The Outcomes of Caudal or Intravenous Addition of Morphine and Clonidine into The Caudal Block Performed with Levobupivacaine In Children; A Retrospective Study

Çocuklarda Levobupivakain ile Yapılan Kaudal Bloğa Kaudal veya İntravenöz Morfin ve Klonidin Eklenmesinin Sonuçları; Geriye Dönük Bir Çalışma

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Öz

Çocuklarda Postoperatif ağrı tedavisinin etkin şeklide yapılamaması kronik ağrı ile ilişkili olabilmektedir. Yaşları 6 ay ile 12 arasında değişen, hipospadias cerrahisi için kaudal levobupivakain uygulanan 98 pediatrik hasta retrospektif olarak değerlendirildi. Kaudal levopubivakaine intravenöz klonidin eklenmiş hastalar grup 1; intravenöz morfin eklenmiş hastalar grup 2, kaudal klonidin eklenmiş hastalar grup 3 ve kaudal morfin eklenen hastalar grup 4 olarak adlandırıldı. İntravenöz morfin grubunda 8 olgu (%40), intravenöz klonidin grubunda 5 olgu (%25) ve kaudal morfin grubunda 3 olgu (%15)'da 1. saatte CHEOPS ağrı skoru 6 ve üzerinde idi. Bununla birlikte kaudal klonidin grubundaki tüm olguların 1. saat CHEOPS değerleri 6'nın altındaydı ($p<0.05$). 12. saatte; intravenöz morfin grubunda 5 olguda (%25), intravenöz klonidin grubunda 10 olguda (%50) ve kaudal morfin grubunda (%20) 4 hastada CHEOPS değerleri 6 ve üzerinde idi. 24. saatte ise; intravenöz morfin grubunda 10 olgu (%50), intravenöz klonidin grubunda 10 olgu (%50), kaudal morfin grubunda 9 olgu (%45) ve kaudal klonidin grubunda 2 olguda (%10) CHEOPS değerleri 6 ve üzerinde idi ($p<0.05$). Sedasyon skorları açısından gruplar arasında tüm saatlerde fark yoktu ($p>0.05$). En düşük ağrı skorları 1., 12. ve 24. saatlerde kaudal klonidin grubunda kaydedildi. Tüm gruplar değerlendirildiğinde 6 saatte en düşük, en iyi ağrı skorları ile karşılaşıldı. Bizim çalışmamızda klonidin grubu lehine analjezinin postoperatif 12 saat boyunca sürdüğünü, böylece çocukların ve ailelerinin postoperatif streslerinin en aza indirilebileceğini kabul ettik.

Anahtar Kelimeler: Intravenöz Klonidin, Kaudal Analjezi, Kaudal Klonidin, Pediatrik Postoperatif Analjezi

Abstract

Ineffective post-operative pain management in children may be associated with chronic pain. 98 pediatric patients aged 6 months to 12 years who underwent caudal levobupivacaine for hypospadias surgery were evaluated retrospectively. The patients who received additional intravenous clonidine were added in group 1; the patients who received additional intravenous morphine were added in group 2, patients who received additional caudal clonidine was added in group 3, and patients who received additional caudal morphine was added in group 4. CHEOPS score was assessed 1, 6, 12 and 24 hours after the operation and patients with score 6 or higher were determined. At the 1st hour, there were 8 cases in the intravenous morphine group (40%), 5cases in the intravenous clonidine group (25%), and 3 cases in the caudal morphine group (15%). At the 12th hour, there were 5 cases in the intravenous morphine group (25%), 10 cases in the intravenous clonidine group (50%), and 4 cases in the caudal morphine group (20%). At the 24th hour, there were 10 cases in the intravenous morphine group (50%), 10 cases in the intravenous clonidine group (50%), 9 cases in the caudal morphine group (45%) and 2 cases in the caudal clonidine group (10%) ($p<0.05$). There was no difference between the groups in terms of sedation scores at all hours ($p>0.05$). The lowest pain scores at the 1st, 12th, and 24th hours were recorded in the caudal clonidine group. It had the lowest pain scores at 6 hours. By these methods, in favor of the clonidine group, we agreed that the analgesia lasts for approximately 12 hours postoperatively, so the postoperative stress that the children and their families have can be minimized.

