Original Article

Evaluation of Analgesic Efficacy of Caudal Bupivacaine with Clonidine versus Bupivacaine Alone in Pediatric Laparoscopic Surgery

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Abstract

Background: Caudal local anesthetics with and without additives are increasingly being used for pain management in children. The primary objective of the present study was to compare intraoperative fentanyl consumption in pediatric patients undergoing laparoscopic surgeries under general anesthesia with supplemental caudal analgesia with and without addition of clonidine. The secondary outcomes were comparison of intraoperative and postoperative hemodynamic changes, postoperative pain, and postoperative analgesic requirements. **Materials and Methods:** In this prospective randomized trial, 32 children aged 6 months to 6 years were recruited. Group B received 2 mg/kg bupivacaine in 1.25 ml/kg, while Group BC received 2 mg/kg bupivacaine with 1 μg/kg clonidine in 1.25 ml/kg as caudal medication after induction of general anesthesia. Chi-square test, independent sample *t*-test, and Mann–Whitney U-test were used as applicable. **Results:** Intraoperative use of fentanyl and percentage of patients who required additional fentanyl intraoperatively and postoperatively were comparable in both groups. Intraoperative heart rate (HR), systolic blood pressure (SBP), and mean arterial pressure (MAP) were comparable in both groups most of the time. HR was significantly higher in Group B at 1 h intraoperatively with significantly higher SBP at 10 min after caudal. Postoperative HR and SBP were comparable in both groups. Group B had significantly higher MAP in the immediate postoperative period. Postoperative pain as assessed by FLACC (Face, Legs, Activity, Cry, Consolability) scale was comparable between groups with the exception of it being lesser in Group B at 8 h postoperatively. **Conclusion:** Clonidine 1 μg/kg added to caudal bupivacaine did not improve analgesia in comparison to bupivacaine alone in children undergoing laparoscopic surgery.

Keywords: Bupivacaine, caudal, clonidine, laparoscopy, pediatric

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Introduction

Caudal analgesia is the most commonly performed regional anesthetic in children as it is simple and provides significant analgesia, particularly in infraumbilical surgeries. Laparoscopic surgeries are progressively replacing open surgical procedures even in children.[1,2] The advantages are lesser pain and earlier postoperative recovery, but disadvantages are longer duration of surgery and anesthesia. Clonidine as an adjuvant to bupivacaine as caudal anesthetic produces superior quality of analgesia without adverse effects in children. However, its role in laparoscopic surgeries remains unclear.

Aims

The primary objective of the present study was to compare the intraoperative fentanyl consumption in pediatric patients undergoing laparoscopic surgeries under general anesthesia with supplemental caudal analgesia using bupivacaine with and without addition of clonidine. The secondary outcomes were comparison of intraoperative and postoperative hemodynamic changes, postoperative pain, and postoperative analgesic requirements in both groups.

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Materials and Methods

This was a prospective randomized double-blinded study conducted on elective pediatric surgical patients. Following approval from the local ethics committee, the trial was registered in the Clinical Trials Registry of India (CTRI/2016/05/006911).

After obtaining consent following explanation of the procedure to the parents, 32 children aged between 6 months and 6 years undergoing elective laparoscopic abdominal surgeries such as pyeloplasty, nephrectomy, ureteric reimplantation, appendicectomy, herniotomy, and orchidectomy were recruited for the study, over a period of 1 year.

Exclusion criteria included children with congenital heart diseases other than atrial septal defect, children with anatomical abnormalities of the sacral region, and children with American Society of Anesthesiologists physical status 3 and above. Children undergoing other surgical procedures in addition to laparoscopy were also excluded from the study.

Children were randomized to two groups by computer-generated random sequence of numbers to receive caudal bupivacaine only (Group B) or caudal bupivacaine with clonidine (Group BC). Allocation concealment was ensured using sequentially numbered opaque sealed envelopes.

All patients received standardized anesthesia care. Intravenous ketamine 1 mg/kg body weight with 0.05 μg/kg glycopyrrolate intravenously was given at the time of separation from parents as per institutional protocol. In the theater, after preinduction, monitors were instituted (pulse oximeter, electrocardiogram, and noninvasive blood pressure monitors), and fentanyl 2 μg/kg and midazolam 0.01 mg/kg were administered. Propofol was administered at 2 mg/kg, and intubation was performed following atracurium 0.5 mg/kg or suxamethonium 1.5 mg/kg. Choice of muscle relaxant depended on the preference between individual consultants.

