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ANALGESIC EFFICACY OF CAUDAL DEXAMETHASONE COMBINED WITH ROPIVACAINE IN CHILDREN UNDERGOING HERNIOTOMY

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ABSTRACT

Background : Epidural administration of dexamethasone might reduce postoperative pain in adults. We evaluated whether a caudal block of 0.1 mg kg– 1 dexamethasone combined with ropivacaine improves analgesic efficacy in children undergoing day-case Herniotomy.

Methods: This randomized, double-blind study included 60 children aged 6 months to 6 yr who underwent day-case, unilateral Herniotomy. Patients received either 1.5 ml /kg of 0.15% ropivacaine (Group R) or 1.5 ml /kg of 0.15% ropivacaine in which dexamethasone of 0.1 mg /kg was mixed (Group RD) for caudal analgesia. Postoperative pain scores, rescue analgesic consumption, and side-effects were evaluated 48 h after operation.

Results: Postoperative pain scores at 6 and 24 h post-surgery were significantly lower in Group RD than in Group R. Furthermore, the number of subjects who remained pain free up to 48 h after operation was significantly greater in Group RD [14 of 28 (50%)] than in Group R [3 of 28 (10.71%); P,0.001]. The number of subjects who received oral analgesic was significantly lower in Group RD [8 of 28 (28.57%)] than in Group R [15 of 28 (53.57%); P¼0.027]. Time to first oral analgesic administration after surgery was also significantly longer in Group RD than in Group R (P¼0.014). Adverse events after surgery including vomiting, fever, wound infection, and wound dehiscence were comparable between the two groups.

KEYWORDS : Caudal anaesthesia, regional, Ropivacaine, Dexamethasone, hormones, corticosteriods, paediatric surgery

Editor's key points

- † Epidural dexamethasone can have analgesic effects, but its effect in children has not been well studied.
- † The efficacy of dexamethasone as an adjunct to caudal ropivacaine was studied.
- † Caudal dexamethasone added to ropivacaine increased the pain-free interval and reduced postoperative oral analgesic use in children undergoing Herniotomy.

Herniotomy is commonly performed in children, and is associated with postoperative pain lasting several days.[1 2] A recent report described pain after day-case herniotomy in detail.1 According to this report, children under-going herniotomy suffered moderate-to-severe pain at home in the first postoperative day requiring analgesics for an additional 3 days after surgery.[1 2] Therefore, the appropriate management of postoperative pain in children undergoing herniotomy needs to be further evaluated with a focus on better pain control.

administration of a_2-agonists can produce hypotension, bradycardia, and sedation.[3 – 6] Because of these adverse effects, such adjuncts might not be appropriate for children undergoing a day-case surgery.[3 4]

Dexamethasone is commonly used perioperatively to manage postoperative pain, nausea, and vomiting, with the overall goal of ensuring a better recovery.[7 – 9] Furthermore, previous reports demonstrated that epidural administration of dexamethasone can reduce postoperative pain and analgesic requirements in adults.[10 11] Therefore, dexamethasone has the potential to be an efficacious adjunct to caudal epidural blocks. However, the analgesic properties of caudal dexamethasone have not been investigated fully in children. We designed this prospective, randomized, double-blind study to examine whether a caudal block of ropivacaine combined with dexa-methasone improves analgesic efficacy in children undergoing day-case herniotomy.

Methods

Subjects

This randomized, double-blind study was conducted at Govt. Tiruvannamalai medical college hospital in Tamilnadu, india. between June 2015 and December 2015. After obtaining approval from Hospital approval committee and written informed consent from parents, we enrolled a total of 60 children aged 6 months to 5 yr of ASA physical status I or II, undergoing day-case, unilateral herniotomy. Exclusion criteria included a history of develop-mental delay or mental retardation, type I diabetes, known or suspected coagulopathy, known allergy to any local anaesthetic or steroid, known congenital anomaly of the spine, or signs of spinal anomaly or infection at the sacral region.

