Original Article

Peri-anal infiltration versus caudal block for multimodal analgesia in paediatric patients with Hirschsprung's disease undergoing transanal endorectal pull-through procedure: A randomised trial

Address for correspondence:
Dr. Fatma Nabil, Department of Anesthesia, Intensive Care, and Pain Management, Assiut University Hospitals, Assiut, 71515, Egypt.
E-mail: fatmanabil2012@aun.edu.eg

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Fatma Nabil, Mohamed S. Rashed, Mohammed H Takrouney[1], Ibrahim A Ibrahim[1], Esam Abdalla, Hany M Osman

Department of Anesthesia, Intensive Care, and Pain Management, Faculty of Medicine, Assiut University, Assiut, [1]Department of General Surgery, Pediatric Surgery Unit, Faculty of Medicine, Assiut University, Assiut, Egypt

ABSTRACT

Background and Aims: Transanal endorectal pull-through (TERPT) is a standard procedure for managing paediatric patients with Hirschsprung's disease (HD). This study aimed to evaluate peri-anal infiltration versus caudal block as a part of multimodal analgesia for paediatric patients with HD undergoing the TERPT procedure. **Methods:** This randomised trial included 60 patients of both genders, aged 6 to 18 months who underwent the TERPT procedure under general anaesthesia. The patients were randomly assigned into two groups to receive either peri-anal infiltration or caudal block with 1 ml/kg bupivacaine 0.25% and dexmedetomidine 1 μg/kg in 0.5 ml normal saline. The primary outcome was the time to the first rescue analgesia. The secondary outcomes were the total consumption, the frequency of nalbuphine administration as rescue analgesia within 24 hours and the level of postoperative sedation. **Results:** The time to first rescue analgesia was significantly shorter in the peri-anal infiltration group versus the caudal block group (median [interquartile range] 10 [7.5–12.5] h versus 16 [13.5–18.5] h, respectively, $P = 0.008$).The frequency of administration and the total dose of nalbuphine was significantly higher in the peri-anal infiltration group ($P = 0.003$ and 0.013, respectively).The sedation score was significantly higher in the caudal block group postoperatively. **Conclusion:** For paediatric patients undergoing the TERPT procedure, peri-anal infiltration was less effective than caudal block in terms of the duration of postoperative analgesia. However, both techniques were comparable during the first 6 hours postoperatively.

Keywords: Analgesia, caudal block, dexmedetomidine, epidural analgesia, Hirschsprung's disease, paediatric, peri-anal infiltration

INTRODUCTION

Hirschsprung's disease (HD) is a congenital anomaly with a worldwide incidence of 1:5000 to 1:10000.[1] Transanal endorectal pull-through (TERPT) is currently a standard procedure for managing HD in neonates and infants aiming to excise the aganglionic non-functioning bowel via the anus.[2] This procedure includes anal retraction and dilatation to expose the distal rectal mucosa for dissection and to pull the colon out through the narrow anal canal.[3] Hence,

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a deep level of anaesthesia is classically required to provide adequate anal relaxation and postoperative analgesia, achieved by combining regional and general anaesthesia.[4]

Caudal block is the most common technique to be combined with general anaesthesia in paediatric patients undergoing sub-umbilical surgeries. However, despite its effectiveness, it has some contraindications, such as local site infection or spinal anomalies.[5] In these conditions, peripheral blocks seem to be good alternatives. Peri-anal anaesthesia has been previously described with different techniques in adults undergoing anal or anorectal surgeries.[6,7]

This study was conducted to test the hypothesis that peri-anal infiltration could be as effective as a caudal block as a part of multimodal analgesia for managing postoperative pain in paediatric patients with HD undergoing the TERPT procedures. The primary objective was the time to first rescue analgesia postoperatively. The secondary objectives included the total consumption and frequency of rescue analgesia, the response of heart rate to skin incision and the level of postoperative sedation.

METHODS

This randomised clinical trial was conducted from August 2021 to July 2022 after obtaining approval from the institutional review board (vide approval number 17101069). The techniques used in the study were explained to the patient's legal guardians before obtaining written informed consent from them to use the patient data for research and educational purposes. This trial followed the ethical principles of the Declaration of Helsinki 1964 (Revised 2013) and was registered at clinicaltrials.gov (vide registration number NCT04367818, dated 29 April 2020).