Keywords: Intravenous Clonidine, Caudal Analgesia, Caudal Clonidine, Pediatric Postoperative Analgesia

Introduction

Postoperative pain is one of the most critical problems affecting morbidity in surgical cases. Postoperative pain can cause a series of complications such as hypoxia and atelectasis by limiting respiratory capacity, thromboembolism due to decreased movement, cardiovascular effects due to increased catecholamine release and undesirable changes in metabolic and neuroendocrine systems (1). It was indicated that newborns and infants have a stronger humoral, metabolic and cardiovascular response to surgical stress and pain than adults (2). However, in studies from various countries, postoperative pain management in children has been revealed to be inadequate (3, 4). Lee et al. reported that one of the main reasons for inadequate treatment of postoperative pain in children is difficulties in pain assessment and concerns about the adverse effects of opioid analgesics (5). Evidence has been presented that it is associated with the inability to provide effective postoperative pain treatment, delayed wound healing, negative perception of pain in the future, and chronic pain in children (3, 4).

Providing analgesia after surgical intervention in children relieves the patient, increases parental satisfaction and provides convenience in

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postoperative follow-up (5). Approximately one-fourth of the anesthesia procedures applied to children include regional anesthesia (6). Approximately 34-40% of these are single-injection caudal blocks (6, 7). Almost 4-6 hours of postoperative analgesia is provided with local anesthetics (LA) through caudal block. Furthermore, additional drugs such as clonidine, ketamine, morphine, and dexmedetomidine are added to intraspinal LAs to reduce the adverse effects of LAs such as toxicity and motor block and extend the postoperative analgesia period (8-12). However, although various additives with LAs increase analgesia, there are also risks of itching, nausea, vomiting, and respiratory depression (13).

The study aimed to reveal the most ideal analgesia method by investigating the postoperative pain and sedation level of the patients to whom we applied caudal block with levobupivacaine combined with caudal morphine, caudal clonidine, intravenous morphine or intravenous clonidine as an adjuvant, using the retrospective file scanning method.

Material and Method

Study design and patient selection

This retrospective study was conducted at the Cerrahpaşa University Faculty of Medicine. After obtaining hospital's ethics committee approval (22.10.2010, protocol number: 31780), medical data were obtained using electronic medical database and medical files of pediatric patients who underwent hypospadias surgery between 2007 and 2010. A total of 98 patients from ASA I and II patients for whom levobupivacaine was used during caudal block were examined within the scope of the study. Among these patients, 18 patients were excluded due to conditions such as preoperative analgesic use, premedication applied, or lack of postoperative follow-up forms, and 20 patients from each group were included. Since we did not perform a caudal block in patients with bleeding diathesis, allergy to local anesthetics, and taking aspirin, these conditions were determined as exclusion criteria. The cases that did not receive premedication after 8 hours of fasting before the operation were included in the study.

Data collection

Standard monitoring (ECG, pulse oximetry, noninvasive arterial pressure) is routinely performed on all patients admitted to the pediatric surgery operating room, and hemodynamic values are recorded. After vascular access is established, 1% dextrose ringer lactate liquid was used as maintenance. The caudal epidural was administered with a 22-gauge needle under sterile conditions after the patients who will undergo caudal analgesia were placed in the lateral decubitus position. After caudal injection, patients were kept in the lateral position for 15 minutes and then taken to the supine position. In our patients, hemodynamic data such as noninvasive blood pressure (BP) and heart rate (HR) were measured every 5 minutes and recorded in anesthesia follow-up forms.

Cases for which levobupivacaine was used as a local anesthetic agent during the caudal block in hypospadias operations between 2007 and 2010 were included. In our clinic, levobupivacaine was administered at a dose of 2 mg/kg 0.5% (1ml/kg, volume) during the caudal block. Moreover, intravenous or caudal clonidine or morphine was usually added to caudal levobupivacaine in hypospadias cases. Patients who received additional intravenous clonidine were added to group 1; patients who received additional intravenous morphine were added to group 2, patients who received additional caudal clonidine were added to group 3, and patients who received additional caudal morphine were added to group 4.