Anaesthesia

All subjects received IM, midazolam (0.5 mg/ kg) 30 min before anaesthesia. The surgery started between 9:00 a.m. and 10:00 a.m. Subjects were hydrated with a multiple electrolytes infusion at a rate of 6 ml/kg/hr. Glycopyrolate (0.01 mg /kg) was administered by i.v. injection to inhibit respiratory secretion.

Ten minutes later, patients received i.v. ketamine at 2 mg kg21. Oxygen was delivered at a rate of 5 litre min21 (FIO2¼1.0). The children were placed in the left lateral decubitusposition, standard monitors including , non-invasive arterial pressure, pulse oximetry, were applied during induction and maintenance of anaesthesia. Child was sent to a post-anaesthetic care unit (PACU)..

Intervention

Enrolled children were randomly assigned to either Group R (control) or Group RD (dexamethasone adjunct) according to a computer-generated randomization table. For caudal blocks, Group R received 1.5 ml kg^{21} of 0.15% ropivacaine (maximum volume 20 ml); Group RD received 1.5 ml kg^{21} of 0.15% ropivacaine in which dexamethasone 0.1 mg kg^{21} was diluted (maximum volume 20 ml). dexamethasone sodium phosphate injectate[w] (4mg ml^{21}), . An investigator who did not participate in the care of the enrolled children prepared all study medications according to group assignment. Another investigator , who was blinded to group assignments, performed caudal blocks in all patients. sacral epidural space was measured, and then a 5 cm short bevelled 22 G block needle was inserted into the sacral epidural space. An aspiration test was conducted to exclude intravascular placement. As the medication was being administered, turbulence in the sacral caudal space on ultrasound imaging of the transverse plane was checked to confirm the spread of injected medications into the epidural space.

Fifteen minutes after performing the caudal block, surgery was initiated. The caudal block was considered to have failed if the patient moved his or her limbs, had an increase in heart rate, had an increase in mean arterial pressure, or both of more than 15% compared with

baseline during the surgery. In such instances, the patient was to be withdrawn from the study and treated with 1 – 2 mg kg^{-21} of fentanyl.

Assessments

Another investigator who was blinded to group allocation provided postoperative care and assessments. Postoperative pain during the hospital stay was assessed using the Children's Hospital of Eastern Ontario Pain Scale (CHEOPS, 0–10)[12] and the Faces Legs Activity Cry Consolability tool (FLACC, 0–10)[13] at 30 min and 1, 2, and 3 h after operation. A child with a score of more than 4 on both CHEOPS and FLACC received 0.5 mg kg^{21} of fentanyl i.v. for rescue analgesia. Motor function was assessed using the following scale: 0, no motor block; 1, able to move legs; 2, unable to move legs. The presence of other adverse events including bradycardia, hypotension, respiratory depression, retching, vomiting, or urinary catheterization was evaluated. Hypotension and respiratory depression were defined as ,80% of baseline arterial pressure and ,95% of pulse oxygen saturation, respectively. The decision to place a urinary catheter for urinary retention and the evaluation of micturition were made by an urologist. Children were discharged from the hospital when they met the following discharge criteria: conscious, haemodynamically stable, tolerating oral intake, voiding, walking in an appropriate manner for age, with the absence of retching, vomiting, and other side-effects.[14]

After discharge, pain was assessed by parents who were also blinded to group assignment. The investigator, who was blinded to group allocations and provided postoperative care, educated the parents on how to rate pain according to verbal and non-verbal expressions of pain and behavioural change after surgery on a numeric rating scale (NRS) from 0 to 10, with 0 representing 'no pain' and 10 representing 'the worst pain possible'.[15] The parents were instructed to assess pain at least once an hour. Oral ibuprofen was prescribed for anal-gesia after discharge. Children received 5 mg kg^{21} of ibuprofen for pain scores of 4 or greater on NRS. Information regarding pain levels and the use of analgesia after discharge was obtained via telephone calls to parents at 6, 24, and 48 h after surgery. The investigator inquired about present NRS, maximal NRS since the previous inquiry, and time and number of ibuprofen administration by parents. For NRS scores of zero at all time-points, the investigator asked the additional question of whether the child had been pain free for 48 h since the surgery. One week after operation, surgeon checked the surgical wound to rule out other problems such as infection.