This study included 60 patients, aged 6 to 18 months of both genders, with American Society of Anesthesiologists (ASA) physical statuses I and II, who had HD and were scheduled for a TERPT procedure. Exclusion criteria were parent refusal, coagulopathy, local infection at the injection site, known allergy to the study drugs, skeletal deformities, neuromuscular disorders or associated cardiac anomalies.

Using computer-generated random numbers, the recruited patients were allocated to the peri-anal infiltration group (n = 30) or the caudal block group (n = 30). The allocation numbers were kept in sequentially numbered opaque sealed envelopes opened on the morning of the surgery by a nurse who would no longer participate in the study. The nurses responsible for assessing postoperative pain and sedation, both in the post-anaesthesia care unit (PACU) and surgical intermediate care unit, were blinded to the group allocation. However, the main anaesthesiologist responsible for monitoring the patients and recording the intraoperative haemodynamics was not blinded to the group allocation.

No sedation was given preoperatively. However, each patient was accompanied by one of their parents or a guardian to the operative theatre. Upon arrival at the operative theatre, pulse oximetry (SpO_2), non-invasive blood pressure (NIBP) and electrocardiogram (ECG) were connected to monitor the patient. Inhalational induction was achieved with sevoflurane in oxygen. Intravenous (IV) propofol (1 mg/kg), fentanyl (1 μg/kg) and cis-atracurium (0.15 mg/kg) were then given to facilitate endotracheal intubation and mechanical ventilation. Anaesthesia was maintained with sevoflurane in a minimum alveolar concentration (MAC) of 1–2% in the oxygen–air mixture (1:1) with incremental doses of IV cis-atracurium (0.03 mg/kg) as needed.

In the peri-anal infiltration group, the patient was placed in lithotomy position with a small sandbag underneath the buttocks to optimise the view of the peri-anal region. Under complete aseptic conditions and after applying a self-retaining Lone Star retractor, the dentate line was identified. A prepared anaesthetic mixture (1 ml/kg bupivacaine 0.25% and dexmedetomidine 1 μg/kg in 0.5 ml normal saline) was injected by the surgeon just above the dentate line at four points (3, 6, 9 and 12 o'clock) with angles of injection between 30 and 45 degrees. During injection, the volume of the anaesthetic mixture was equally distributed between the four points and the needle was tilted to the right and left to ensure circumferential spread of the anaesthetic mixture.

In the caudal block group, the patient was turned to the lateral decubitus position with flexion of the hips and knees. Under, complete aseptic conditions, the caudal epidural block was performed using a 22-gauge needle with a single shot of the same anaesthetic mixture.

The surgical incision was allowed after at least 10 minutes from the caudal block or the peri-anal

infiltration. By the end of the surgery, IV paracetamol (15 mg/kg) was given to the patients in both groups, and the neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and atropine (20 μg/kg). After extubation, the patients were transferred to the PACU.

The PACU patients were routinely monitored for consciousness level, haemodynamics, respiratory rate, oxygen saturation and temperature. The Face, Legs, Activity, Cry and Consolability (FLACC) behavioural scale was used to assess pain.[8] The University of Michigan Sedation Scale (UMSS) was used to determine sedation in the PACU.[9] The postoperative pain and sedation assessments were performed by trained nurses at 30 minutes and then at 2 hours of admission using the FLACC scale and the UMSS, respectively. The patients were then transferred to the paediatric surgical intermediate care unit, where the postoperative pain was repeatedly assessed every 2 hours till 24 hours from arrival to the PACU. IV paracetamol (15 mg/kg) was given regularly every 6 hours on the first postoperative day. In comparison, IV nalbuphine (0.1 mg/kg) was given as rescue analgesia if the FLACC score was ≥4 at any point.

The primary outcome was the time to the first rescue analgesia based on the FLACC score ≥4 starting from arrival to the PACU. The secondary outcomes were the total consumption and the frequency of administration of nalbuphine during the first 24 hours postoperatively, intraoperative heart rate in response to the skin incision, the level of sedation in the PACU and the incidence of side effects, such as repeated vomiting or severe bradycardia (<60 beats/min).