Anesthesia was maintained with 1 minimum alveolar concentration (MAC) of isoflurane in air–oxygen mixture (1:1). The initial gas flows were 3.0 L/min until end-tidal 1 MAC of isoflurane was reached, then the flows were reduced to 1.0 L/min, and the dial concentration was adjusted to maintain 1 MAC end-tidal concentration. Neuromuscular relaxation was obtained with intermittent top ups of atracurium.

Caudal analgesia was performed after intubation. The primary investigator in charge of the study selected a random envelope and loaded the appropriate drug in one or two 10 ml syringes and placed them on the caudal tray prepared for administering caudal anesthesia. Group B received 2 mg/kg bupivacaine to a volume of 1.25 ml/kg in normal saline and Group BC received 1.0 μg/kg clonidine in addition to 2 mg/kg bupivacaine to a volume of 1.25 ml/kg in saline caudally at the start of surgery. The final concentration of bupivacaine in the reconstituted solution administered caudally was approximately 0.16%.

The heart rate (HR), systolic blood pressure (SBP), and mean arterial pressure (MAP) were recorded at baseline, after intubation, at the time of caudal, and 10 min after caudal administration. Then, HR and blood pressure were recorded at 30-min intervals during surgery. Any increase in HR (20% above baseline) without increase in blood pressure was treated with intravenous fluids at 5 ml/kg bolus and any increase in HR with rise in SBP was treated as pain. This was treated with intravenous fentanyl in increments of 0.5 μg/kg, administered to a maximum of 2 μg/kg/h. The total dose of fentanyl consumption during surgery was calculated.

All children received rectal paracetamol at a dose of 20 mg/kg at extubation and then at 10 mg/kg 6th hourly for the first 24 h in the postoperative period. At the end of surgery, after reversal of neuromuscular blockade, the patients were extubated, shifted to the postoperative intensive care unit (ICU), and managed as per standard protocols. An ICU nurse who was blinded to the intraoperative management performed the assessment of pain and scored it as per the FLACC (Face, Legs, Activity, Cry, Consolability) scale[3] from the time of arrival in the ICU, until the child was shifted from the ICU. Any patient with score >3 despite paracetamol treatment was considered to have pain and was treated with intravenous fentanyl at 0.5 μg/kg and repeated if required, not exceeding 1 μg/kg in 1 h. If children were comfortable postoperatively, no additional analgesic was given. Intervention was provided when they had pain as judged by the FLACC score.

The sample size calculation for our study was obtained from a pilot study conducted on twenty patients. Based on the total fentanyl consumption between the two groups, as 40.9 ± 11.0 μg versus 19.6 ± 3.2 μg in the B and BC groups, with 95% CI and 90% power, the sample size was calculated. With the ratio of sample size as 1, variance in each group as 121 and 110.24, respectively, and mean difference as 21.3, the sample size was calculated four per group (results from OpenEpi, Version 3, open source calculator – SSMean). However, we were able to include 16 patients in each group during our study period of 1 year.

The Chi-square test was used to compare the categorical values between the groups. Independent sample *t*-test or Mann–Whitney U-test was used to compare the analgesic usage and hemodynamic changes between the two groups. Analysis was performed using SPSS software IBM SPSS Statistics for Windows, Version 20.0. (IBM Corp., Armonk, NY, USA).

Results

The data of 32 patients were analyzed [Figure 1], of which the demographic variables and the duration of surgery were found to be comparable between the groups [Table 1]. The intraoperative use of fentanyl between Groups B and BC did not show any statistically significant difference between the groups. Nine patients in Group BC and eight patients in Group B needed additional fentanyl, however this difference was not significant statistically (50 vs. 56.25%, $P = 0.727$). The percentage of patients who required fentanyl in the postoperative

