/kg) was given to provide the analgesia.

After the completion of the surgery, the volatile anesthesia disconnected and patients were extubated when adequate spontaneous ventilation was established. Patients were be transferred to recovery room and then to the surgical ward.

The demographic data (age, weight, ASA status, type of operation and duration of surgery) were recorded.

The following parameters were assessed: the intraoperative and postoperative heart rate (HR) and mean arterial blood pressure (MAP) at base line, after induction, after caudal block and every 15 min for 3 h from the start of operation in the operative room.

In the postoperative anesthesia care unit (PACU), the modified objective pain score (MOPS) [10] was assessed at 30 min, 1, 2, 3, 6 and 12 h in the surgical ward.

The MOPS consists of 5 parameters: crying (0 = none, 1 = consolable, 2 = non consolable), movements (0 = none, 1 = restless, 2 = thrashing), agitation (0 = asleep or calm, 1 = mild, 2 = hysterical), posture (0 = normal, 1 = flexed, 2 = holds injury site), verbal (0 = asleep or not complaint, 1 = complaint but cannot localized, 2 = complaint but can localize).

If the (MOPS) ≥ 4, the patient was given supplementary paracetamol i.v. injection in a dose of 15 mg/kg as analgesia. The first time to require analgesia was calculated (the time from caudal block to the first time to paracetamol injection), and also the number of patients require analgesia in the first 12 h postoperative was calculated.

Ramsay sedation score was assessed at the time of the pain (1 = anxiety and completely awake, 2 = completely awake, 3 = awake but drowsy, 4 = asleep but responsive to verbal commands, 5 = asleep but responsive to tactile stimulus, and 6 = asleep and not responsive to any stimulus) [11].

The adverse effects in PACU also were assessed: hypotension (decrease in basal mean arterial blood pressure by 20%) treated with i.v. fluid and incremental dose of ephedrine 5 mg/kg, bradycardia (defined by decrease in basal heart rate by 20%) treated by i.v. atropine .01–.02 mg/kg), respiratory

depression (the SPO2 < 95% and need O2 supplementation), vomiting and itching.

3.1. Statistical data analysis

Data were obtained from the previous studies that the addition of caudal dexmedetomidine had prolonged duration of analgesia than the caudal local anesthetic alone or in combination with caudal fentanyl. So the power calculation according to data obtained from our previous studies. The number of sample size was adequate (120 patients) with $\alpha = 0.05$ and a power of 0.8. Statistical analysis of data was carried out as for all comparisons $P < 0.05$ was considered significant. The minitab version 1.6 program was used in the statistical analysis. ANOVA test used for numerical values as data expressed in mean and standard deviation (age, duration of surgery, duration of analgesia, MAP, HR, and chi-square test used for categorical values as data expressed in number of patients or ratio (type of operation, number of patients required analgesia and adverse effects). Kruskal–Wallis test used for postoperative pain and sedation score as data expressed as median and range.

4. Results

This study was conducted on 120 patients underwent lower abdominal surgeries in pediatrics. 8 patients were excluded because of failed caudal analgesia (one in the control group, 2 in the fentanyl and dexmedetomidine groups and 3 in the dexamethasone group).

The demographic data were comparable in the 4 groups as shown in Table 1.

The means of heart rate changes among the studied groups were comparable at all times and until 3 h from the start of surgery as shown in Fig. 1.

The means of Mean arterial blood pressure changes among the studied groups were comparable at all times and until 3 h from the start of surgery as shown in Fig. 2.

Table 2 shows modified objective pain score that was comparable in the first 2 h, in the 3rd, 6th and 12 h the pain score was significantly decreased in both dexmedetomidine group and the dexamethasone group without significant difference in between them.

Table 3 shows prolonged duration of analgesia significantly in both dexmedetomidine group and the dexamethasone group without significant difference in between them. Also the number of patients need analgesia in the first 6 h postoperative was significantly increased in control group and fentanyl group (79.3% and 50%) respectively.

Table 4 shows increased sedation score significantly in the 1st 2 h in the fentanyl and dexmedetomidine groups. Sedation score in the 3rd, 6th and 12 h was comparable.