Based on a previous study[10] using G*Power 3 software, the sample size was calculated as a minimum of 24 participants in each group to detect an effect size of 0.9 in the time to first rescue analgesia, with an error of probability of 0.05 and a power of 85% on the two-tailed test. The sample was increased to 30 participants in each group to compensate for dropouts.

The data were analysed by Statistical Package for the Social Sciences (SPSS) version 23.0 (International Business Machines, Armonk, New York, USA). The variables were presented as numbers, median (interquartile range (IQR)) or mean (standard deviation (SD)). The categorical data were analysed using the Chi-square or Fisher's exact test as appropriate. The time to first rescue analgesia was presented as a Kaplan–Meier plot and analysed using the log-rank test. The Shapiro–Wilk test was used to test the normality of the continuous data. Accordingly, the Mann–Whitney U-test was used to compare the non-parametric data, while the Student's *t*-test was used to compare the normally distributed data. The Bonferroni correction was performed for multiple comparisons. A P value <0.05 was considered statistically significant.

RESULTS

Of the 87 patients with HD screened for the previously mentioned inclusion criteria, 60 were included in this trial and randomly allocated into two groups. Three patients were excluded from the final analysis due to the conversion from the TERPT procedure to laparotomy. Hence, the final analysis included 29 patients in the peri-anal infiltration group versus 28 patients in the caudal block group [Figure 1]. The demographic variables and the duration of surgery were comparable in both groups [Table 1].

In the PACU, only one patient in each group received nalbuphine as a rescue analgesia based on a FLACC score ≥4. The percentage of patients with the FLACC score <4 at 30 minutes of PACU arrival and during the first 6 hours postoperatively did not differ significantly between both groups. However, it was significantly lower in the peri-anal infiltration group versus the caudal block group during the first 12 and the first 24 postoperative hours (P = 0.018 and 0.041, respectively) [Table 2].

Heart rate measurements were comparable between both groups before and at 1 and 5 minutes after the skin incision. Moreover, the percentage of patients with ≥ 20% increase in heart rate after skin incision did not differ significantly between both groups [Table 2].

The Kaplan–Meier survival analysis showed that the time to first rescue analgesia was significantly shorter

Table 1: Demographic and surgical data

Parameters	Peri-anal infiltration group (*n*=29)	Caudal block group (*n*=28)
Age (months)	9.0 (6.5–12.0)	8.0 (7.0–11.8)
Gender (male/female)	20/9	21/7
Weight (kg)	8.0 (7.0–8.5)	8.5 (7.5–9.0)
Height (cm)	71.5 (5.6)	70.6 (5.7)
Duration of surgery (min)	80 (70–90)	87.5 (70–90)

Values are presented as median (interquartile range), mean (standard deviation) or number. n: Number