Statistical analysis

Based on previous data[16] from our centre, a target sample size was calculated. Among patients who received caudal block with 1.5 ml kg^{21} of 0.15% ropivacaine alone, 50% needed oral analgesics after discharge. To demonstrate a 35% differnce in this study, at least 36 subjects in each group were required (a¼0.05, b¼0.1). Assuming an estimated 10% drop-rate, a total of 80 subjects were enrolled. Comparisons between the groups were performed with Student's t-test, the Mann –Whitney rank-sum test, the x^2 test, and Fisher's exact test when appropriate. A P-value of ,0.05 was consid-ered significant.

Results

A total of 60 subjects were enrolled in the study and five were excluded in total. Four subjects (two in Group R and Two in Group RD) were excluded because of failed caudal .. they are all excluded from the study (Fig. 1). The two groups did not differ in terms of patient characteristic data and surgical profiles (Table 1). .

Until discharge from hospital, FLACC scores were comparable between the groups. CHEOPS scores at 1, 2, and 3 h after surgery were higher in Group R than in Group RD with statistical significance (Table 2). However, the differences in CHEOPS scores between the groups were ,1 point. There was no difference in the number of subjects who had rescue analgesia with fentanyl [five subjects in Group R (17.85%) and Two in GroupRD (7.14%), P¼0.304].

There were no cases of motor block after surgery. Vomiting was observed in only one subject from Group R in the PACU. No other adverse events occurred. Similarities between the two groups were observed regarding time to micturition [174 (77) min in Group R and 156 (43) min in Group RD, mean (SD); P¼0.224] and time to discharge after surgery [239 (70) min in Group R and 219 (40) min in Group RD, mean (SD); P¼0.134].

Figure presents pain scores determined by parents during the 48 h postoperative period. Group RD had significantly lower NRS scores than Group D, with the exception of scores at the 48 hr postoperative mark. The number of subjects who were pain free during the 48 h postoperative period was significantly greater in Group RD (14 of 28, 50%) than in Group R (3 of 28, 10.8%, P,0.001). Consumption of oral analgesics during the postoperative 48 h is shown in Figure and Table 3. According to a Kaplan–Meier curve depicting time to first oral analgesic administration after surgery, analgesic duration of Group RD was significantly longer than that of Group R (P¼0.014). The number of subjects who had oral analgesic during the post-operative 48 h was significantly less in Group RD (9 of 28, 28.7%) than in Group R (15 of 28, 53.57%, P¼0.027) and so was the number of oral analgesic administration (P¼0.013).

Table demonstrates adverse events after hospital discharge with no significant differences between the two groups. Postoperative wound dehiscence was seen in one case from each group, and the two patients recovered with conservative care within the 3 month follow-up period. Two subjects experienced vomiting in Group R, with no cases of vomiting in Group RD after discharge.

Discussion

This study demonstrates the analgesic efficacyof caudal dexa-methasone in children undergoing day-case Hernioplasty. The addition of dexamethasone can increase the analgesic duration of caudal block with ropivacaine. Furthermore, pain severity and analgesic consumption decreased by the post-operative 48 h. Among subjects who received dexamethasone in their caudal block, half experienced no pain and 71% required no oral analgesics during the 48 h postoperative period—a significantly higher proportion compared with subjects who did not receive dexamethasone.