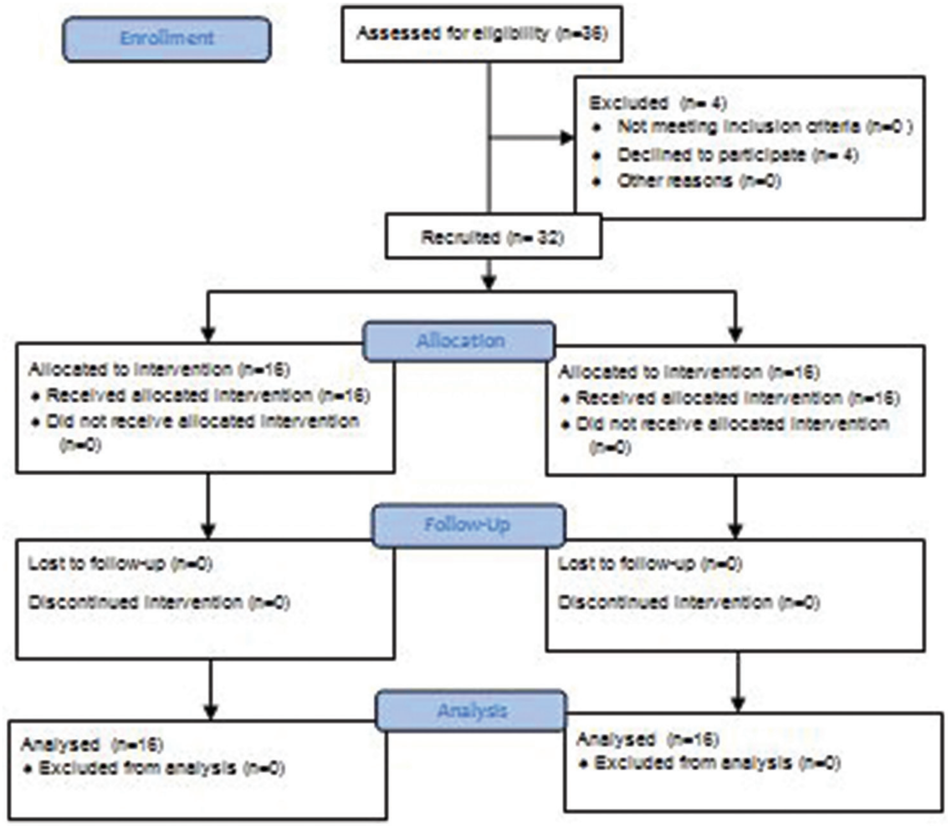

Figure 1: CONSORT flowchart

Table 1: Comparison of age, weight, and duration of surgery

Variables	Mean±SD		*P*
	Group B	Group BC	
Age (months)	23.9±18.3	28.9±21.1	0.474
Weight (kg)	10.8±3.6	11.1±3.5	0.822
Duration of surgery (min)	211.9±112.9	169.6±94.6	0.251

SD: Standard deviation

Table 2: Comparison of fentanyl consumption

Intraoperative fentanyl consumption			
Variables	Group B	Group BC	*P*
Intraoperative fentanyl requirement (µg/kg/min), mean±SD	0.02±0.01	0.02±0.01	0.827
Patients required additional fentanyl intraoperatively, *n* (%)	8 (50)	9 (56.25)	0.727
Patients required fentanyl postoperatively, *n* (%)	2 (12.5)	3 (18.75)	0.632

SD: Standard deviation

period (independent sample *t*-test) was also comparable between the groups [12.5 vs. 18.75%, *P* = 0.632, Table 2].

The mean intraoperative HR, SBP, and MAP were comparable in both groups most of the time. Only at two time points, a significant difference was observed such as the mean HR being significantly higher in Group B at 1 h intraoperatively [131.3 ± 15.7 vs. 120.1 ± 12.7, *P* = 0.028, Figure 2] and a significantly higher SBP at 10 min after caudal compared to Group BC [89.8 ± 6 vs. 98.40 ± 8.8, *P* = 0.054, Figure 3].

Postoperative HR and SBP were comparable in both groups. However, Group B patients showed a statistically significantly higher MAP in the immediate postoperative period compared to Group BC [76.0 ± 9.8 vs. 68.2 ± 6.8, *P* = 0.006, Table 3]. The postoperative pain as assessed on the FLACC scale using Mann–Whitney U-test was comparable between the groups, with the exception of it being lesser in Group B compared to Group BC at 8 h postoperatively [Table 4]. Two children in Group B and three in Group BC required bolus fentanyl 0.5 µg/kg once during the postoperative period.

