Original Article

Comparison of the effectiveness of intravenous fentanyl versus caudal epidural in neonates undergoing tracheoesophageal fistula surgeries

ABSTRACT

Background: Caudal epidural has become an inseparable part of pediatric pain relief as it depresses the stress response better than any other form of analgesia, resulting in the reduction in the need for systemic opioids; in addition, it facilitates early recovery and promotes good postoperative respiratory functions.

Aim: To evaluate the effectiveness of epidural analgesia in neonates undergoing tracheoesophageal fistula repair in terms of requirement of perioperative fentanyl opioid, postoperative neonatal infant pain score (NIPS), on-table extubation, duration of intubation, reintubation, perioperative hemodynamic response, and any other side effects.

Materials and Methods: A comparative, prospective, single-blind, randomized trial on 30 neonates scheduled for tracheoesophageal surgeries were randomly allocated to two groups: group I: neonates receiving caudal epidural block with ropivacaine 0.2%, 1 mg/kg bolus followed by infusion 0.1 mg/kg/h; group II: neonates receiving initial intravenous [IV] fentanyl 1 ug/kg and maintenance with 0.5 μg/kg/h IV bolus.

Results: None of the neonates received opioids in group I. There were statistically significant differences in the mean NIPS at 30, 60, 90, 120 150, and 240-min intervals between group I and group II. Further, 80% of neonates were extubated in group 1 compared to 50% in group II, which was statistically significant ($P = 0.025$). The duration of intubation was more in group II compared to group I, with a suggestive significance of $P = 0.093$.

Conclusion: Caudal epidural infusion provides adequate perioperative analgesia, promotes rapid weaning from the ventilator, and contributes to a successful outcome.

Key words: Analgesia, caudal catheter, neonates

Introduction

Tracheoesophageal fistula occurs in about 1:3000 to 4500 births and continues to be a major challenge for the anesthesiologist. With surgical repair, the rate of survival exceeds 90% even in low-birth-weight infants.[1] Significant mortality is now limited to infants with severe coexisting congenital or chromosomal abnormalities.[1-3] As many complex factors are involved, anesthetic management for

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surgical repair of TEF is based on individual experience and confidence in handling the case. Regional analgesia for thoracotomy in neonates has many advantages: it reduces the need for systemic opioids, facilitates early recovery, and promotes good postoperative respiratory functions.[4] The caudal catheter can be advanced to T6–T7 to supplement the general anesthesia and provide excellent postoperative analgesia without the use of opioids and facilitates extubation.[5,6] Pain protocol included in our hospital is intravenous fentanyl, which has got its disadvantages such as respiratory depression, delay in extubation, prolonged hospital stay, nausea, vomiting, and pruritus. This study aims to evaluate the effectiveness of caudal epidural block intraoperatively and postoperatively for tracheoesophageal fistula repair in neonates in terms of perioperative requirement of fentanyl, postoperative neonatal infant pain score (NIPS),[7] on-table extubation, duration of intubation, reintubation, perioperative hemodynamic response, and any other side effects.

Methodology

Institutional ethics clearance was taken; CTRI number: CTRI/2020/03/023882.

This study design was a prospective, single-blind, randomized trial started on 30 neonates undergoing tracheoesophageal surgery from November 2019 to September 2020.

Spitz classification system [Table 1] was used to predict perioperative risk, which is based on the finding that cardiac disease is the most important risk factor for mortality. In group 1, Spitz was included to reduce the selection bias. Neonates (preterm and term) weighing more than 1.5 kg, not on ventilator support, and hemodynamically stable were included in the study. Parental refusal, neonates less than 1.5-kg weight, those on ventilator support before surgery, coagulation abnormalities, and cyanotic heart disease were excluded from the study. The primary objective was to observe the requirement of opioids intraoperative and postoperative. The secondary objective was to observe the time for on-table extubation, neonatal infant pain score (NIPS), hemodynamic parameters, duration of intubation, and reintubation.