After day-case orchiopexy, children without caudal block reported clinically significant pain, and about 90% of them needed analgesia. Furthermore, about 70% required more than one type of analgesic.[1] Caudal block using ropivacaine alone can reduce pain and analgesic consumption after herniotomy in children. About 46% of subjects in Group R with ropivacaine alone needed no analgesic after discharge, which is consistent with the finding of a previous study for paediatric orchiopexy, which demonstrated that caudal block with 1.5 ml kg^{21} of 0.15% ropivacaine provided prolonged analgesia and reduced analgesic consumption after discharge, compared with that with 1.0 ml kg^{21} of 0.225% ropivacaine.[16] Based on this study,[16] we selected the former concentration and dose of ropivacaine for caudal analgesia. Because the analgesic duration of ropivacaine is 4–6 h[17] and caudal block with ropivacaine could provide sufficient analgesia in children undergoing herniotomy for the immediate postoperative period, additional rescue analgesia might not be required.[16] Hence, postoperative pain during hospital stay was assessed with two types of pain scales for infants and children to avoid inappropriate administration of rescue fentanyl. Differences in pain scores were not clinically significant between the groups for postoperative 3 h, and this was probably due to the analgesic durationof ropivacaine, thus adding dexamethasone would not make any clinically significant difference in pain scores and rescue fentanyl administration for several hours after operation. Clinically relevant differences in pain scores and analgesic consumption between the groups occurred after 6 h after surgery, and this is consistent with the end of analgesic duration of ropivacaine. Adding dexamethasone can significantly increase the analgesic duration of caudal block with ropivacaine and reduce pain scores and analgesic consumption for postoperative 48 h. Unlike other adjuvants to caudal block investigated in previous studies,[3 – 6] no adverse events were observed with dexamethasone during postoperative recovery.

Dexamethasone is commonly used in the perioperative period to reduce postoperative nausea and vomiting.[18] additionally, it has been reported to have analgesic effects.[7 – 9] Recently, several studies have demonstrated that epidural administration of dexamethasone prolonged analgesic effects and reduced analgesic requirements in adults.[10 11] Also, the use of dexamethasone as an adjuvant to local anaesthetics during brachial plexus block effectively improved the quality of analgesia without side effects.[19 20] The precise mechanism of analgesic effect of epidural or perineural dexamethasone administration is not clearly understood. Dexamethasone might have a local anaesthetic effect on nerve by direct membrane action.21 Therefore; dexamethasone might potentiate the effect of ropivacaine and prolong the duration of analgesia. Another possible mechanism involves the effect of dexamethasone on the spinal cord. The

transcription factor nuclear factor-k B (NF-kB) is expressed throughout the nervous system and plays an important role in the develop-ment of pathological pain.

22 Dexamethasone could regulate NF-kB;23 more specifically, epidural injection of corticosteroid has been reported to inhibit development of hyperalgesia with associated reduction in NF-kB levels.24 These findings suggest that dexamethasone might prevent central sensitiza-tion after surgery and strengthen the preventive analgesia of caudal block. Our finding that a higher proportion of children in Group RD were without pain during the postoperative 48 h

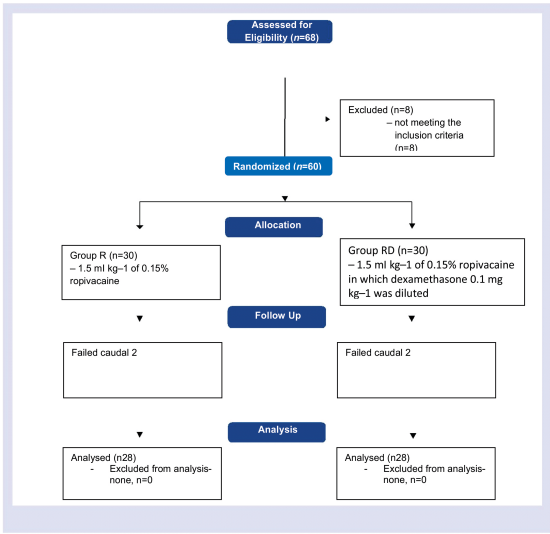

Table 1 Patient characteristics and intraoperative data. Data are shown as mean (range) or mean (SD). C, control; D, dexamethasone adjunct; T1, immediately after induction of anaesthesia; T2, 5 min after skin incision; T3, end of surgery

	Group C (n537)	Group D (n538)
Age (months)	14.1(7–48)	14.3 (6– 53)
Weight (kg)	10.5(1.9)	10.8 (2.1)
Height (cm)	76.5(7.4)	77.9 (8.6)
Duration of surgery (min)	38 (14)	34 (11)
Duration of anaesthesia (min)	64 (13)	60 (10)
Fluid administered (ml)	74 (21)	73 (17)
Mean arterial pressure (mm Hg)		
T1	67 (13)	65 (9.7)
T2	63 (9.7)	66 (7.8)
T3	57 (7.5)	56 (6.2)
Heart rate (beats min^{21})		
T1	141 (18)	140 (14)
T2	143 (15)	140 (15)
T3	131 (14)	130 (16)
Sevoflurane concentration (end-tidal vol%)		
T1	3.4 (0.6)	3.4 (0.8)
T2	2.7 (0.4)	2.6 (0.3)
T3	2.2 (0.6)	2.0 (0.7)