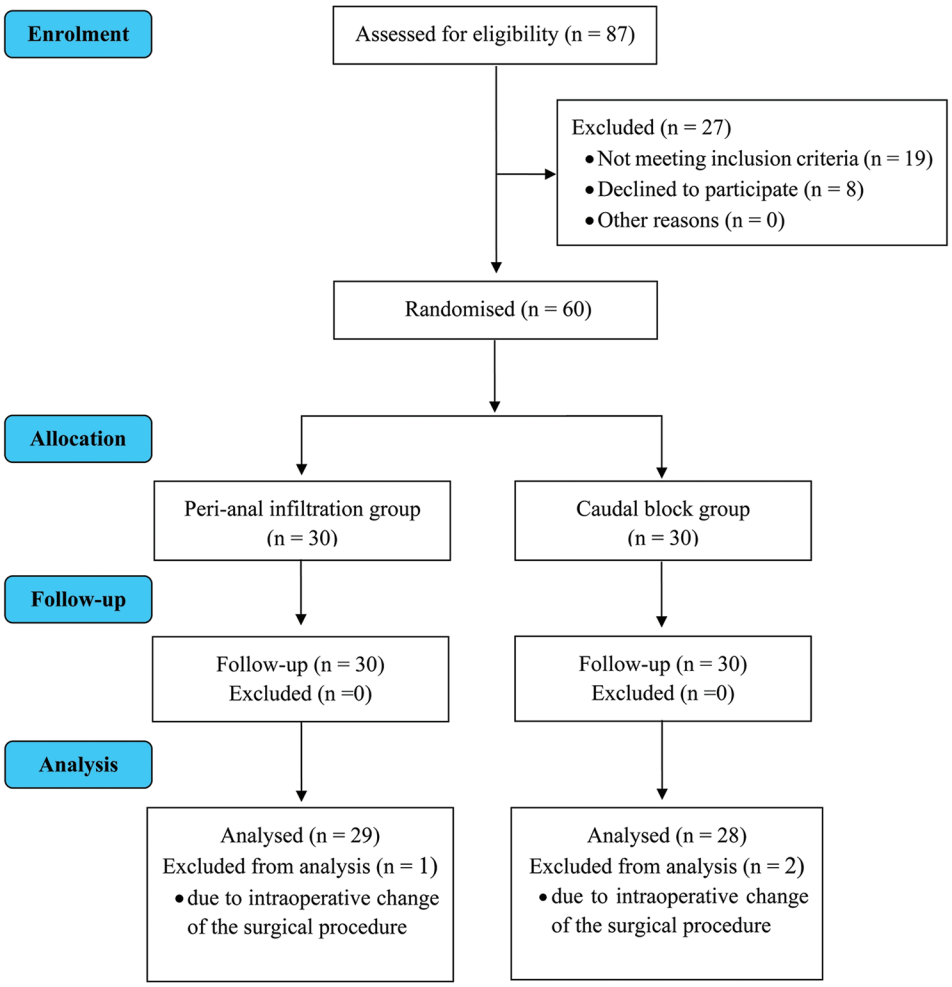

Figure 1: Consolidated standards of reporting trials (CONSORT) flow diagram of the participants. n: Number of patients

Table 2: Intraoperative heart rate and postoperative pain and sedation

Parameters	Peri-anal infiltration group (*n*=29)	Caudal block group (*n*=28)	*P*
Heart rate (beats/min)			
Before skin incision	104.0 (100.0–114.5)	105.0 (98.3–122.0)	0.670
1 minute after skin incision	110.0 (105.5–122.5)	122.5 (106.3–131.5)	0.075
5 minutes after skin incision	105.0 (104.0–117.8)	112.0 (99.0–122.0)	0.538
Patients with ≥20% increase in heart rate after skin incision	2	4	0.423
FLACC scale score <4 without any rescue analgesia			
At 30 minutes of PACU arrival	28	28	1.000
During the first 6 postoperative hours	25	26	0.670
During the first 12 postoperative hours	14	22	0.018
During the first 24 postoperative hours	2	8	0.041
Rescue analgesia during the first 24 hours			
Frequency of rescue analgesia	2 (2–3)	1.5 (0–2)	0.003
Total dose of nalbuphine (mg)	1.7 (1.3–2.8)	1.1 (0–1.8)	0.013
UMSS score			
At 30 minutes of PACU arrival	0.0 (0.0–1.0)	1.0 (0.0–2.0)	0.030
At 2 hours of PACU arrival	0.0 (0.0–0.0)	0.5 (0.0–1.0)	0.004

Values are presented as median (interquartile range) or number. FLACC=Face, Legs, Activity, Cry and Consolability; UMSS=University of Michigan Sedation Scale; PACU=post-anaesthesia care unit, n: Number of patients

in the peri-anal infiltration group versus the caudal block group (10 [7.5–12.5] hours versus 16 [13.5–18.5] hours, respectively, $P = 0.008$, log-rank test) [Figure 2]. Subsequently, the frequency of rescue analgesia and the