In our clinic, intravenous morphine at a dose of 0.02 mg/kg, caudal morphine at a dose of 0.02 mg/kg, intravenous clonidine at a dose of 1 µg/kg, and caudal clonidine at a dose of 1 µg/kg were routinely added to caudal levobupivacaine.

Hypospadias cases are followed for at least 24 hours in the postoperative pediatric surgery service, and their follow-up forms were recorded. For postoperative pain, CHEOPS (The Children's Hospital East Ontario Pain Scale) was routinely used for children aged 6 months to 12 years in our clinic, and analgesics were added when CHEOPS score was 6 or more. Ramsey Sedation Scoring System (RSS) was used for sedation (1: Awake, restless and/or crying 2: Awake, Calm, watching normal surroundings, 3: Tired, sleepy, immobile, uninterested to the surroundings, 4: Asleep, but easily awakened, 5: Asleep, but can hardly be awakened, 6: Sleeping, no response to shouting and glabellar stimulation) and the data was recorded in forms. Postoperative pain and sedation scales were examined from the data obtained from the follow-up forms at the 1st, 6th, 12th, and 24th hours. Also, adverse effects (nausea, vomiting, pruritus, respiratory depression, and others) occurring in the postoperative period were recorded in the follow-up forms as "yes" or "no." If the oxygen saturation was below 95% in the postoperative 24-hour period, it was recorded as respiratory depression. In postoperative hypospadias patients, the first dose of Paranox suppository (paracetamol 120 mg, phenobarbital 15 mg) to the patients aged one year and younger and Ibufen syrup (ibuprofen 100 mg/5 ml) to the patients aged 1 to 12 years was routinely administered 6 hours after the operation at 6-hour intervals/4 times a day. Furthermore, additional paracetamol (20 mg/kg suppository) was given in cases when more analgesics were requested from patients' relatives. As a result of file reviewing, the time elapsed until the CHEOPS value was 6 and

above was considered as the effectiveness of the applied analgesia method.

Statistical analysis

The shapes of distribution of the variables were demonstrated using the Shapiro-Wilk test. Analysis of variance (ANOVA) test was used for group-wise differences on parametric data, and mean and standard deviation values were shared. Kruskal-Wallis test was used for non-parametric data and detailed with median and interquartile range. The inter-group differences for categorical variables were tested using Chi-square test, and both percentages and observation numbers were detailed. Statistical analyses were performed using the SPSS version 25 (SPSS Incorporated, Chicago, Illinois, USA) software. A p value of < 0.05 was considered statistically significant for all tests results presented.

Results

The following data were compiled by examining the files and forms of 80 children who underwent surgery between January 2007 and June 2010. The children's ages ranged from 6 months to 11 years.

Twenty (25%) of the cases were in the intravenous clonidine group, 20 (25%) were in the intravenous morphine group, 20 (25%) were in the caudal clonidine group, and 20 (25%) were in the caudal morphine group.

There was no statistically significant difference between the ages (Table 1) and the duration of surgery (Table 2) according to the groups (p>0.05).

Systolic blood pressure values before caudal block were 102.10±14.47 in group 1, 103.15±22.55 in group 2, 95.10±12.51 in group 3, and 101.60±15.30 in group 4, which was not statistically significant (p>0.05).

The groups showed no statistically significant difference between the systolic blood pressure levels before the caudal block and at the 5th, 10th, 15th, and 20th minutes after the caudal block induction (p>0.05). However, in all groups, the systolic blood pressure levels decreased significantly after the caudal block (p>0.01).

Table 1. Evaluation of age (month) according to groups

Variable	Group	N	Mean Rank	Median	IQR	*p*
Age (month)	Iv clonidine	20	36.17	22	27	0.407
	Iv morphine	20	36.6	24	18	
	Caudal clonidine	20	42.43	36	42	
	Caudal morphine	20	46.8	30	45.75	

IQR: Interquartile range. p value is obtained with Kruskal-Wallis test.

Table 2. Evaluation of surgery duration (min.) according to groups

				95% CI		
Variable	Group	Mean	sd	LB	UB	*p*
Surgery Duration (min.)	Iv clonidine	113.05	24.97	101.36	124.74	0.553
	Iv morphine	122.75	39.18	104.41	141.09	
	Caudal clonidine	128	43.78	107.51	148.49	
	Caudal morphine	128.25	40.98	109.07	147.43	

sd: standard deviation, LB: Lower boundary, UB: Upper boundary. p value is obtained with ANOVA test.