Table 2 Immediate postoperative CHEOPS and FLACC scores. Data are shown as mean (SD). CHEOPS, Children's Hospital of Eastern Ontario Pain Scale; FLACC, Faces Legs Activity Cry Consolability tool

	Group C (n537)	Group D (n538)	P-value
CHEOPS			
30 min after surgery	2.3 (0.9)	2.2 (0.8)	0.554
1 h	2.4 (1.1)	2.0 (1.0)	0.049
2 h	2.1 (1.1)	1.3 (1.0)	0.002
3 h	1.6 (1.0)	1.1 (1.0)	0.023
FLACC			
30 min after surgery	0.9 (1.6)	0.5 (1.3)	0.313
1 h	1.2 (1.2)	0.7 (1.4)	0.175
2 h	0.8 (1.5)	0.3 (0.8)	0.057
3 h	0.3 (0.8)	0.0 (0.2)	0.066

period compared with Group C could be due to the prevention of hyperalgesia at the spinal cord level.

Epidural corticosteroids have a long history of safe use in the treatment of low back and radicular pain.[25] To date, no signifi-cant side-effects have been reported for epidural dexametha-sone.[26] Although there is no direct evidence regarding the safety of dexamethasone administered through an epidural route in children or young animals, as far as we know, an in vitro experiment demonstrated that direct exposure to neural cell cultures dexamethasone for 12 h was not neurotoxic.[27] In a study of the neurotoxicity of adjuvants

used in regional anaesthesia, dexamethasone attenuated bupivacaine-induced neuronal injury[28] and did not significant-ly increase ropivacaine-induced neuronal death.[29] The safety of methylparaben and propylparaben, the preservatives included in dexamethasone injectate, has been proven even in intrathecal injection of human and animal models.[30,31] However, high-dose dexamethasone is associated with com-plications such as hyperglycaemia,[32] wound infection,[33] post-operative bleeding,[34] and transient adrenal suppression.[35]

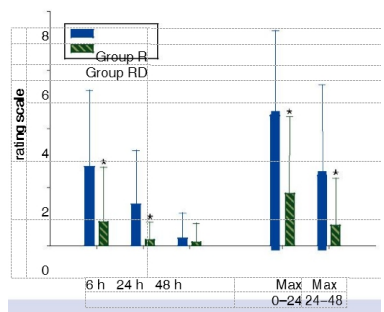

Fig 2 Pain scores during the 48 h postoperative period. Max 0 –24, maximal NRS score during postoperative 0– 24 h; Max 24 –48, maximal NRS score during postoperative 24 –48 h. *P,0.005 vs GroupR.

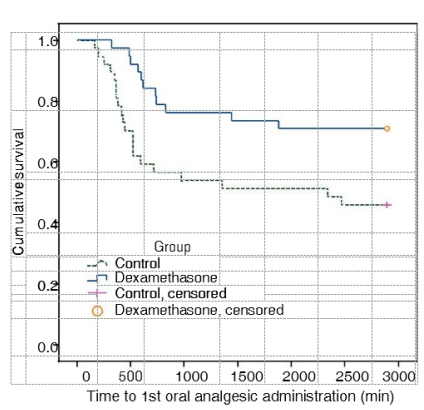

Fig 3 Kaplan – Meier curve for time to first oral analgesic administration. The proportion of the patients who did not receive oral analgesic over time after the surgery was significantly higher in Group D than in Group C (P¼0.014).