Discussion

Laparoscopic surgeries are replacing open surgeries in children with acceptable advantages.[1,2] The pain following open abdominal procedures benefits from caudal analgesia with both local anesthetics and additives. Various additives have been used successfully in the caudal space, such as clonidine, ketamine, dexmedetomidine, morphine, and dexamethasone.[4-8]

However, the benefits of caudal analgesia in laparoscopic abdominal surgeries are poorly understood. The pain

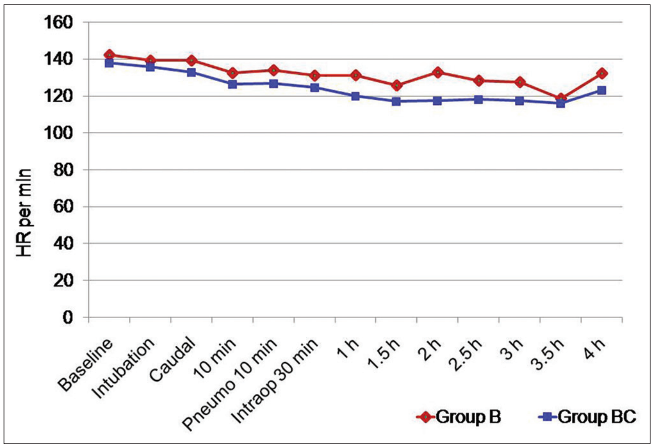

Figure 2: Changes in intraoperative heart rate

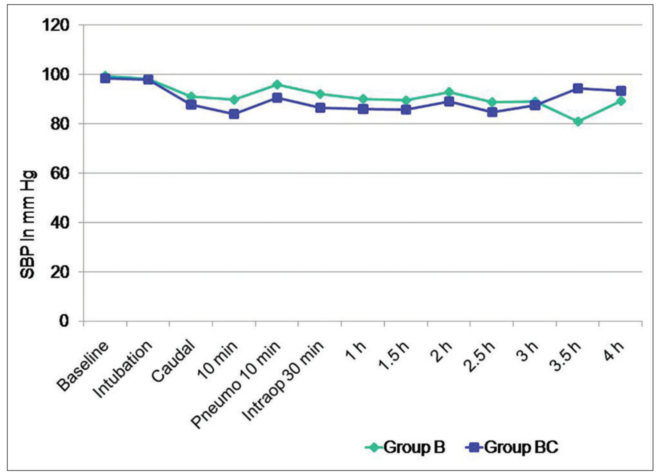

Figure 3: Changes in intraoperative systolic blood pressure

following laparoscopy is believed to be due to the stretch of the peritoneum, injury to the nerves, and the release of inflammatory mediators. The filum terminale and the terminal sacral nerves emerge in the caudal space piercing the dura. Administration of local anesthetics in children produces analgesia by blocking these nerve roots in lower abdominal and pelvic surgery.

Clonidine as an additive in caudal enhances analgesia by increasing the potassium conductance around the A delta fibers and also by prolonging the action of local anesthetic by producing vasoconstriction. Alpha 2 agonists such as clonidine can activate the spinal cholinergic neurons, resulting in acetylcholine release.[9] The mechanism of action of caudal dexamethasone includes a direct action on unmyelinated nerve fibers, vasoconstriction, action on potassium channels, and inhibition of the release of inflammatory mediators.[10]

There is very little published literature on the validity of a caudal block in pediatric laparoscopic surgery. Borkar and Dave[11] compared the effects of caudal block with bupivacaine 1 mL/kg after anesthetic induction versus diclofenac suppository 3 mg/kg postinduction and local anesthetic infiltration at the port sites at the end of the procedure in children undergoing laparoscopy for diagnostic and therapeutic purposes. They concluded that there was no significant benefit in a caudal in laparoscopic procedures in children.

Kundu *c*.[12] administered caudal morphine with bupivacaine and concluded that caudal administration decreased the postoperative pain and pain on skin incision for port insertion, but did not affect the response to pneumo-peritoneum during laparoscopic surgery. In a systematic review and meta-analysis with trial sequential analysis by Kawakami *et al*.,[13] the effect of magnesium added to local anesthetics for caudal anesthesia on postoperative pain in pediatric surgical patients was assessed. They were of the opinion that caudal magnesium may reduce the need for rescue analgesia after surgery, but pointed out the need for further research for more conclusive results.

There is no clear consensus on the optimal pain management in pediatric laparoscopy. Although it is generally stated that the pain in laparoscopy is less than that of open surgery, there are other reports that the pain in the initial 24 h may

Table 3: Comparison of postoperative hemodynamic variables

Time (h)	HR, mean±SD		*P*
	Group B	Group BC	
Postoperative HR			
0	126.4±22.2	129.2±31.8	0.732
4	116.8±16.3	110.6±21.7	0.626
8	111.7±10.0	113.7±18.4	0.498
12	109.3±8.1	109.0±24.7	0.620
16	112.6±7.7	127.0±13.5	0.053
Postoperative SBP			
0	101.9±12.0	96.1±11.1	0.139
4	105.6±16.6	101.9±10.1	0.256
8	105.6±11.3	97.6±8.5	0.076
12	102.8±10.4	103.6±11.4	0.895
16	106.4±7.2	104.7±18.5	0.846
Postoperative MAP			
0	76.0±9.8	68.2±6.8	0.006
4	75.3±13.0	76.6±14.3	0.942
8	73.2±11.3	72.0±10.3	0.776
12	76.1±10.2	77.2±10.9	0.817
16	79.0±8.9	77.0±16.7	0.699