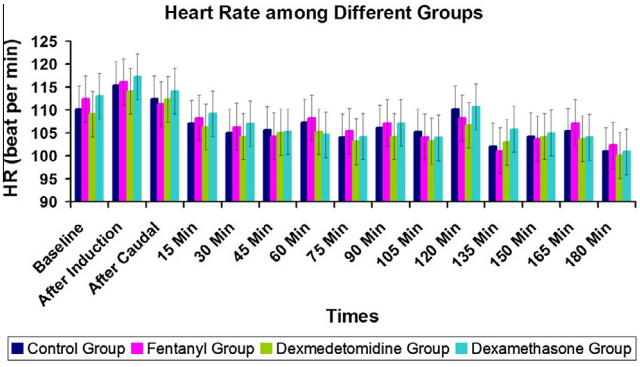

Figure 1 HR changes among the studied groups, data expressed by means and standard deviation.

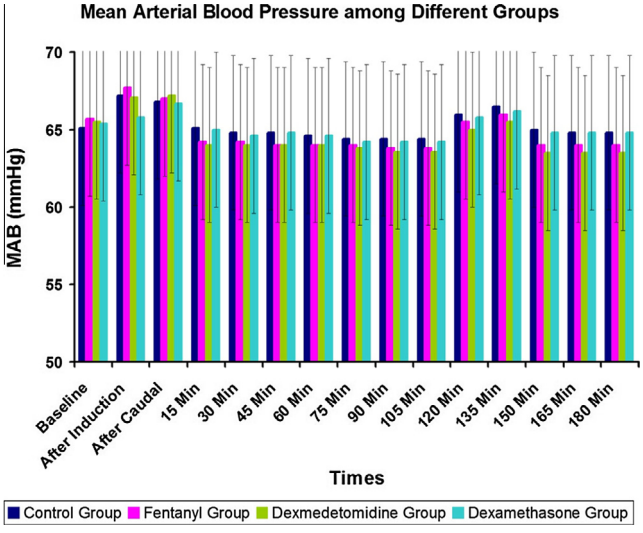

Figure 2 MAP changes among the studied groups, data expressed by the mean and standard deviation.

Table 1 Demographic data.

	Control No = 29	Fentanyl No = 28	Dexmedetomidine No = 28	Dexamethasone No = 27	Test	*P* value
Age (years)	6.7 ± 2.5	6.5 ± 2.3	6.1 ± 2.1	6.2 ± 2.7	$f = 0.016$	0.997
Weight (kg)	21.2 + 5.7	20.8 + 4.9	19.8 + 5.2	20.6 + 5.5	$f = 0.343$	0.793
ASA (I/II)	20/9 (70%)	18/10 (64.2%)	17/11 (60.7%)	18/9 (66.7%)	$X = 0.46$	0.926
Type of operation						
Hypospadias	14 (48.3%)	12 (42.9%)	15 (53.6%)	13 (48.1%)	$X = 0.64$	0.886
Inguinal herniotomy	10 (34.5%)	13 (46.4%)	11 (39.3%)	10 (37%)	$X = 0,94$	0.816
Orchiopexy	5 (17.2%)	3 (10.7%)	2 (7.1%)	4 (14.9%)	$X = 1.54$	0.672
Duration of surgery (min)	115.1 + 10.5	111.4 + 10.8	113.3 + 8.7	112.2 + 9.9	$f = 0.458$	0.712

Data expressed as mean and standard deviation (Mean ± SD), Anova (*F*) test used or data expressed as number (%), Chi-square test used (*X*) (ASA status and type of operation).

Table 2 Modified objective pain score (MOPS).

	Control No = 29	Fentanyl No = 28	Dexmedetomidine No = 28	Dexamethasone No = 27	Test	*P* value
	Median (interquartile range)					
At 30 min	3 (2–3)	3 (2–3)	3 (3–3)	3 (2–3)	0.514	0.916
At 1 h	3 (2–3)	3 (2–3)	3 (3–3)	3 (2–3)	2.49	0.477
At 2 h	3 (2–3)	3 (2–3)	3 (3–3)	3 (2–3)	21.9	0.916
At 3 h	4 (4–4)	4 (3–4)	3 (3–3)	3 (3–3)	57.5	< 0.001*
At 6 h	4 (4–4)	4 (3–4)	3 (3–3)	3 (3–3)	48.2	< 0.001*
At 12 h	5 (4–5)	4.5 (4–5)	4 (4–4)	4 (4–4)	10.64	0.014*

Data expressed as median and interquartile range, Kruskal–Wallis test used.
* Statistical significance ($P < 0.05$).

