



Evaluation of Adding Dexmedetomidine to Ropivacaine in Pediatric Caudal Epidural Block: A Randomized, Double-blinded Clinical Trial

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Abstract

Background: Caudal block is one of the methods of pain management performed following lower abdominal surgery, though having its own limitations.

Objectives: In the present study, the effects and side effects of adding dexmedetomidine to ropivacaine in the caudal epidural block were investigated in children after lower abdominal surgery.

Methods: In this randomized, double-blinded clinical trial, 46 children aged three to six years were divided into two groups to perform a caudal block following lower abdominal surgery under general anesthesia. The injectable solution contained ropivacaine in the R group (1 mL/kg ropivacaine 0.2%), as the control group, and dexmedetomidine (2 µg/kg) and ropivacaine 0.2% (1 mL/kg) in the DR group. The pain score (modified CHEOPS score), duration of analgesia, amount of analgesia consumed (i.v. paracetamol), hemodynamic changes, and possible adverse effects were assessed at one, two, and six hours in both groups.

Results: The pain score at one and two hours showed no significant difference between the two study groups ($P > 0.05$). In the DR group, however, the pain score at the sixth hour was significantly lower, and the duration of analgesia was longer ($P = 0.001$). The amount of analgesic consumption was also lower in the DR group ($P = 0.001$). However, there was no significant difference in systolic blood pressure and heart rate ($P < 0.05$), in the case of diastolic blood pressure, a significant difference ($P < 0.05$) was seen (DR group lower than the R group). There was no statistically significant difference between the study groups in the duration of surgery, recovery time, and side effects ($P < 0.05$).

Conclusions: In the present study, the addition of dexmedetomidine to ropivacaine in the caudal epidural blockade improved postoperative analgesia without significant adverse effects in pediatric patients.

Keywords: Caudal Block, Pediatric, Postoperative Pain, Dexmedetomidine, Ropivacaine

1. Background

Various methods, including administration of opioids, non-opioids, peripheral nerve blocks, and central nerve blocks, have been used so far to manage postoperative pain in pediatric lower abdominal surgery (1). Caudal block, as a central nerve block technique, is one of the common methods performed to manage perioperative pain in pediatric lower abdominal surgeries, particularly hernia and orchidopexy (2). Local anesthetics have usually been the main drug in such cases, and if administered alone in the caudal blockade, they do not usually provide prolonged analgesia. Thus, several studies have been conducted to investigate the possibility of increasing the analgesic effect of cau-

dal local anesthetics in children (3, 4). Ropivacaine is one of the most common drugs in this group, with a similar structure to bupivacaine, but it has a shorter duration of motor block, better hemodynamic stability, fewer cardiac and hemodynamic effects, and less neurotoxicity, thereby allowing for faster discharge from the recovery room, especially in pediatric outpatient surgery (5, 6).

Dexmedetomidine as a strong selective alpha-2 adrenergic receptor agonist, is eight times stronger than clonidine. Stimulation of alpha-2 adrenergic receptors induces sedative and analgesic effects without respiratory depression (7). The addition of dexmedetomidine to local anesthetics or its administration as an adjunct for pain management in a variety of techniques enhances their effects

without increased frequency of side effects (8-10).

2. Objectives

Despite studies in this area, the optimal dose of dexmedetomidine added to caudal ropivacaine in pediatrics has not yet been determined. This study investigated the effects and side effects of adding dexmedetomidine to ropivacaine in the caudal epidural block in children undergoing lower abdominal surgery.

3. Methods

The present clinical trial was conducted in a pediatric population scheduled for lower abdominal surgery, lasting one to three hours, under general anesthesia. After receiving the approval of the ethics committee (ref: IR.IUMS.FMD.REC.1398.077) and getting a clinical trial code (ref: IRCT20111102007984N30), as well as obtaining the written consent of the parents, a total of 46 children aged three to six years of both sexes, with ASA class I or II, were included in the study. The study was conducted using the following exclusion criteria: complicated surgeries (i.e., prolonged or associated with bleeding requiring transfusion), sacral abnormalities, bleeding disorders, systemic or local infections, history of reaction to study drugs, and parental dissent.

