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Caudal dexmedetomidine combined with bupivacaine inhibit the response to hernial sac traction in children undergoing inguinal hernia repair

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Editor's key points

- Hernial sac traction, as occurs in hernia surgery, can cause undesired haemodynamic changes.
- This study investigated the analgesic effects of adding caudal dexmedetomidine, an α_2 agonist, to bupivacaine.
- Caudal dexmedetomidine reduced the need for ketamine rescue analgesia.
- There was an increase in sedation and a reduction in postoperative fentanyl consumption in patients receiving dexmedetomidine.

Background. Caudal bupivacaine is widely used for inguinal hernia repair in children, but often cannot totally eliminate responses to hernial sac traction. The current study examined whether supplementation of caudal bupivacaine with dexmedetomidine could achieve better results.

Methods. Sixty children aged 12–72 months undergoing unilateral inguinal hernia repair received standardized premedication with midazolam, i.v. ketamine anaesthesia, and then were randomly assigned to receive either bupivacaine 0.25% (1 ml kg^{-1}; Group B) or bupivacaine plus dexmedetomidine (1 $\mu g\ kg^{-1}$; Group BD). The response to hernial sac traction was defined as an increase in heart rate or systolic arterial pressure by >20%, and was treated with ketamine rescue (2 mg kg^{-1}). After the surgery, fentanyl was administered as needed with a nurse-controlled analgesia pump.

Results. Only one subject in Group BD (3.33%) needed ketamine rescue, as opposed to 13 subjects in Group B (43.33%; $P<0.001$). The first fentanyl injection occurred at a much later time point in Group BD (median: 860 *vs* 320 min in Group B; $P<0.001$). Total fentanyl consumption of fentanyl was significantly lower in Group BD [2.5 (1.2) *vs* 6.9 (1.6) $\mu g\ kg^{-1}\ 24\ h^{-1}$ in Group B; $P=0.008$].

Conclusions. The addition of dexmedetomidine to caudal bupivacaine could reduce the response to hernial sac traction, and prolong the duration of postoperative analgesia in children undergoing inguinal hernia repair.

Keywords: anaesthesia, caudal; analgesia; dexmedetomidine; hernia, inguinal; sympathetic nervous system

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Single-shot caudal anaesthesia is widely used for inguinal hernia repair in children.[1 2] In order to achieve an effective caudal block, local anaesthetic agents must often be given at the maximum recommended dosage. To maximize the efficacy and extend the duration of analgesia, caudal bupivacaine may be co-administered with other agents such as epinephrine, clonidine, midazolam, ketamine, neostigmine, morphine, tramadol, fentanyl, and sufentanil.[3 4] Dexmedetomidine is a specific α_2 adrenergic receptor agonist with sedative, anxiolytic, and analgesic properties which enables it to prevent emergence agitation in children.[5 6] Recent studies suggested that caudal administration of dexmedetomidine could prolong postoperative pain relief in children,[7 8] but the perioperative effects of caudal dexmedetomidine have not been adequately examined.

The current study is a randomized, double-blinded clinical trial, and its aim was to examine whether supplementation of caudal bupivacaine with dexmedetomidine can eliminate the responses to hernial sac traction.

Methods

The current study was approved by the Institutional Ethics Committee. Written informed consents were obtained from parents of all subjects. The study was registered at the Chinese Clinical Trial Registry (http://www.chictr.org; ID: ChiCTR-TRC- 11001785). Sixty children (ASA status I, age: 12–72 months) undergoing elective surgery to repair unilateral inguinal hernia were randomly assigned into two groups using a computer-generated randomization table (Fig. 1).