The diastolic blood pressure values measured before the block were not different between the groups.

At the 1st hour; There was statistically significant difference between the postoperative CHEOPS pain scores between the groups. As a result of the pairwise comparisons performed to determine which group the difference originates from, pain scores of Group 1, Group 2, and Group 4 were significantly higher than Group 3 (p=0.020).

At 6th hour; There was also no statistically significant difference between the postoperative CHEOPS pain scores between the groups (p>0.05) (Table 3).

At the 12th hour; There was statistically significant difference between the postoperative CHEOPS pain scores (p=0.010). As a result of the pairwise comparisons made to determine which group the difference originates from, pain scores of Group 1 were significantly higher than Group 3 (p=0.010).

At the 24th hour; no statistically significant difference was determined between the postoperative CHEOPS pain scores (p> 0.05). But the pain scores of Group 3 were lower compared to other groups (Table 3).

There was a statistically significant difference between the groups' CHEOPS 1st hour pain levels (p>0.05). While there were 5 patients (25%) with a pain score of 6 or higher in group 1, 8 patients (40%) in group 2, and 3 patients (15%) in group 4, all patients in group 3 had a pain score less than 6 (Table 4).

No statistically significant difference was determined between the CHEOPS 6th hour pain levels between groups (p>0.05) (Table 4).

There was a statistically significant difference between CHEOPS 12th hour pain levels in the intergroup comparison (p>0.01). While there were 10 patients (50%) with a pain score of 6 or higher in group 1, five patients (25%) in group 2 and 4 patients

(20%) in group 4, all patients in group 3 had a pain score less than 6 (Table 4).

A statistically significant difference was observed between CHEOPS 24th hour pain levels between the groups (p>0.05). There were 10 (50%) patients with a pain score of 6 or higher in group 1, 10 (50%) in group 2, 2 (10%) in group 3, and 9 (45%) in group 4 (Table 4).

There was no statistical difference between the groups' postoperative 1st hour, 6th hour, 12th hour, and 24th-hour sedation scores (p>0.05) (Table 5).

The incidence of nausea, vomiting, pruritus, respiratory depression, and other adverse effects did not differ statistically between the groups (p>0.05). Since bradycardia developed in the 1st hour after caudal block in one patient in Group 1, atropine administration was obtained from the follow-up forms in which 0.1mg intravenously was administered (Table 6).

Discussion

Caudal epidural block application is a reliable technique widely used in pediatric surgery, especially in sub umbilical and genitourinary operations, and is routinely applied in many clinical centers (6, 7, 9, 10, 11, 13, 14). In studies performed using caudal morphine and clonidine in different doses in children, the results show variability (13, 15, 16). In our retrospective file review study, the postoperative pain score was significantly lower in the group with caudal levobupivacaine (2mg/kg) + caudal clonidine (2mg/kg). No statistically significant difference was found in postoperative complication rates.

Table 3. CHEOPS Postoperative Pain Scale Evaluation by Groups

Variable	Group	N	Mean Rank	Median	IQR	*p*
CHEOPS_1	Iv clonidine	20	41.4	4	1.75	0.020
	Iv morphine	20	48.25	5	2	
	Caudal clonidine	20	28.4	4	0	
	Caudal morphine	20	43.95	5	1	
CHEOPS_6	Iv clonidine	20	39.85	4	0	0.061
	Iv morphine	20	47.3	4	1	
	Caudal clonidine	20	37.42	4	0	
	Caudal morphine	20	37.42	4	0	
CHEOPS_12	Iv clonidine	20	48.75	5	2	0.010
	Iv morphine	20	41.88	4	1.75	
	Caudal clonidine	20	29	4	0	
	Caudal morphine	20	42.38	4	1	
CHEOPS_24	Iv clonidine	20	45.73	5.5	1.75	0.054
	Iv morphine	20	44.95	5.5	3.5	
	Caudal clonidine	20	28.98	4	1	
	Caudal morphine	20	42.35	4	3.75	

IQR: Interquartile range. p value is obtained with Kruskal-Wallis test.