Considering a deviation error of 90% and a difference of 301 between the hypothetical means, a total of 46 people were studied in two equal groups of 23 individuals. To double-blind the study, the researchers who performed the block and evaluated the patients were not aware of the type of intervention.

The same method of general anesthesia was used for all the patients (induction with propofol, fentanyl, and atracurium, and maintenance with isoflurane). At the end of surgery and before extubation, a caudal block was administered to the subjects in a randomized order in both groups (R and DR), under sterile conditions, in the lateral position, using a 20 G needle (Dr. J, China) under ultrasound guidance with a linear probe (high frequency 6 - 13 MHz; Sonosite, USA). After the correct position of the needle at the caudal space in ultrasound guidance view, 3 mL was injected slowly. If there were no hemodynamic changes, the rest of the injectate was slowly administered.

In group R, the injectable solution contained 1 mL/kg ropivacaine 0.2% (Ropivacaine, Molteni, Italy), up to a maximum volume of 15 mL, and in group DR, the solution contained 2 µg/kg dexmedetomidine (Precedex®, Hospira, Illinois, USA) added to 1 mL/kg ropivacaine 0.2%. After performing the caudal block, the neuromuscular block was

reversed with neostigmine and atropine, and the patients were extubated. The patients were evaluated at one, two, and six hours after the surgery, and if the pain score exceeded three, the patients received 15 mg/kg paracetamol (Paracetamol Zolben, Switzerland) intravenously. The pain was scored using the CHEOPS score (Children's Hospital of Eastern Ontario Pain Scale), and hemodynamic changes (blood pressure and heart rate) were evaluated using non-invasive monitoring before and after the block (Table 1). In addition, the duration of analgesia (pain score < 3), amount of analgesic medications consumed, duration of stay in the recovery room, and potential adverse effects were assessed in both groups.

Table 1. Modified CHEOPS (Children's Hospital of Eastern Ontario Pain Scale)

| Score | 0 | 1 | 2 |
|---------------|----------|--------------------------|----------------|
| Cry | No cry | Crying, moaning | Scream |
| Facial | Smiling | Composed | Grimace |
| Verbal | Positive | None or other complaints | Pain complaint |
| Torso | Neutral | Shifting, tense, upright | Restrained |
| Legs | Neutral | Kicks, squirm, drawn up | Restrained |

Data analysis was carried out using the SPSS software (version 25). For quantitative variables (age, weight, pain score, duration of analgesia, duration of surgery, amount of analgesic consumption, heart rate, and blood pressure), the data were expressed as means and standard deviation (SD), and for qualitative variables (sex, complications), they were expressed as percentages. Quantitative variables were compared utilizing the independent *t*-test in the case of normal data distribution; otherwise, the comparison was performed using the Mann-Whitney test if the distribution was abnormal. For qualitative variables, the comparison was carried out employing the chi-square or Fisher's exact test. A *p* value less than 0.05 was considered as the significance level.

4. Results

Demographic information and other criteria included in the study are summarized in Table 2. According to the results obtained, the mean pain score measured at one and two hours was not remarkably different between the study groups ($P > 0.05$); nevertheless, at the sixth hour, a significant difference ($P < 0.05$) was seen (DR group lower than R group). Additionally, the DR group was proven to have a longer analgesia duration and lower analgesic consumption than the R group ($P < 0.05$). Meanwhile, no statistical difference was found in the systolic blood pressure, and heart rate ($P > 0.05$), but the diastolic blood pressure was

meaningfully lower in the DR group than in the R group ($P < 0.05$). There was no statistical difference between the study groups in the duration of surgery, recovery time, and adverse effects ($P > 0.05$).

Table 2. Demographic Information, Pain Score, Analgesia, Analgesic Consumption, Hemodynamic Changes, and Adverse Effects^a