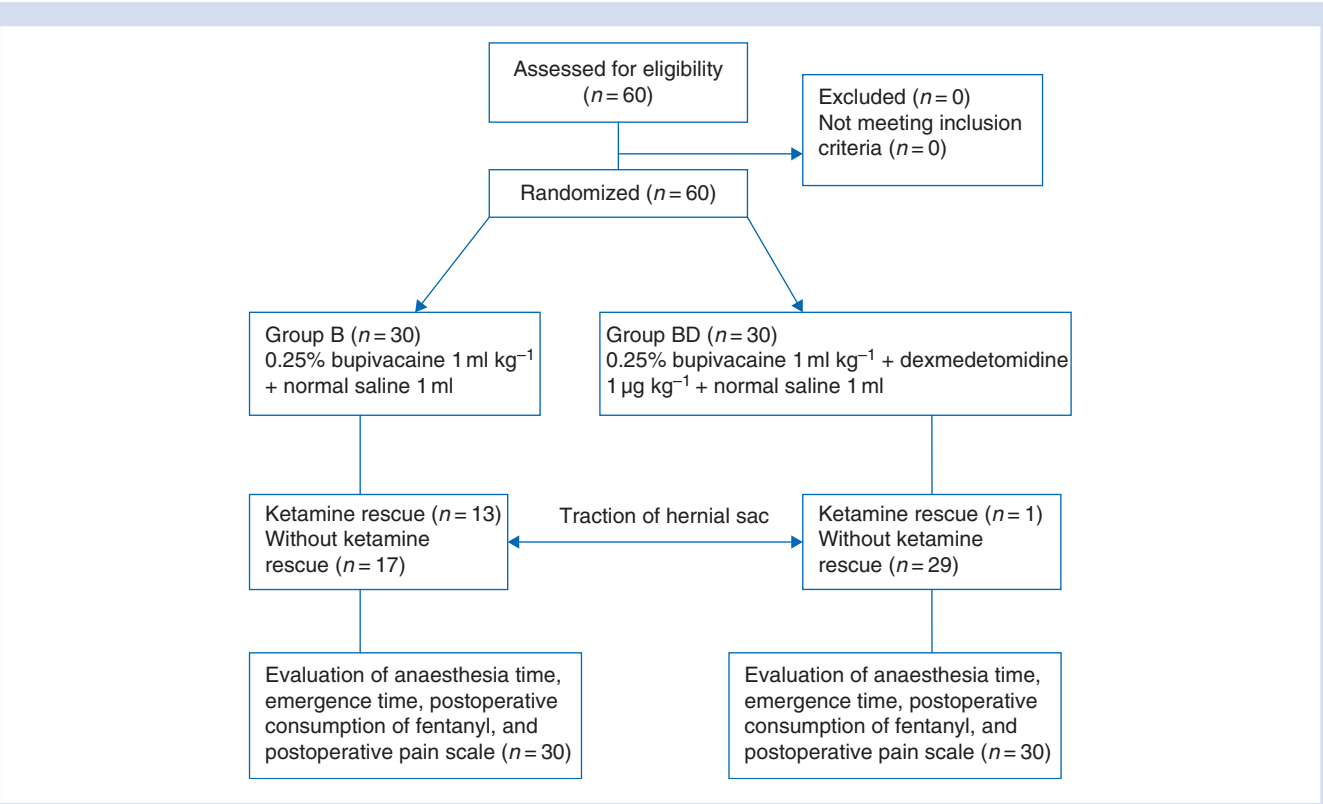

Fig 1 The study design: a CONSORT style diagram.

Exclusion criteria included developmental delay, bleeding diathesis, exposure to aspirin within 1 week before the surgery, known allergy to any of the study drugs, congenital anomaly of the lower back, any signs of local infection in the caudal area, systemic illnesses, or common cold.

All subjects received oral midazolam (0.5 mg kg^{-1}) 30 min before anaesthesia. The surgery started between 8:00 a.m. and 9:00 a.m. Subjects were hydrated with a multiple electrolytes infusion (Baxter Healthcare, China) at a rate of 6 ml kg^{-1} h^{-1}. Penehyclidine hydrochloride (0.01 mg kg^{-1}) was administered by i.v. injection to inhibit respiratory secretion. Ten minutes later, patients received i.v. ketamine at 2 mg kg^{-1}. Oxygen was delivered at a rate of 5 litre min^{-1} (F_{IO_2} = 1.0). The children were placed in the left lateral decubitus position, and a single-dose caudal block was achieved via a 22 G caudal needle.

Group 'BD' received: bupivacaine 0.25% (1 ml kg^{-1}) combined with dexmedetomidine 1 μg kg^{-1} in normal saline 1 ml (the concentration of dexmedetomidine is no more than 1 μg ml^{-1}) (Group BD; n=30); Group 'B' received: bupivacaine 0.25% (1 ml kg^{-1}) with normal saline 1 ml (Group B; n=30). The operation started 15 min later, and was carried out by the same surgeon. The block was deemed as successful if the increase in heart rate (HR) or systolic arterial pressure (SAP) in response to skin incision was ≤20%. HR, ECG, and peripheral oxygen saturation were monitored continuously. Non-invasive arterial pressure was monitored every 5 min. Adequate intraoperative analgesia was defined by haemodynamic stability, as reflected by ≤20% fluctuation of HR or SAP from the preoperative baseline. Inadequate anaesthesia was defined as >20% increase in HR or SAP upon hernial sac traction, and was treated with a rescue dose of ketamine (2 mg kg^{-1}). An intraoperative decline of HR and SAP by >30% from the preoperative value was defined as hypotension and bradycardia, respectively, and was managed accordingly with fluid bolus, ephedrine injection, and/or atropine. No other anaesthetics, analgesics, sedatives, or antiemetics were allowed during the operation. At the conclusion of the operation, patients were awakened and transported to a post-anaesthesia care unit (PACU).