Table 4. Evaluation of the Groups According to the CHEOPS (6) Score

Variable	Group		Iv clonidine	Iv morphine	Caudal clonidine	Caudal morphine	*p*
Cheops1 grup	<6	N	15	12	20	17	0.014
		%	75.00%	60.00%	100.00%	85.00%	
	≥6	N	5	8	0	3	
		%	25.00%	40.00%	0.00%	15.00%	
Cheops6 grup	<6	N	18	19	20	20	0.283
		%	90.00%	95.00%	100.00%	100.00%	
	≥6	N	2	1	0	0	
		%	10.00%	5.00%	0.00%	0.00%	
Cheops12 grup	<6	N	10	15	20	16	0.003
		%	50.00%	75.00%	100.00%	80.00%	
	≥6	N	10	5	0	4	
		%	50.00%	25.00%	0.00%	20.00%	
Cheops24 grup	<6	N	10	10	18	11	0.024
		%	50.00%	50.00%	90.00%	55.00%	
	≥6	N	10	10	2	9	
		%	50.00%	50.00%	10.00%	45.00%	

p value is obtained with chi-square test.

In the literature, the studies of Motsch et al. (16), which used caudal 0.175% of 1 ml/kg bupivacaine and the highest caudal clonidine (5 μg.kg-1) in children, reported a significant decrease in postoperative heart rate and blood pressure in the clonidine-added group compared to the control group, and they observed bradycardia requiring atropinization in one child. In our series, bradycardia requiring atropinization was determined in only one patient in the group where intravenous (1 μg/kg) clonidine was used. However, no arrhythmia and hypotension requiring vasopressors were detected.

Bonnison et al. (14) also revealed lower heart rate levels in the group in which they administered 3 µg.kg-1 caudal clonidine compared to the group that didn't receive caudal clonidine or received 1-2 µg.kg-1 caudal clonidine.

Hypertension, although rare, may occur with the administration of clonidine. It was reported that this effect develops since clonidine stimulates alpha 2 postsynaptic vascular receptors and causes an increase in systemic vascular resistance, and it can only developed when clonidine is administered at high concentrations (17). Hypertension was not determined in our patients who received intravenous or caudal clonidine. In general, when we evaluated SBP, DBP, and HR in all groups, compared to pre-block, the decrease lasted from 10 to 15 minutes, and was statistically significant but not clinically significant. Afterward, the decrease did not continue at the 15th and 20th minutes, and the monitored parameters began to stabilize. We attributed these results to decreased anesthetic requirement and cardiovascular stress reaction. Therefore, we interpreted it as creating a situation in favor of the patient.

Table 5. Postoperative Ramsey Sedation Scale (RSS) Evaluation by Groups

Variable	Group	N	Mean Rank	Median	IQR	df	$\chi 2$	*P*
RAMSEY_1	Iv clonidine	20	32.95	3	3	3	3.16	0.367
	Iv morphine	20	43.25	3	2.5			
	Caudal clonidine	20	41.8	3	2.5			
	Caudal morphine	20	44	3	1			
RAMSEY_6	Iv clonidine	20	34.2	2	2.75	3	2.26	0.520
	Iv morphine	20	42.6	3	2			
	Caudal clonidine	20	41.5	2.5	2			
	Caudal morphine	20	43.7	3	2			
RAMSEY_12	Iv clonidine	20	42.55	2	0	3	6.72	0.081
	Iv morphine	20	38.5	2	0			
	Caudal clonidine	20	36.63	2	0			
	Caudal morphine	20	44.33	2	0			
RAMSEY_24	Iv clonidine	20	40.98	2	0	3	3.79	0.285
	Iv morphine	20	40.98	2	0			
	Caudal clonidine	20	37.1	2	0			
	Caudal morphine	20	42.95	2	0			

IQR: Interquartile range. p value is obtained with Kruskal-Wallis test.