| | R | DR | P-Value |
|---------------------------------|--------------|--------------|---------|
| Age, y | 4.5 ± 1.2 | 4.8 ± 1.1 | 0.372 |
| Sex, N | | | 0.76 |
| Male | 14 | 15 | |
| Female | 9 | 8 | |
| Duration of surgery, min | 122 ± 28.3 | 127.5 ± 39.5 | 0.741 |
| Pain score | | | |
| 1st h | 2.5 ± 0.6 | 2.4 ± 0.6 | 0.826 |
| 2nd h | 3.2 ± 1.1 | 3.1 ± 0.9 | 0.571 |
| 6th h | 7.8 ± 1.9 | 4.7 ± 1.5 | 0.001 |
| Duration of analgesia, h | 2.7 ± 0.7 | 4.2 ± 0.8 | 0.001 |
| Paracetamol, mg | 250.9 ± 59.3 | 179.6 ± 55.5 | 0.001 |
| Blood pressure, mmHg | | | |
| Systolic | 96.7 ± 5.3 | 94.5 ± 9.7 | 0.356 |
| Diastolic | 62.3 ± 3.7 | 59.3 ± 4.8 | 0.037 |
| Heart rate, bpm | 104.7 ± 9.7 | 103.7 ± 7.9 | 0.679 |
| Recovery time, min | 60 ± 25.1 | 64.4 ± 27.9 | 0.579 |
| Side effects | | | |
| None | 20 (86.8) | 18 (72.8) | |
| Hypotension | 1 (4.4) | 1 (4.4) | |
| Tachycardia | 1 (4.4) | 2 (7.8) | |
| Nausea/vomiting | 1 (4.4) | 2 (7.8) | |

^aValues are expressed as mean ± SD or No. (%).

5. Discussion

This study demonstrated that the addition of dexmedetomidine (2 µg/kg) to ropivacaine 0.2% in the caudal block enhanced analgesia and diminished analgesic consumption after lower abdominal surgery performed under general anesthesia in children without influencing the incidence of adverse effects.

Clonidine (a non-selective alpha-2 adrenergic receptor agonist) is commonly used as an adjuvant in the caudal block (11). A recent meta-analysis of the pediatric population showed that the addition of clonidine to local anesthetics resulted in prolonged postoperative analgesia and reduced analgesic consumption. Nevertheless, no statistical difference was seen in the incidence of side effects be-

tween the addition of clonidine to local anesthetics and the use of local anesthetics alone (12).

In a study conducted by Saadawy et al. (13), the caudal block with bupivacaine 0.25% with or without dexmedetomidine was performed preoperatively in children undergoing herniotomy under general anesthesia with sevoflurane. Their results demonstrated that the need for intraoperative sevoflurane and postoperative agitation reduced in subjects who received the combination of bupivacaine and dexmedetomidine. The duration of postoperative analgesia and the amount of analgesic consumed was also diminished in this group. Accordingly, they concluded that considering the lack of hemodynamic changes between the two groups, the addition of dexmedetomidine to bupivacaine in the caudal block could be applied as a useful method.

She et al. (14) evaluated the preoperative administration of various doses of dexmedetomidine added to levobupivacaine in children candidates for herniotomy under general anesthesia with sevoflurane. The results indicated that the addition of dexmedetomidine to levobupivacaine reduced the required concentration of the local anesthetic without any changes in the quality of analgesia (14). Moreover, the need for anesthetic drugs to maintain general anesthesia, the need for supplemental drugs to blunt the response to surgical stimulation, and the prevalence of postoperative agitation decreased in the participants.

On the contrary, in some studies, the addition of s-ketamine or clonidine to levobupivacaine not only did not affect postoperative pain in hypospadias but also increased postoperative sedation (4). The study by Gupta and Sharma (15) investigated the addition of 2 mg/kg tramadol versus 2 µg/kg dexmedetomidine to caudal ropivacaine 0.25% administered preoperatively in children who were candidates for infra-umbilical surgery under general anesthesia. The results indicated that the addition of dexmedetomidine, as compared to tramadol, induced prolonged analgesia, but changes in the heart rate and mean BP before and after the block, as well as side effects, were alike (15). Notwithstanding, although adequate analgesia (FLACC score < 4) existed in both groups within the first four hours after the surgery, the analgesia decreased rapidly in the tramadol group afterward. In addition, the time to the first request for analgesia (acetaminophen suppository) was longer in the dexmedetomidine group than in the tramadol group (15 vs. 11.5 hours). Therefore, it was concluded that the addition of dexmedetomidine was more effective than tramadol to ropivacaine for postoperative pain management. Although the ropivacaine concentration and dexmedetomidine dosage were lower in our study than in theirs, the results were similar; thus, it may

be concluded that lower doses of the drug could be administered for the caudal block.