Table 3 First time of analgesia and number of patients require analgesia in 1st 6 h.

	Control No = 29	Fentanyl No = 28	Dexmedetomidine No = 28	Dexamethasone No = 27	Test	*P* value
Time of analgesia (min)	323.8 ± 10.2	330.4 ± 14.7	490.4 ± 13.6	498.2 ± 15.4	$f = 1417.5$	< 0.001*
Does not require analgesia	23 (79.3%)	14 (50%)	9 (32.1%)	7 (25.9%)	$X = 19.5$	< 0.001*

Data expressed as mean and standard deviation (Mean ± SD), Anova (*F*) test used, or data expressed as number (%), Chi-square (*X*) test used.
* Statistical significance ($P < 0.05$).

Table 4 Ramsay sedation score.

	Control No = 29	Fentanyl No = 28	Dexmedetomidine No = 28	Dexamethasone No = 27	Test	*P* value
	Median (interquartile range)					
At 30 min	4 (1)	4 (1)	4.5 (1)	4 (1)	8.34	0.04*
At 1 h	3 (1)	4 (1)	4 (1)	3 (1.5)	31.9	< 0.001*
At 2 h	2 (1)	4 (1)	4 (1)	3 (1)	28.6	< 0.001*
At 3 h	2 (0)	2 (0)	2 (1)	2 (0)	6.33	0.097
At 6 h	1 (1)	1 (1)	1 (1)	1 (1)	2.15	0.54
At 12 h	1 (1)	1 (1)	1 (1)	1 (1)	2.15	0.54

Data expressed as median and interquartile range (IQR), Kruskal–Wallis test used.
* Statistical significance ($P < 0.05$).

Table 5 Adverse effects.

	Control No = 29	Fentanyl No = 28	Dexmedetomidine No = 28	Dexamethasone No = 27	Test	*P* value
Hypotension	1 (3.4%)	2 (7.1%)	2 (7.1%)	0 (0%)	$X = 2.27$	0.512
Does not require ephedrine	0 (0%)	1 (3.6%)	2 (7.1%)	0 (0%)	$X = 3.77$	0.288
Bradycardia	0 (0%)	2 (7.1%)	3 (10.7%)	0 (0%)	$X = 5.65$	0.13
Does not require atropine	0 (0%)	2 (7.1%)	3 (10.7%)	0 (0%)	$X = 5.65$	0.13
Respiratory depression	0 (0%)	9 (32.1%)	2 (7.1%)	0 (0%)	$X = 22.1$	< 0.0001*
Itching	0 (0%)	7 (25%)	0 (0%)	0 (0%)	$X = 22.4$	< 0.0001*
Vomiting	1 (3.4%)	7 (25%)	2 (14.3%)	2 (7.4%)	$X = 8.26$	0.041*

Data expressed as number (%), Chi-square test used.
* Statistical significance ($P < 0.05$).

Table 5 shows postoperative vomiting, itching and respiratory depression were significantly occurred in the fentanyl group compared to other groups. The other adverse effects were comparable among studied groups.

5. Discussion

Fentanyl is most common additive to local anesthetics to caudal block, but it has undesirable side effects [5].

Dexmedetomidine is α_2 adrenergic receptor agonist which prolongs the duration of analgesia when added to caudal bupivacaine. This effect due to local vasoconstriction, increases potassium conductance in *Aδ* and *C* fibers, entering the central nervous system either via systemic absorption or by diffusion into the cerebrospinal fluid and reach α_2 receptors in the superficial laminae of the spinal cord and brainstem or indirectly activating spinal cholinergic neurons [12,7,13,14].

Caudal dexamethasone prolongs the duration of analgesia. The mechanism of analgesic effect may be due to the local anesthetic action of corticosteroids, and also it inhibits the transcription factor nuclear factor-kB (NF-kB) which expressed in the nervous system and causes pain [15,16].

The current study compared some of different caudal additives to the local anesthetics (fentanyl 1 μg/kg, dexmedetomidine 1 μg/kg and dexamethasone 0.1 mg/kg) in pediatrics underwent lower abdominal surgeries as regards hemodynamics, duration of analgesia, pain score, sedation score and adverse effects.

In the present study the results of *demographic data* were comparable between the studied groups.