Table 6. Adverse Effect Evaluation by Groups

Variable	Group		Iv clonidine	Iv morphine	Caudal clonidine	Caudal morphine	*p*
Nausea	yes	N	19	15	17	17	0.354
		%	95.00%	75.00%	85.00%	85.00%	
	no	N	1	5	3	2	
		%	5.00%	25.00%	15.00%	10.00%	
Vomiting	yes	N	18	13	19	17	0.054
		%	90.00%	65.00%	95.00%	85.00%	
	no	N	2	7	1	3	
		%	10.00%	35.00%	5.00%	15.00%	
Itching	yes	N	20	20	20	18	0.104
		%	100.00%	100.00%	100.00%	90.00%	
	no	N	0	0	0	2	
		%	0.00%	0.00%	0.00%	10.00%	
Respiratory Depression	yes	N	20	20	20	20	n/a
		%	100.00%	100.00%	100.00%	100.00%	
	no	N	0	0	0	0	
		%	0.00%	0.00%	0.00%	0.00%	
Other	yes	N	20	20	20	19	0.386
		%	100.00%	100.00%	100.00%	95.00%	
	no	N	0	0	0	1	
		%	0.00%	0.00%	0.00%	5.00%	

p value is obtained with chi-square test.

Although studies have demonstrated that clonidine administered in different doses in addition to bupivacaine in caudal block applications prolongs the duration of analgesia and increases the quality of analgesia (11, 19), there are also studies reporting that when clonidine is used together with bupivacaine, it does not provide a change in the duration of caudal analgesia (18). In this study, which reported that clonidine (2 µg/kg) did not prolong the duration of analgesia, the researchers reported that this result might be due to the insufficient volume of the solution (0.5 ml/kg) or the fact that epinephrine given as an adjuvant that prolongs the duration of analgesia and masks the contribution of clonidine (17).

In a study in which 0.25% caudal bupivacaine (0.5 ml/kg) was combined with 2 µg/kg caudal or 2 µg/kg intravenous clonidine were compared in hypospadias repair surgery, both groups did not need postoperative analgesia, and no difference was reported in terms of adverse effects and sedation (9). Likewise, the study of Potti et al. (21), in which caudal levobupivacaine was combined with intravenous clonidine or caudal clonidine, reported that they achieved the longest analgesia time in the caudal clonidine added group.

The study of Jamali et al. (19), the first to report positive results of the additional effect of clonidine, revealed that the duration of analgesia with caudal 0.25% levobupivacaine 1 ml/kg was 7.6 hours in children aged 1-7 years who underwent sub umbilical or urological surgery and 16.5 hours when clonidine 1 µg/kg was added to levobupivacaine and 5.7 hours when 5 µg/kg epinephrine was added to levobupivacaine. As a result, clonidine doubled the analgesic effect of levobupivacaine. They even reported that half of the children in the clonidine group, 13% of those who took only levobupivacaine, and 6% of those in the epinephrine group did not need analgesics for 24 hours.

The caudal clonidine group had the lowest value among the 1st-hour values of the CHEOPS scale, which we used for pain assessment, and there was no significant difference between the 6th-hour values. In the 12th hour CHEOPS scores, the score of the caudal clonidine group was lower than the intravenous clonidine group, and there was no difference between the intravenous morphine and caudal morphine groups. This result may be an evidence that the presence of clonidine in the spinal area, not in the plasma level, contributes to analgesia. In the 24th hour scores, the lowest pain score was found in the caudal clonidine group. On the contrary, in the study of Singh et al. (20) in which they compared the use of caudal 2 µg kg^{-1} clonidine and caudal 30 µg kg^{-1} morphine as an adjuvant to caudal 0.2% bupivacaine, they indicated that the duration of analgesia and sedation were longer in the caudal morphine group. The meta-analysis published by Yang et al. (22) also reported that postoperative analgesia time was prolonged in patients using clonidine, and the need for additional analgesics was less.

In the study of Vetter et al. (14) in the children aged 6 months to 6 years who had undergone ureteral reimplantation operation in which they added caudal clonidine, caudal morphine, or caudal hydromorphone to caudal ropivacaine, although longer analgesia time was provided in the caudal morphine group, adverse effects of postoperative nausea, and vomiting and pruritus were more common. Similarly, in another study comparing caudal clonidine and caudal morphine, pruritus adverse effects were observed at a higher rate in the caudal morphine group (20). In our study, we expected better analgesic results in the caudal morphine group compared to our experience. However, the fact that we used a lower dose by moving away from our classical epidural morphine dose caused us not to be able to prove this prediction. It is possible to provide much longer analgesia by increasing the dose of morphine. However, these doses also cause adverse effects such as vomiting and itching (23). While interpreting our results, it should be considered that children were administered paracetamol or ibuprofen at 6-hour intervals in the ward.