Postoperative pain was assessed by an experienced nurse who was unaware of the patient's allocation using Children's and Infant's Postoperative Pain Scale (CHIPPS),[9] every 2 h for the first 6 h, every 3 h for the following 12 h, and once at 24 h. Fentanyl (i.v. bolus of 0.5 μg kg^{-1}, with a 60 min lockout period) was administered as needed (if the CHIPPS exceeded 3) using a nurse-controlled analgesia pump. Sedation was assessed using a sedation score: 0, awake, alert; 1, mild sedation, easy to rouse; 2, asleep, easy to rouse; 3, moderate sedation, unable to remain awake; 4, difficult to rouse. The emergence time was defined as the time from the end of surgery to eye opening on calling the children's name. Quality of night rest was assessed as previously described.[10] Side-effects of postoperative analgesia were also recorded.

Table 1 Subject characteristics and intraoperative clinical data. Data are presented as mean (SD), or as frequency (%). *$P<0.05$ *vs* Group B. #$P<0.05$ *vs* subgroup of ketamine rescue. Group B: bupivacaine alone; Group BD; bupivacaine plus dexmedetomidine

	Group B ($n=30$)	Group BD ($n=30$)	*P*-value
Gender			
Male	21 (70%)	22 (73%)	
Female	9 (30%)	8 (27%)	
Age (months)	41.4 (15–70)	42.6 (14–69)	
Weight (kg)	14.8 (4.4)	13.9 (4.5)	
Duration (min)			
Surgery	27.6 (8.9)	26.3 (9.4)	0.547
Anaesthesia	52.2 (10)	46.2 (5.5)	0.007*
Ketamine			
Rescue	13 (43.33%)	1 (3.33%)	<0.001*
Without rescue	17 (56.67%)	29 (96.67%)	
Emergence time (min)			
Ketamine rescue	16.4 (3.1)	14.6	0.062
Without ketamine rescue	4.1 (1.4)	3.4 (1.2)	0.112
P-value	0.043#	<0.001#	

Statistical analysis

The primary endpoint of the study was the proportion of the children who needed ketamine rescue. Before the study, the number of patients required in each group was determined after a power calculation according to data obtained from our previous studies. The calculation of sample size revealed that at least 29 patients in each group would be required for appropriate study with $\alpha=0.05$ and a power of 0.8. Data are presented as mean or median with range or 95% confidence interval (CI) as appropriate. Student's *t*-test or the Mann–Whitney *U*-test was used as appropriate. Categorical data are presented as absolute numbers (%) and were analysed with a χ^2 analysis. Fisher's exact test was used as appropriate. $P<0.05$ was considered statistically significant.

Results

The two groups did not differ in gender, age, body weight, and duration of surgery (Table 1). The caudal block was deemed successful (≤20% increases in HR or SAP upon skin incision) in all 60 subjects.

Thirteen subjects (43.3%) in Group B needed ketamine due to inadequate anaesthesia as reflected by >20% increase in HR or SAP upon hernial sac traction. The emergence time for the 13 patients receiving ketamine rescue was significantly longer than that in subjects without ketamine rescue [16.4 (3.1) *vs* 4.1 (1.4) min; $P<0.001$]. All patients in Group B who did not receive any ketamine rescues had a similar emergence time to those in Group BD [4.1 (1.4) *vs* 3.4 (1.2); $P=0.112$; Table 1]. Only one subject (3.33%) in Group BD needed ketamine rescue with a *P*-value of <0.001 compared with in Group B (Table 1). The emergence time in Group BD as a whole was significantly shorter than that in Group B [9.9 (4.6) *vs* 3.6 (1.6) min; $P=0.006$].

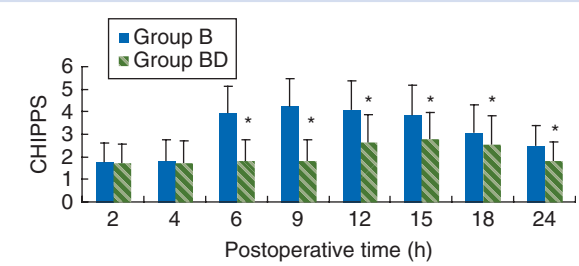

Fig 2 CHIPPS score after the surgery. *$P<0.01$ *vs* Group B.