After taking informed consent from parents, neonates were shifted to the operation theater and baseline vitals were noted. Preoperatively, adequate hydration was achieved with normal saline 10 mL/kg bolus and then maintenance with Ringer's lactate solution 4 mL/kg/h. Hypothermia was prevented by wrapping the baby with cotton rolls, and the pooling of secretions in the pouch was drained using a catheter on low suction in the pouch. The airway was secured by intubating with 2.5–3-mm ID uncuffed endotracheal tubes after induction with sevoflurane in 100% O_2, supplemented by fentanyl 1 ug/kg, thiopentone 5 mg/kg, and atracurium 0.5 mg/kg. The endotracheal tube was fixed so that the tip lay below the tip of the fistula but above the carina and confirmed by bilateral equal breath sounds. Induction neonates were randomly allocated into two groups by computer randomization: Group I: patients received caudal epidural block with injected ropivacaine 0.2% 1 mg/kg bolus and maintenance infusion 0.1 mg/kg/h for 48 h; Group II: patients received intravenous fentanyl 1 μg/kg initially and maintained with 0.5 μg/kg/h by IV bolus.

Patients in group I were placed in the lateral position. Under aseptic precautions, a 19-G epidural catheter set with a Tuohy 50-mm cannula, and a 24 G catheter (Smiths Medical India Pvt. Ltd.) was placed in the caudal space by loss of resistance using the saline technique and advanced 11–14 cm to reach T4 level, which was estimated by measuring the distance on the skin from the caudal hiatus to the target level for the catheter tip (epidural catheter was easily advanced to a premeasured distance from the caudal space to the mid-thoracic area). Then, the catheter was fixed over the back by employing micropore plasters without tunneling. The caudal space was confirmed by negative aspiration for blood and cerebrospinal fluid and the meniscus test. Anesthesia was maintained with sevoflurane 1.5%–2% to keep an adequate depth of anesthesia. Paracetamol suppository 40 mg/kg was inserted for all patients at the end of surgery. After emergence from general anesthesia, all neonates were assessed for adequacy of ventilation and NIPS by another anesthetist (observer), who was blinded to the procedure and hemodynamic parameters by nursing staff in neonatal intensive care (NICU). Postoperatively, all neonates were on paracetamol 15 mg/kg every 8th hourly and IV fentanyl 0.5 μg/kg bolus was the rescue analgesia in the postoperative period when the NIPS score was ≥3, for 48 h, in both groups. In group II, ropivacaine infusion was started at 0.1 mg/kg/h for 48 h in group I by using a 20-mL syringe pump. The epidural catheter was removed after 48 h. Demographic data and hemodynamic parameters such as heart rate (HR) and mean blood pressure (MBP) were recorded before the block and starting IV fentanyl, which was considered as the baseline and at regular intervals of 10, 30, 60, 90,120, 240, 480, 720, 1440, and 2880 min intraoperatively and postoperatively. In the postoperative period, opioid requirement, NIPS, on-table extubation, duration of intubation, reintubation, and complications were documented. A pilot study following the identical study design was performed to assess feasibility, safety, recruitment, consent rate, and sample size. Based on

a pilot study and outcome variables in the previous study on mean analgesia and hemodynamic parameters[4] with a difference of 0.3% and standard deviation of 0.34%, 90% statistical power, and 5% statistical significance, the sample size of 30 [15 in each group] was considered adequate. Statistical methods include the Chi-Square test, Fisher's exact test, and Students's *t* test.