In a study, Jarineshin et al. (16) performed caudal block after induction of anesthesia in children undergoing elective hernioplasty under general anesthesia, and compared the effects of adding dexmedetomidine 2 $\mu\text{g}/\text{kg}$ and fentanyl 2 $\mu\text{g}/\text{kg}$ to caudal bupivacaine 0.25%. The results indicated that dexmedetomidine than fentanyl more effectively enhanced the analgesic effects of postoperative bupivacaine without causing considerable adverse effects or hemodynamic changes. Furthermore, studies in adult patients have shown that performing caudal block before spinal surgery under general anesthesia, with the addition of 1 $\mu\text{g}/\text{kg}$ dexmedetomidine to 20 ml ropivacaine 0.25%, prolongs postoperative analgesia without causing severe hemodynamic changes or side effects, which is consistent with the results of published studies on children (17).

Al-Zaben et al. (18) examined the effects of adding different doses of dexmedetomidine (1 and 2 $\mu\text{g}/\text{kg}$) to 0.8 mL/kg caudal bupivacaine 0.25% in the pediatric caudal block and concluded that despite a shorter postoperative sedation period and fewer side effects, the quality of analgesia with low doses of dexmedetomidine was similar to the quality of analgesia with its high doses. In another study, Bharti et al. (19) evaluated the addition of dexmedetomidine at various doses (0.5, 1, and 1.5 mcg/kg) to 0.75 mL/kg ropivacaine 0.2% preoperatively administered in the pediatric caudal block. The children aged one to eight years were candidates for lower abdominal and perineal surgery under general anesthesia with sevoflurane (19). They concluded that postoperative analgesia within the first 3 - 5 hours was longer in all dexmedetomidine groups than in the group that had received ropivacaine alone. Moreover, within the first six hours after the surgery, all the patients who had received ropivacaine alone needed additional analgesics, while none of the dexmedetomidine groups required further analgesics. However, children who received dexmedetomidine at a dose of 1.5 mg/kg had higher sedation, but it did not affect their discharge time. On the other hand, some patients in the ropivacaine group developed agitation. Although the addition of these three doses of dexmedetomidine prolonged the duration of analgesia, no statistical difference was seen between the study groups.

5.1. Conclusions

Overall, the findings of our study showed that the addition of dexmedetomidine (2 $\mu\text{g}/\text{kg}$) to ropivacaine enhanced the effectiveness of the caudal epidural block in children but did not increase adverse effects and therefore, its administration in combination with ropivacaine is recommended.

Footnotes

Authors' Contribution: Study concept and design: FI and RFR. Analysis and interpretation of data: AM and RS. Drafting of the manuscript: MA, FI, RFR, and AM. Critical revision of the manuscript for important intellectual content: FI, RFR, and NDN. Statistical analysis: ZMJ and AM.

Clinical Trial Registration Code: The clinical trial registration code was IRCT20111102007984N30.

Conflict of Interests: The authors have no conflict of interest.

Ethical Approval: The ethical approval code was IR.IUMS.FMD.REC.1398.077.