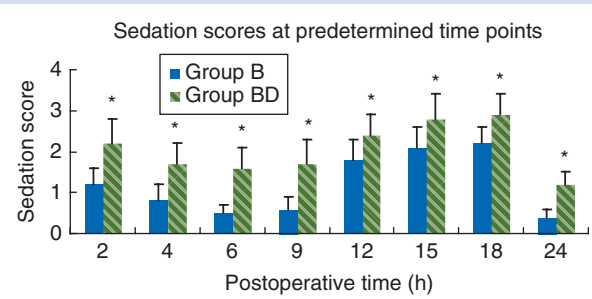

Fig 3 Sedation score after the surgery in the two groups. Sedation score: 0, awake, alert; 1, mild sedation, easy to rouse; 2, asleep, easy to rouse; 3, moderate sedation, unable to remain awake; 4, difficult to rouse. *$P<0.01$ *vs* Group B.

During the first 4 h after the surgery, analgesia was adequate in all subjects of both groups. However, during the next 20 h, the number of subjects with satisfactory analgesia decreased in both groups, but at a much slower rate in Group BD. The pain score was significantly lower in Group BD

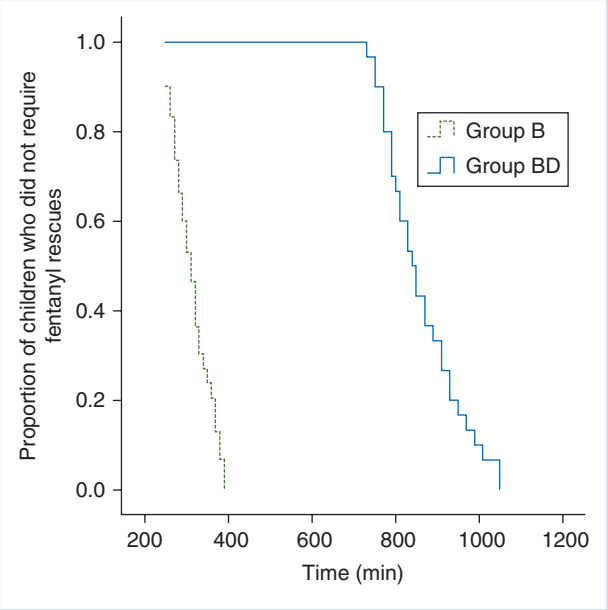

Fig 4 Kaplan–Meier analysis showing the proportion of children who did not require fentanyl rescues during the postoperative period.

Table 2 Postoperative clinical data. Data are presented as mean (SD), or as frequency (%). Quality of night rest: 1, normal sleep; 2, occasionally interrupted; 3, frequently interrupted; 4, awake.[9] *$P<0.05$ *vs* Group B

	Group B	Group BD	*P*-value
Total consumption of fentanyl (μg kg^{-1} 24 h^{-1})	6.9 (1.6)	2.5 (1.2)	0.008*
Quality of night rest	2.2 (0.8)	1.3 (0.6)	0.03*
Incidence of vomiting [*n* (%)]	2 (6.67)	2 (6.67)	1
Urinary retention [*n* (%)]	1 (3.33)	1 (3.33)	1

($P<0.01$ *vs* Group B; Fig. 2). The sedation score was significantly higher in Group BD at all time points ($P<0.01$ *vs* Group B; Fig. 3). The median time to first fentanyl injection was significantly longer in Group BD (860 min, 95% CI: 720–1040 *vs* 320 min, 95% CI: 240–380 min in Group B, $P<0.001$; Fig. 4). Total fentanyl consumption was significantly lower in Group BD [2.5 (1.2) *vs* 6.9 (1.6) μg kg^{-1} 24 h^{-1} in Group B, $P=0.008$; Table 2].

The two groups did not differ in the incidence of vomiting. Quality of night rest was better in Group BD [2.2 (0.8) *vs* 1.3(0.6) in Group B, $P=0.03$; Table 2]. One subject in each group required bladder catheterization. No hypotension, bradycardia, or bradypnoea ($Sp_{O_2}<95\%$) was noted.

Discussion

We have demonstrated that supplementation of caudal bupivacaine with dexmedetomidine (1 μg kg^{-1}) reduced the haemodynamic response to hernial sac traction in children undergoing inguinal hernia repair. The drug combination also significantly prolonged the duration of postoperative analgesia.