HR: Heart rate, SBP: Systolic blood pressure, MAP: Mean arterial pressure, SD: Standard deviation

Table 4: Comparison of postoperative FLACC score

Time	Postoperative FLACC score: Median (minimum-maximum)		*P*
	Group B	Group BC	
Postoperative 0	1 (0-4)	0 (0-6)	0.331
4 h	0 (0-4)	0 (0-2)	0.619
8 h	0 (0-4)	1 (0-4)	0.022
12 h	0 (0-4)	0 (0-3)	0.338

FLACC: Face, Legs, Activity, Cry, Consolability be in accordance to that of open surgery.[14] Guidelines, however, recommend that a combination of a nonsteroidal anti-inflammatory drug and local infiltration or a transverse abdominal plane block may be adequate in pain management in children.

We used 1.25 ml/kg volume for caudal as it is the standard practice at large-volume centers for upper abdominal surgeries. We believed that pain in laparoscopy resulting from stretch could extend to the higher segments and hence chose this volume. This was combined with the standard dose of local anesthetic to avoid potential toxicity. In our study, we assessed consumption of fentanyl in μg/kg/min taking into account the different duration of surgical procedures.

Contrary to the study by Kundu *et al*.,[12] we were unable to document the benefits of adjuncts added to local anesthetic on analgesic requirements in laparoscopy. It is possible that use of morphine in the caudal had contributed to the positive response in their study. It appeared that clonidine at a dose of 1 μg/kg in combination with local anesthetic did not have a beneficial effect on hemodynamic responses or postoperative pain in laparoscopic surgery. The addition of clonidine did not appear to have a beneficial response on hemodynamic responses, and this was similar to the study by Borkar *et al.*[11] While the benefits of caudal local anesthetics and additives remain unchallenged in open surgery, its role in laparoscopy remains unclear.

The management of pain may be confounded by difficulties in the assessment of children who may not be able to communicate clearly. Hence, the interpretation of pain is prone to significant interobserver variability.[15] We had used the FLACC scale for postoperative pain and the assessment performed by the nurse assigned to the care of the patient,[3] who was blinded to the drugs given caudally. This was chosen as it is simple and uses definite points of assessment. Most of the scores recorded in all groups were low in our study, which was indicative of minimal or no discomfort to the child.

The present study was limited by the fact that there were no objective pain indices intraoperatively and hemodynamic responses were used as a surrogate marker of pain responses. In the postoperative pain evaluation, the drawback we had perceived was that anxiety from strange location in a child could falsely be misinterpreted as pain. Children who were crying could sometimes be calmed just by the presence of the parent, not an additional analgesic. As postoperative pain in children is difficult to assess, the ICU nurse assessed it using FLACC score whenever the child had discomfort and analgesics were administered if required. In fact, the pain assessment was a continuous process and the FLACC score recorded at fixed time points might not have represented the actual score the child had during a time frame. This was a drawback of our study.

More than the FLACC score, the requirement of postoperative analgesics represents the quality of the postoperative analgesia. As the requirement of additional analgesics in both groups in our study was minimal and comparable, it could be interpreted as lack of an additional analgesic effect of clonidine in the dose we used when added to caudal local anesthetic agents.

If the present study had been conducted with three groups having one group without caudal and the others with caudal, it could have been possible to prove if caudal actually helped in this subset of surgeries. The caudal was performed by an anesthetist with >4 years' experience in anesthesia. Though the cases that were technically difficult were excluded, we might have missed those patients with a block failure. All patients in the study received rectal paracetamol at extubation and 6 hourly in the postoperative period as this was the standard of care for minimally invasive surgeries at our institute. Because both groups received this intervention, it could not be considered a confounding factor in the interpretation of pain score as reduction in the intensity of pain would be same in both groups.

Conclusion

Clonidine 1 μg/kg added to caudal bupivacaine did not improve analgesia in comparison to bupivacaine alone in pediatric patients undergoing laparoscopic versus local anaesthetic with clonidine did not appear to affect the pain during laparoscopy surgery.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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