As regards *postoperative pain score*, *duration of analgesia and number of patients required analgesia in the first 6 h*, there was a significant decrease in pain score after 3 h and number of patients required analgesia in first 6 h in both dexmedetomidine and dexamethasone groups in comparison with the other 2 groups. Also the 1st time to rescue analgesia was significantly prolonged in them compared to control and fentanyl groups.

These results come with agreement with the study done by Xiang et al. who studied the effect of addition of dexmedetomidine to ropivacaine in caudal block in children underwent inguinal hernia repair and concluded that the addition of dexmedetomidine to caudal bupivacaine could reduce the response to hernial sac traction, prolong the duration of postoperative analgesia and decrease postoperative analgesic requirements [17].

Another 2 studies were done by Dutt et al. and Nasr et al. who compared caudal fentanyl or dexmedetomidine on lower abdominal and limb surgeries and cardiac surgery in pediatrics respectively and concluded that in dexmedetomidine group the pain score was decreased and the duration of postoperative analgesia was prolonged [18,19].

The study done by Kim et al. who studied the effect of addition of dexamethasone to ropivacaine in children underwent orchiopexy and found that Postoperative pain scores at 6 and 24 h post-surgery were significantly lower in dexamethasone group. Furthermore, the number of patients who received oral analgesic was significantly lower in the dexamethasone group and time to first oral analgesic administration after surgery was also significantly longer in dexamethasone group [20].

The *hemodynamic variables* (*MAP & HR*) were comparable in between the studied groups.

These results were supported by the study done by Mahendru et al. who compared the intrathecal administration of fentanyl, clonidine and dexmedetomidine in the lower limb surgeries and concluded that the mean values of mean arterial pressure (MAP) and heart rate (HR) were comparable between the studied groups throughout the intraoperative and postoperative periods [21].

Dutt et al. compared the addition of fentanyl or dexmedetomidine to caudal ropivacaine in pediatrics underwent lower abdominal and lower limb surgeries and concluded that hemodynamics was comparable between the two studied groups [18].

Mohammed et al. compared caudal ropivacaine or dexamethasone in normal labor and found the HR and MAP were comparable in both groups at baseline and intrapartum [22].

Nasr et al. compared the efficacy of the caudal dexmedetomidine or caudal fentanyl on the stress response and postoperative analgesia and concluded that the HR & MAP were significantly decreased in the dexmedetomidine group [19]. This difference may due to the high volume used in caudal block (1.6 ml/kg), the younger age and the type of operation (open heart).

As *regards sedation score*, there was a significant increase in the first 2 h in sedation score which more pronounced in the fentanyl and dexmedetomidine groups compared to the control and dexamethasone. But in the dexamethasone group the sedation score is little but in the level which is acceptable to the parents as there was no crying.

These results come with agreement of the study done by Anand et al. who evaluated the effects of dexmedetomidine added to caudal ropivacaine in pediatric lower abdominal surgeries, and found that dexmedetomidine group achieved significant postoperative pain relief with better quality of sleep and prolonged duration of arousal sedation [23].

Saadawy et al. studied the addition of dexmedetomidine to bupivacaine in caudal block in children concluded that the dexmedetomidine group had better quality of sleep and a prolonged duration of sedation [24].

However, Dutt et al. compared caudal fentanyl versus dexmedetomidine and concluded that sedation score was more pronounced in dexmedetomidine group. But this difference was due to high dose of dexmedetomidine (2 μg/kg) [18].

As regards the *postoperative adverse effects* (respiratory depression, vomiting and itching), they were increased significantly in the fentanyl group.

Constant et al. compared caudal clonidine and caudal fentanyl and concluded that the adverse effects especially vomiting occurred mainly in the fentanyl group [25].

Bajwa et al. evaluated the addition of either fentanyl or dexmedetomidine to epidural analgesia in lower limb surgeries and revealed that the incidence of postoperative nausea and vomiting was significantly occurred in the fentanyl group [26].

6. Conclusion

Both caudal dexmedetomidine and caudal dexamethasone added to local anesthetics are good alternatives in prolongation of postoperative analgesia with less pain score compared to caudal local anesthetic alone or added to caudal fentanyl. Also they showed less side effects compared to caudal fentanyl.

Conflict of Interest

No relations with people or organization as regards this work and no any type of financial support.

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