Results

The demographic profiles including age, weight, gender, ASA grade, and duration of surgery in the two groups were comparable. Most neonates were 2 days old at the time of surgery and in that 22 were term and 8 were preterm[Table 2]. The average weight was 2.46 ± 0.32 kg (mean ± SD) [Table 3]. There were 14 male and 16 female neonates. Five required supplemental oxygen. None of them had major cardiac disease [Table 4], which was ruled out by 2D ECHO. All neonates had a proximal esophageal pouch and a distal TEF. Preoperatively, the mean body weight in group I was 2.46 ± 0.38 kg, whereas it was 2.46 ± 0.27 kg in group II. Sixteen neonates were enrolled in group I; 15 epidural catheters were placed in 16 neonates via the caudal route. One was excluded from the study due to persistent hemodynamic instability. There was no hypotension due to sympathetic blockade or complications associated with the threading of the catheter. In two cases, blood was aspirated from the catheter on initial insertion; however, this cleared following 0.5-cm withdrawal of the catheter and flushing with 0.9% saline. There was only one case of fecal soiling of the catheter, which occurred at catheter removal, without leading to any further complications.

The mean concentration of sevoflurane was 1.7 ± 0.34% in group I and 1.9 ± 0.8% in group II. There were no statistically significant differences in the mean sevoflurane concentration in both groups. None of the neonates who received caudal epidural analgesia intraoperatively required IV fentanyl in group I compared to group II. The mean and standard deviation of intraoperative fentanyl use in group II was 3.733 ± 1.41 μg.

There was statistically significant lower NIPS in group I with mean and standard deviation at immediate postoperative (IMPO) as 0.53 ± 0.92 ($P = 0.001$), 30 min: 0.73 ± 0.96 ($P = 0.001$), 60 min: 0.87 ± 1.13 ($P = 0.001$), 120 min: 0.60 ± 0.63 ($P = 0.001$), 240 min: 0.27 ± 0.46 ($P = 0.001$), 480 min: 0.93 ± 0.80 ($P = 0.001$), 720 min: 0.87 ± 0.99 ($P = 0.004$), 1440 min: 1.00 ± 0.65 ($P = 0.001$), and 1880 min: 0.80 ± 0.77 ($P = 0.0025$) in group I when compared to group II [Table 5, Figure 1].

Table 1: Spitz classification

Spitz Classification	Birth Weight (in kg)	Major Cardiac Disease	Survival
Group I	>1.5	None	97%
Group II	<1.5	Yes*	59%
Group III	<1.5	Yes	22%

*Group II includes neonates weighing less than 1.5 kg OR those having major cardiac disease

Table 2: Age distribution of patients

Age (in days)	Group I *N*	Group II *N*	Total *N*
1	3 (20%)	5 (33.3%)	8 (26.7%)
2	9 (60%)	5 (33.3%)	14 (46.7%)
3	1 (6.7%)	1 (6.7%)	2 (6.7%)
4	1 (6.7%)	3 (20%)	4 (13.3%)
5	1 (6.7%)	1 (6.7%)	2 (6.7%)
Total	15 (100%)	15 (100%)	30 (100%)

P=0.654, Not Significant, Fisher's exact test *N*=Number

Table 3: Weight (kg) distribution in the two groups of patients

Weight (kg)	Group I *N*	Group II *N*	Total *N*
2-2.5	7 (46.7%)	10 (66.7%)	17 (56.7%)
2.5-3	8 (53.3%)	5 (33.3%)	13 (43.3%)
Total	15 (100%)	15 (100%)	30 (100%)
Mean±SD	2.46±0.38	2.46±0.27	2.46±0.32

P=0.991, Not Significant, Student *t* test *N*=Number

Table 4: Preoperative variables

Variables	Values
Age	2.46±0.32
Sex	
Male	14
Female	16
Length of gestation	37.7±2.6
Requiring oxygen	5
SpO_2 >95%	25
>80% to <90%	5
Minor cardiac disease	
PDA	12
VSD	3
ASD	1
Types of fistula	
Type C	30
Other congenital anomalies	4
Pressor support	0

Nine infants were extubated on the table in group I compared to three infants in group II, which was statistically significant ($P = 0.025$) [Figure 2].