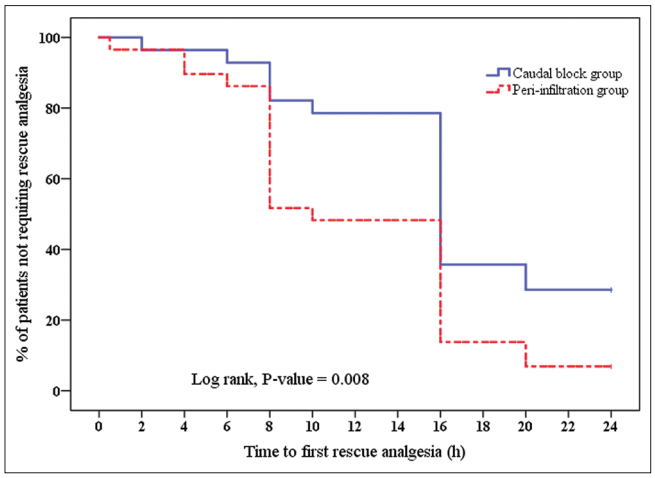

Figure 2: Kaplan-Meier survival plot illustrating the time to first rescue analgesia in both groups

total dose of nalbuphine given as rescue analgesia during the first 24 postoperative hours were significantly higher in the peri-anal infiltration group versus the caudal block group (P = 0.003 and 0.013, respectively) [Table 2].

Regarding sedation in the PACU, the UMSS scores were significantly higher in the caudal block group versus the peri-anal infiltration group at 30 minutes and 2 hours of arrival to the PACU (P = 0.030 and 0.004, respectively) [Table 2]. Furthermore, there were no reported incidents of repeated vomiting, severe bradycardia or respiratory depression.

DISCUSSION

This trial demonstrated that peri-anal infiltration was less effective than caudal block regarding the time to first rescue analgesia and the frequency and the total dose of rescue analgesia during the first 24 hours postoperatively. Nevertheless, peri-anal infiltration was comparable to caudal block during the first 6 postoperative hours. Furthermore, intraoperatively, the heart rate response to the skin incision did not differ between groups.

In agreement with these results, in a previous meta-analysis, the caudal block has been reported to be superior to non-caudal regional blocks or local anaesthetic infiltration for postoperative analgesia in children undergoing inguinal surgeries.[11] However, other studies reported that some peripheral blocks were superior to caudal blocks in other surgeries.[12-15] Regarding pull-through surgery in patients with HD, a previous study reported better postoperative analgesia and more stable intraoperative haemodynamics in the patients who underwent the surgery under combined general–caudal anaesthesia compared with those who underwent the surgery under only general anaesthesia.[16]

Unlike caudal block, peri-anal anaesthesia is less common in paediatric patients and is mainly used for short procedures such as drainage of peri-anal abscesses.[17] However, there is a recently observed transition from central to peripheral blocks because they have a lower incidence of complications.[18]

In this study, dexmedetomidine was added, in the same dose, as an adjuvant to bupivacaine in both groups. Adding dexmedetomidine, a selective α2-adrenergic agonist, to the caudally administered local anaesthetic has been reported to increase the duration of postoperative analgesia.[19-22] Similarly, adding dexmedetomidine to the locally infiltrated local anaesthetic effectively relieved pain for adult and paediatric patients.[23,24] The main concern concerning dexmedetomidine is the associated bradycardia reported in previous studies on adult and paediatric patients.[25,26] In the current study, no significant bradycardia was observed intraoperatively or postoperatively. This is consistent with the results of other previous studies on paediatric patients in which dexmedetomidine was added to bupivacaine during caudal block or local infiltration.[21,23,27]

Another finding in the current study was the higher sedation score in the caudal block group at 30 minutes and 2 hours of arrival to the PACU. This is similar to previous studies in which dexmedetomidine was added to the caudally administered local anaesthetic.[25,28] This sedative effect is primarily due to the action of dexmedetomidine on the central α2-adrenergic receptors in the locus coeruleus.[28]

This study has limitations. First, the primary surgeon was not blinded to the technique, which rendered the assessment of surgeon satisfaction with the relaxation of the anal sphincter unfeasible. Second, the anaesthesiologist responsible for recording the heart rate before and after the skin incision was not blinded to the intervention.

CONCLUSION

For paediatric patients undergoing the TERPT procedure, peri-anal infiltration was less effective than caudal block in terms of the duration of postoperative analgesia. However, both techniques were comparable during the first 6 hours postoperatively.

Study data availability

De-identified data may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared after approval as per the authors' institution policy.

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Conflicts of interest

There are no conflicts of interest.

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