Sedation is common with clonidine administration during regional blocks (15, 16). In our study, when the sedation score was evaluated at the postoperative 1st, 6th, 12th, and 24th hours, we encountered the highest (3.10) sedation score at the 1st hour in the intravenous morphine group. The statistical analysis indicated that the wakefulness at the 12th and 24th hours was significant compared to the 1st hour. When we compared the groups, there was no difference in sedation scores between the morphine and clonidine groups at all hours. As a result, we could not demonstrate the sedating effect of epidural clonidine at the dose we used (1 µg/kg).

A decrease in peripheral oxygen saturation due to clonidine and respiratory depression can be observed. However, it has been reported that these adverse effects occur due to caudal clonidine used at a high dose of 700 µg (17). Another study (16), in which 5 µg/kg caudal clonidine was administered in children, demonstrated decreased respiratory rate and peripheral oxygen saturation, although respiratory depression was not encountered. Although the amount of clonidine administered by the caudal route of these researches was quite high compared to other studies, the absence of respiratory depression supports that clonidine is a safe agent for caudal block. The fact that the caudal clonidine dose we used in our study was very low compared to other researches makes it necessary to say that we did not encounter postoperative respiratory depression without the need for additional interpretation.

Although there are publications indicating respiratory depression with epidural morphine (22), we did not observe any respiratory depression in our clinical experience, although we used a dose much higher than the dose specified in this study.

Motsch et al. (16) stated that using a lower concentration of bupivacaine and clonidine during caudal block reduced the incidence of adverse effects such as paresthesia, motor weakness, and urinary retention, which are common as a result of administration of 0.25% bupivacaine. In this regard, levobupivacaine also provides selective analgesia, so it is possible to avoid motor blocks with low concentrations. Although the motor block was not evaluated in this retrospective study, we do not determine motor block at the doses we traditionally use.

With the addition of clonidine to local anesthetic in caudal anesthesia, a prolongation in the duration of analgesia has been demonstrated by causing less nausea and vomiting than fentanyl (23). Associated with epidural use of morphine, complaints of nausea, vomiting, and itching have been reported (24). The study by Kelleher et al., which added caudal bupivacaine and diamorphine to caudal bupivacaine, observed more urinary retention in the group to which they added caudal diamorphine and applied urinary catheterization (24). In the study of Parikh et al. (25), in which they added morphine or clonidine to epidural bupivacaine in adults, they found a significant increase in the complaints of nausea and vomiting treated with ondansetron and itching treated with antihistamines in the morphine group. Since all of our patients had urinary catheters, we could not detect the possibility of urinary retention. Although nausea and vomiting occurred in the intravenous morphine group at a rate of 25%-30%, nausea and vomiting with a minimum rate of 5% in the intravenous clonidine group, and vomiting at least 1% in the caudal clonidine group in the groups, no statistical significance was found in the statistical evaluation. The frequencies of nausea and vomiting (34 ±36 at 0.05 mg/kg dose), pruritus (57%), urinary retention (6±30%) were associated with epidural morphine dosage used usually as in respiratory depression (26). In our patients, pruritus was detected in only one patient in the intravenous morphine group, and there seems to be an evaluation error in this regard.

The most important limitation of our study was its retrospective design, but since our records were kept very well, it did not cause any problems in accessing the data.

In this study, in the children who underwent hypospadias repair under general anesthesia, we demonstrated that hemodynamic stabilization was achieved with caudal morphine (0.02 mg/kg) or clonidine (1 µg/kg) added to levobupivacaine in the preoperative caudal block, and postoperative analgesia was prolonged up to 12 hours with minimal adverse effects in favor of clonidine for postoperative analgesia. We determined that the hour with the lowest pain scores is the 6th hour after the surgery, which can be the most distressing as we concluded that this might have a critical role in reducing the stress reactions of families and children.

Ethics Committee Approval: The study was approved by the Cerrahpaşa University Faculty of Medicine (22.10.2010, protocol number: 31780).

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