The intraoperative hemodynamic parameters (heart rate and mean blood pressure) were compared with the baseline parameters in two groups. The mean heart rate as beats per minute [bpm] in group I, where caudal block was given, was 142.33 ± 9.48 bpm at baseline, 142.33 ± 9.48 bpm at 10 min,

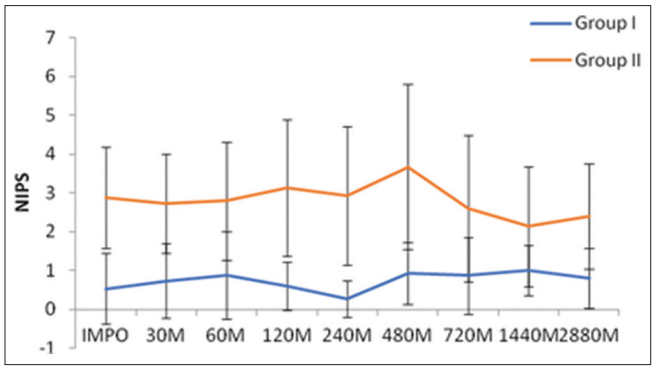

Figure 1: NIPS- Comparison in the two groups of patients

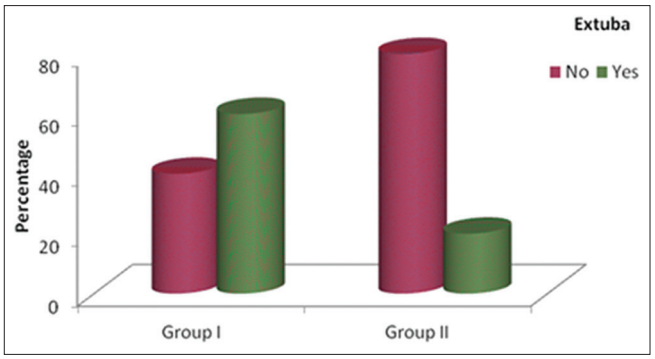

Figure 2: Extubation- Distribution in the two groups of patients

140.00 ± 12.21 bpm at 30 min, 135.53 ± 12.74 bpm at 60 min, 133.73 ± 10.93 bpm at 90 min, and 131.60 ± 11.06 bpm at 120 min compared to group II, wherein it was 138.07 ± 8.17 bpm at baseline, 138.07 ± 8.17 bpm at 10 min, 139.87 ± 11.10 bpm at 30 min, 142.53 ± 12.01 bpm at 60 min, 142.07 ± 12.30 bpm at 90 min, and 141.6 ± 12.99 bpm at 120 min. There was a constant decrease in the intraoperative heart rate compared to neonates in group II and statistically significant at 120 min ($P = 0.031$) [Table 6].

The mean blood pressure in group I was 58.20 ± 9.62 mm Hg at baseline, 56.60 ± 9.85 mm Hg at 10 min, 54.13 ± 7.61 mm Hg at 30 min, 51.80 ± 6.04 mm Hg at 60 min, 51.40 ± 5.15 mm Hg at 90 min, and 50.73 ± 4.74 mm Hg at 120 min compared to group II, wherein it was 61.20 ± 9.67 mm Hg at baseline, 61.33 ± 10.44 mm Hg at 10 min, 60.73 ± 9.14 mm Hg at 30 min, 59.20 ± 9.64 mm Hg at 60 min, 58.20 ± 9.84 mm Hg at 90 min, and 56.60 ± 9.05 mm Hg at 120 min. The intraoperative mean blood pressure in group I was statistically significant at 30 min ($P = 0.040$), 60 min ($P = 0.018$), 90 min ($P = 0.025$), and 120 min ($P = 0.034$) [Table 7].

Postoperatively, none of the patients received fentanyl in group I compared to group II. The mean and standard deviation of fentanyl use in group II postoperatively was 1.46 ± 1.06 μg over 48 h. The mean heart rate as beats per minute was statistically significant during IMPO ($P = 0.002$), 30 min ($P = 0.001$), 60 min ($P = 0.016$), and 240 min ($P = 0.044$) in group I compared to group II [Table 6]. No significant difference was noted in the mean blood pressure between the two groups postoperatively [Table 7].