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References

1. Ferland CE, Vega E, Ingelmo PM. Acute pain management in children: challenges and recent improvements. *Curr Opin Anaesthesiol*. 2018;**31**(3):327-32. doi: [10.1097/ACO.0000000000000579](https://doi.org/10.1097/ACO.0000000000000579). [PubMed: [29432292](https://pubmed.ncbi.nlm.nih.gov/29432292/)].
2. Lloyd-Thomas AR. Pain management in paediatric patients. *Br J Anaesth*. 1990;**64**(1):85-104. doi: [10.1093/bja/64.1.85](https://doi.org/10.1093/bja/64.1.85). [PubMed: [2405898](https://pubmed.ncbi.nlm.nih.gov/2405898/)].
3. Tsui BC, Berde CB. Caudal analgesia and anesthesia techniques in children. *Curr Opin Anaesthesiol*. 2005;**18**(3):283-8. doi: [10.1097/O1.aco.0000169236.91185.5b](https://doi.org/10.1097/O1.aco.0000169236.91185.5b). [PubMed: [16534352](https://pubmed.ncbi.nlm.nih.gov/16534352/)].
4. Davies K, Wilson G, Engelhardt T. Caudal additives do not improve the analgesia afforded by levobupivacaine after hypospadias repair. *Anesth Pain Med*. 2012;**1**(3):174-7. doi: [10.5812/kowsar.22287523.2629](https://doi.org/10.5812/kowsar.22287523.2629). [PubMed: [24904788](https://pubmed.ncbi.nlm.nih.gov/24904788/)]. [PubMed Central: [PMC4018700](https://pubmed.ncbi.nlm.nih.gov/PMC4018700/)].
5. Suksompong S, von Bormann S, von Bormann B. Regional Catheters for Postoperative Pain Control: Review and Observational Data. *Anesth Pain Med*. 2020;**10**(1). e99745. doi: [10.5812/aapm.99745](https://doi.org/10.5812/aapm.99745). [PubMed: [32337170](https://pubmed.ncbi.nlm.nih.gov/32337170/)]. [PubMed Central: [PMC7158241](https://pubmed.ncbi.nlm.nih.gov/PMC7158241/)].
6. Kumar M, Chawla R, Goyal M. Topical anesthesia. *J Anaesthesiol Clin Pharmacol*. 2015;**31**(4):450-6. doi: [10.4103/0970-9185.169049](https://doi.org/10.4103/0970-9185.169049). [PubMed: [26702198](https://pubmed.ncbi.nlm.nih.gov/26702198/)]. [PubMed Central: [PMC4676230](https://pubmed.ncbi.nlm.nih.gov/PMC4676230/)].
7. Imani F, Zaman B, De Negri P. Postoperative Pain Management: Role of Dexmedetomidine as an Adjuvant. *Anesth Pain Med*. 2021;**10**(6). doi: [10.5812/aapm.112176](https://doi.org/10.5812/aapm.112176).
8. Imani F, Rahimzadeh P, Faiz HR, Nowruzina S, Shakeri A, Ghahremani M. Comparison of the Post-Caesarean Analgesic Effect of Adding Dexmedetomidine to Paracetamol and Ketorolac: A Randomized Clinical Trial. *Anesth Pain Med*. 2018;**8**(5). e85311. doi: [10.5812/aapm.85311](https://doi.org/10.5812/aapm.85311). [PubMed: [30538943](https://pubmed.ncbi.nlm.nih.gov/30538943/)]. [PubMed Central: [PMC6252045](https://pubmed.ncbi.nlm.nih.gov/PMC6252045/)].
9. Akhondzadeh R, Rashidi M, Gousheh M, Olapour A, Baniahmad A. The Effect of Adding Dexmedetomidine as an Adjuvant to Lidocaine in Forearm Fracture Surgeries by Supraclavicular Block Procedure Under Ultrasound-Guided. *Anesth Pain Med*. 2018;**8**(4). e74355. doi: [10.5812/aapm.74355](https://doi.org/10.5812/aapm.74355). [PubMed: [30250821](https://pubmed.ncbi.nlm.nih.gov/30250821/)]. [PubMed Central: [PMC6139532](https://pubmed.ncbi.nlm.nih.gov/PMC6139532/)].
10. Imani F, Rahimzadeh P, Khademi SH, Narimani Zamanabadi M, Sadegi K, Abolfazli-Karizi A. Comparison of Transforaminal Triamcinolone and Dexmedetomidine in Radicular Low-Back Pain: A