Table 3 Consumption of oral analgesics atpostoperative 48 h. Data are shown as number of subjects (proportion, %)

	Group R (n28)	Group R D (n28)	P-value
Number of subjects who had oral analgesic	15(54%)	8 (28%)	0.027
Number of oral analgesic administrations for postoperative 48 h			0.013
0	14 (50%)	20(71%)	
1	8 (29%)	7 (25%)	
2	2 (7%)	1 (3.57)	
3	2 (7%)	0 (0%)	
≥4	2 (7%)	0 (0%)	

Table 4 Incidence of complications after hospital discharge. Data are shown as number of subjects (proportion, %). NA, not applicable

	Group R (n28)	Group RD (n28)	P-value
Vomiting	1(3.57%)	0 (0%)	0.240
Fever (.38.38C)	2(7%)	1(3.5%)	0.829
Wound infection	0 (0%)	0 (0%)	NA
Wound dehiscence	1 (3.5%)	0	1.0

Therefore, there is a bodyof opinion that prefers lowerdose epi-dural steroids due to concern for corticosteroid-related side-effects.[36] In our study with low dose of dexamethasone, there were no differences in the incidence of adverse effects including postoperative fever, wound infection, or dehiscence.

Our study has several limitations. First, we cannot completely exclude the possibility that caudal dexamethasone exerts analgesic effects through systemic absorption because i.v. dexamethasone has been reported to have analgesic effects.[7 – 9] The dose of caudal dexamethasone (0.1 mg kg^{21}) in our study was selected based on a previous study regarding the analgesic effect of epidural dexamethasone in adults.[11] In the previous study, effective analgesia was provided by 5 mg of epidural dexamethasone but not 5 mg of i.v. dexamethasone in patients undergoing laparoscopic cholesy stectomy,[11] which implied that epidural dexamethasone has greater anal-gesic efficacy than i.v. dexamethasone at the same dose. Although the dose of i.v. dexamethasone for analgesia is con-troversial,[78] a meta-analysis demonstrated that more than 0.1 mg kg^{21} of i.v. dexamethasone is needed for postoperative analgesia.[7] Therefore, we did not consider administration of i.v. dexamethasone in a control group.

In a paediatric population, another meta-analysis that focused on the effects of systemic dexamethasone on nausea, vomiting, and pain after tonsillec-tomy demonstrated that the dose of i.v. dexamethasone leading to pain reduction was 0.5– 1.0 mg kg^{21}, and 0.4 mg kg^{21} of systemic dexamethasone produced only an antiemetic effect without analgesic effects.[9] Although only two placebo-controlled studies investigated the analgesic effect of i.v. dexa-methasone of ,0.4 mg kg^{21} in paediatrics,[37 38] 0.15 mg kg^{21} of i.v. dexamethasone reduced severe pain only on the second postoperative day, not on the operation day and first post-operative day after tonsillectomy;[37] moreover, i.v. dexametha-sone at a dose of 0.3 mg kg^{21} did not reduce postoperative pain in dental rehabilitation.[38] Therefore, 0.1 mg kg^{21} of systemic dexamethasone does not seem to provide clinically relevant an-algesia in children. Although the effect of caudal dexametha-sone through systemic absorption on analgesia cannot be excluded in this design, our study clearly demonstrates that caudal dexamethasone can provide clinically relevant analgesia even at a low dose in children undergoing herniotomy

Secondly, the mean age of our population was 14 months. Thus, the infants and children in this study might not be able to express their pain fully to parents. We assessed pain using NRS scores evaluated by parents. Presumably, parental perception of paediatric pain was based on an interpretation of their child's behavioural expression of pain. Hence, this method may not have been as accurate as self-reported pain scores.[39] Despite these limitations, NRS scores by parents in paediatric patients have been validated and correlated well with medical observers.[15]

Thirdly, we did not evaluate some potential adverse effects of dexamethasone such as hyperglycaemia and adrenal suppression. Because the children in day-case herniotomy did not require postoperative laboratory testing, we did not want to introduce invasive techniques for further blood sampling. However, previous studies have demonstrated that a single small dose of dexamethasone is not associated with significant side-effects.[26]

In conclusion, the addition of 0.1 mg kg^{21} dexamethasone to ropivacaine for caudal blocks could significantly improve analgesic efficacy in children undergoing herniotomy.

Declaration of interest
None declared.

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