In terms of the duration of intubation (DOI) in group I, two neonates were extubated on the first day, two neonates extubated on the second day, one neonate each on the fourth and fifth day, and one neonate on the eighth day. In contrast, in group II, two neonates were extubated on the first day, two neonates on the second day, two neonates on the fifth day, three neonates on the sixth day, and one neonate each on the seventh, tenth, and fifteenth day [Table 8]. The DOI was more in group II compared to group I, with a suggestive significance of $P = 0.093+$ [Figure 3]. Two neonates returned to the OT for an anastomotic leak in group II. One neonate each from group I and group II were reintubated in NICU after on-table extubation. There were no cases of catheter-related infection such as hypersensitivity, local inflammation, or

Table 5: Neonatal Infant Pain Score- Comparison in two groups of patients postoperatively

Postoperative period (in min)	Group I NIPS	Group II NIPS	*P*
Baseline	0.53±0.92	2.87±1.30	<0.001
30	0.73±0.96	2.73±1.28	<0.001
60	0.87±1.13	2.80±1.52	<0.001
120	0.60±0.63	3.13±1.77	<0.001
240	0.27±0.46	2.93±1.79	<0.001
480	0.93±0.80	3.67±2.13	<0.001
720	0.87±0.99	2.60±1.88	0.004
1440	1.00±0.65	2.13±1.55	0.015
2880	0.80±0.77	2.40±1.35	<0.001

Table 6: Heart rate (bpm) - Comparison in two groups of patients

Time (in min)	Group I HR	Group II HR	*P*
BL/10	142.33±9.48	138.07±8.17	0.198
30	140.00±12.21	139.87±11.10	0.975
60	135.53±12.74	142.53±12.01	0.133
90	133.73±10.93	142.07±12.30	0.060+
120	131.60±11.06	141.6±12.99	0.031*
IMPO	131.93±10.52	144.93±10.4	0.002**
30	129.27±9.07	142.47±10.96	0.001**
60	130.13±9.22	139.93±11.68	0.016*
120	130.60±8.51	136.73±9.41	0.072+
240	128.47±10.79	135.93±8.49	0.044*
480	129.07±10.58	133.53±10.49	0.255
720	128.93±9.11	135.20±11.34	0.106
1440	129.67±11.34	134.47±10.04	0.230
2880	130.13±11.89	134.47±10.21	0.293

HR=heart rate, Bpm=beats per minute, BL=baseline, and IMPO=immediate postoperative. +Yes suggestive significant, *Yes significant, **Yes significant

Table 7: Mean arterial pressure (in mm Hg) - Comparison in two groups of patients

Time (in min)	Group I MAP	Group II MAP	*P*
BL	58.20±9.62	61.20±9.67	0.402
10	56.60±9.85	61.33±10.44	0.212
30	54.13±7.61	60.73±9.14	0.040*
60	51.80±6.04	59.20±9.64	0.018*
90	51.40±5.15	58.20±9.84	0.025*
120	50.73±4.74	56.60±9.05	0.034*
IMPO	59.20±9.87	61.13±10.58	0.609
30	56.00±9.55	58.67±7.95	0.413
60	57.33±9.18	57.13±9.13	0.953
120	56.20±7.12	56.27±8.36	0.981
240	54.47±6.77	56.40±8.52	0.497
480	55.00±7.25	55.73±6.34	0.770
720	56.33±8.66	54.27±6.78	0.473
1440	56.93±7.76	56.27±7.37	0.811
2880	58.20±9.62	61.20±9.67	0.325

Mm Hg=millimeter of mercury, BL=baseline, IMPO=immediate postoperative.
*Yes significant

Table 8: Duration of intubation- distribution in two groups of patients

DOI in days	Group I	Group II	Total Number
	Number	Number	
0	8 (53.3%)	3 (20%)	11 (36.7%)
1-5	6 (40%)	6 (40%)	12 (40%)
6-10	1 (6.7%)	5 (33.3%)	6 (20%)
>10	0 (0%)	1 (6.7%)	1 (3.3%)
Total	15 (100%)	15 (100%)	30 (100%)

P=0.093+, Significant, Fisher's exact test

urinary retention in any neonate. No episode of vomiting, hypotension, and skin rashes was noted in group I, whereas three neonates had vomited in group II.