- Randomized Double-Blind Clinical Trial. *Anesth Pain Med.* 2019;**9**(5):e96117. doi: [10.5812/aapm.96117](https://doi.org/10.5812/aapm.96117). [PubMed: [31903335](https://pubmed.ncbi.nlm.nih.gov/31903335/)]. [PubMed Central: [PMC6935293](https://pubmed.ncbi.nlm.nih.gov/PMC6935293/)].
11. Eich C, Strauss J. Prompt and powerful effect of a practice guideline on caudal additives. *Paediatr Anaesth.* 2009;**19**(3):271-2. doi: [10.1111/j.1460-9592.2009.02926.x](https://doi.org/10.1111/j.1460-9592.2009.02926.x). [PubMed: [19236648](https://pubmed.ncbi.nlm.nih.gov/19236648/)].
 12. Schnabel A, Poepping DM, Pogatzki-Zahn EM, Zahn PK. Efficacy and safety of clonidine as additive for caudal regional anesthesia: a quantitative systematic review of randomized controlled trials. *Paediatr Anaesth.* 2011;**21**(12):1219-30. doi: [10.1111/j.1460-9592.2011.03715.x](https://doi.org/10.1111/j.1460-9592.2011.03715.x). [PubMed: [22023418](https://pubmed.ncbi.nlm.nih.gov/22023418/)].
 13. Saadawy I, Boker A, Elshahawy MA, Almazrooa A, Melibary S, Abdellatif AA, et al. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. *Acta Anaesthesiol Scand.* 2009;**53**(2):251-6. doi: [10.1111/j.1399-6576.2008.01818.x](https://doi.org/10.1111/j.1399-6576.2008.01818.x). [PubMed: [19076110](https://pubmed.ncbi.nlm.nih.gov/19076110/)].
 14. She YJ, Zhang ZY, Song XR. Caudal dexmedetomidine decreases the required concentration of levobupivacaine for caudal block in pediatric patients: a randomized trial. *Paediatr Anaesth.* 2013;**23**(12):1205-12. doi: [10.1111/pan.12278](https://doi.org/10.1111/pan.12278). [PubMed: [24383602](https://pubmed.ncbi.nlm.nih.gov/24383602/)].
 15. Gupta S, Sharma R. Comparison of analgesic efficacy of caudal dexmedetomidine versus caudal tramadol with ropivacaine in paediatric infraumbilical surgeries: A prospective, randomised, double-blinded clinical study. *Indian J Anaesth.* 2017;**61**(6):499-504. doi: [10.4103/jija.IJA_712_16](https://doi.org/10.4103/jija.IJA_712_16). [PubMed: [28655957](https://pubmed.ncbi.nlm.nih.gov/28655957/)]. [PubMed Central: [PMC5474920](https://pubmed.ncbi.nlm.nih.gov/PMC5474920/)].
 16. Jarineshin H, Fekrat F, Kargar Kermanshah A. Treatment of Post-operative Pain in Pediatric Operations: Comparing the Efficiency of Bupivacaine, Bupivacaine-Dexmedetomidine and Bupivacaine-Fentanyl for Caudal Block. *Anesth Pain Med.* 2016;**6**(5): e39495. doi: [10.5812/aapm.39495](https://doi.org/10.5812/aapm.39495). [PubMed: [27847704](https://pubmed.ncbi.nlm.nih.gov/27847704/)]. [PubMed Central: [PMC5101645](https://pubmed.ncbi.nlm.nih.gov/PMC5101645/)].
 17. Kalappa S, Sridhara RB, Kumaraswamy S. Dexmedetomidine as an Adjuvant to Pre-Emptive Caudal Epidural Ropivacaine for Lumbosacral Spine Surgeries. *J Clin Diagn Res.* 2016;**10**(1):UC22-4. doi: [10.7860/JCDR/2016/15286.7145](https://doi.org/10.7860/JCDR/2016/15286.7145). [PubMed: [26894155](https://pubmed.ncbi.nlm.nih.gov/26894155/)]. [PubMed Central: [PMC4740683](https://pubmed.ncbi.nlm.nih.gov/PMC4740683/)].
 18. Al-Zaben KR, Qudaisat IY, Abu-Halaweh SA, Al-Ghanem SM, Al-Mustafa MM, Alja'bari AN, et al. Comparison of caudal bupivacaine alone with bupivacaine plus two doses of dexmedetomidine for postoperative analgesia in pediatric patients undergoing infra-umbilical surgery: a randomized controlled double-blinded study. *Paediatr Anaesth.* 2015;**25**(9):883-90. doi: [10.1111/pan.12686](https://doi.org/10.1111/pan.12686). [PubMed: [26033312](https://pubmed.ncbi.nlm.nih.gov/26033312/)].
 19. Bharti N, Praveen R, Bala I. A dose-response study of caudal dexmedetomidine with ropivacaine in pediatric day care patients undergoing lower abdominal and perineal surgeries: a randomized controlled trial. *Paediatr Anaesth.* 2014;**24**(11):1158-63. doi: [10.1111/pan.12478](https://doi.org/10.1111/pan.12478). [PubMed: [25040840](https://pubmed.ncbi.nlm.nih.gov/25040840/)].