Caudal anaesthesia is common, safe, and effective but may not adequately block the haemodynamic response to peritoneal traction during lower abdominal surgery at conventional doses. Increasing bupivacaine dosage, however, could potentially lead to increased toxicity and inadvertent high block.[11]

α_2 Adrenergic receptor agonists could prolong the duration of action of bupivacaine and improve the quality of analgesia,[7 8] by causing local vasoconstriction[7] and increasing the potassium conductance in Aδ and C fibres.[12 13] They may also potentiate the action of local anaesthetic by entering the central nervous system either via systemic absorption or by diffusion into the cerebrospinal fluid and reach α2 receptors in the superficial laminae of the spinal cord and brainstem,[14] or indirectly activating spinal cholinergic neurones.[15]

A previous study in rabbits suggested that epidural injection of dexmedetomidine at a dose of 4.8–6.1 μg kg^{-1} and a concentration of 10 μg ml^{-1} could cause neurotoxicity and demyelinate oligodendrocytes in the white matter.[16] However, studies in children indicated that neuraxial administration of dexmedetomidine at no more than 2 μg kg^{-1} and a concentration of no more than 2 μg ml^{-1} does not cause neurotoxicity.[7 8] Although accumulating evidence demonstrates the safety of dexmedetomidine as a caudal or epidural adjunct for human beings, acting as a caudal additive, the risk or the benefit for its use still need to receive adequate attention.[17] Indeed, another animal study suggested that dexmedetomidine could provide neuroprotective effects through activating α_2 adrenergic receptors, imidazoline 1 and 2 receptors.[18]

The sedative effects of dexmedetomidine are mainly attributable to stimulation of the α_2 adrenoceptor in the locus coeruleus.[13 19] Results from the current study indicate that supplementation of bupivacaine anaesthesia with dexmedetomidine could provide more satisfying levels of postoperative sedation than bupivacaine alone.

The inguinal region receives sensory innervation from the ilioinguinal/iliohypogastric nerves and the genitofemoral nerves. All these nerves are derived from the spinal nerve roots at T_{12}–L_2 level.[20] As a part of the parietal peritoneum, the hernial sac also receives a segmental innervation together with the abdominal wall.[21] To achieve complete anaesthesia for inguinal hernia repair, afferent blockade must be complete at the T_6 through L_2. Using real-time ultrasound scanning, Lonnqvist and his team confirmed in their research that the median level of cranial spread directly after the caudal block (with 1.5 ml kg^{-1}, ropivacaine 0.2%) was T_{10} (range T_{12}–T_9). At 15 min after the caudal injection, the cranial level can be increased to a median level of T_8 (range T_{11}–T_4), and the cranial level of sensory block was in median T_4 (range T_{10}–T_3). Thus, even at a relatively high dose of 1.5 ml kg^{-1} of caudal ropivacaine, a sensory block up to T_6 is unlikely to be achieved.[22] This may explain the fact that a significant proportion of the subjects receiving bupivacaine alone still responded to hernia sac traction,

despite apparently sufficient dosing. The better intraoperative analgesia observed in Group BD is most probably caused by the central nervous system effects of dexmedetomidine and possibly a synergic or additive action with i.v. ketamine. Previous research demonstrated that the small volume (0.5 ml kg^{-1}) of local anaesthetic was insufficient to carry the clonidine (another α_2 adrenoreceptor agonist) to the spinal cord when used in combination caudally. Since the sacral nerve routes are much more difficult to penetrate than lumbar nerve routes, the analgesic action of clonidine in this site is often very small. Therefore, the caudal addition of clonidine may be ineffective if a volume of only 0.5 ml kg^{-1} is administered.[23 24] So we choose 1 ml kg^{-1} as the volume of local anaesthetic, a commonly used volume in previous published research, to perform our study.

Bradycardia and hypotension are the most common adverse effects of i.v. α_2 adrenoreceptor agonists, but appear to be less pronounced in children than in adults.[7 8] These problems could also be readily managed with volume expansion, sympathomimetic drugs, or both.[7]

In conclusion, caudal bupivacaine in combination with dexmedetomidine provided a more satisfactory level of anaesthesia than bupivacaine alone in children undergoing inguinal hernia repair. This drug combination also extended the duration of postoperative analgesia. We speculate that dexmedetomidine could also be useful for other types of surgery that involves manipulation of the peritoneum in children.

Declaration of interest

None declared.

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