Discussion

Caudal extradural catheterization is a technique that is being increasingly used among pediatric anesthetists[8] and can be easily mastered with a low major complication rate.[9,10] Thoracic surgery may result in more pain than abdominal surgery. The placement of catheters up to thoracic levels via the caudal route is feasible and safe; this has allowed many children to receive analgesia with a decreased risk of spinal cord injury or dural puncture.[11] Advantages of this technique include reduced requirements for opioids and volatile agents, dense intraoperative analgesia, and analgesia continuing into the postoperative period. It also helps avoid the need for direct needle placement at lumbar and thoracic levels as this may reduce the risk of traumatic damage to the spinal cord, especially in infants who have a relatively narrow depth to the extradural space and in whom the spinal cord may extend as low as L3[12] and also contains less fat and fibrous tissue.[13]

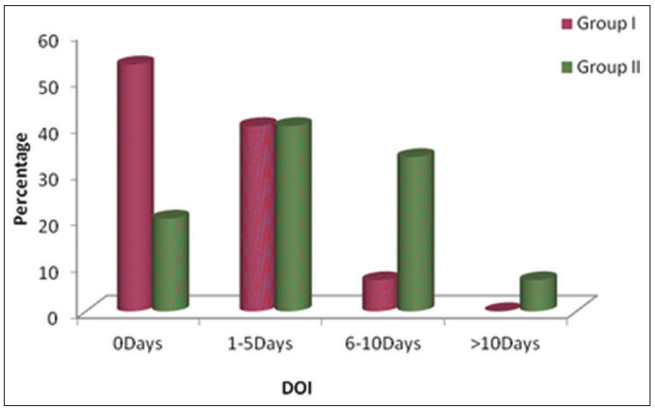

Figure 3: Duration of intubation (DOI) distribution in the two groups of patients

In our study, an epidural catheter was placed successfully in 15 neonates via the caudal route confirmed by the meniscus test. Bösenberg *et al*.,[14] using an unstyled 20-G catheter through an 18 gauge cannula, had a success rate of 95% in infants <6 months of age. Rasch *et al*.[15] reported a 96% success rate in infants <2 years of age. The result of the present study demonstrated nil use of opioids intraoperative and postoperatively in group I with good postoperative analgesia after thoracotomy, which was demonstrated by the neonatal infant pain score (NIPS) of <3 points up to 2440 min (2 days) postoperatively in the epidural group compared to the intravenous group. This study detected a longer duration of analgesia in the caudal epidural group than in the intravenous group. Diaz *et al*.[2] report 15 extubation of 38 neonates not intubated preoperatively, whereas in our study, nine were extubated in group I compared to three in group II, which is statistically significant ($P = 0.025^{*}$).

Compared with intravenous techniques, epidural analgesia is associated with less use of opioids; lower pain scores; reduced need for postoperative ventilator support;[14] and reduced incidence of postoperative anastomosis leak, nausea, and vomiting.[16-19] Warschkow[20] and Rigg[21] in the MASTER trial demonstrated a decrease in respiratory complications in pediatric epidural analgesia, which was also found in our study. Finally, this study has shown that epidural analgesia can be provided for neonates undergoing major surgery with a low risk of complications. Further advantages include the reduced need for both muscle relaxants, opioid analgesics, and postoperative ventilator support.

The limitation of this study was that no method was used to confirm the level of placement of the tip of the catheter.[22] The future of the study is ultrasound-guided placement and confirmation of epidural catheter tip.

Conclusion

Caudal epidural catheterization is a safe and effective technique for achieving intraoperative and postoperative pain control and improved recovery profile in neonates undergoing tracheoesophageal fistula repair.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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