

A Study of Comparison of Post-Operative Analgesia after Single-Shot Caudal Epidural Block Using Bupivacaine with or without Clonidine in Children

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Abstract

Introduction: Lower abdominal surgeries are one of the most frequently performed surgeries in the pediatric age group. A large number of these operations are done as day-care procedures.

Caudal block is one of the most common regional anesthetic techniques in children being used to supplement general anesthesia for a wide variety of sacral-segment surgery. The local anesthetics currently in use are safe and their pharmacological effects have been well evaluated. There is no fear of neurological sequelae as in the past.

Several studies have demonstrated that Clonidine added to the local anesthetic in caudal block both enhances and prolongs the analgesia produced by the block without the unpleasant or hazardous side-effects associated with the use of other adjuvant drugs like opioids, epinephrine and some newer adjuvants like neostigmine and dexmedetomidine. Our study aimed to evaluate the efficacy of single-dose caudal epidural Clonidine in prolonging the post-operative analgesia when mixed with Bupivacaine in children.

Materials and Methods

Sixty children of ASA I and ASA II physical status, between 1 and 12 years of age, who underwent elective lower abdominal surgeries, were randomly divided into two groups B (N=30) and C (N=30). All the children were administered general anesthesia. After induction, a single-shot caudal block was administered using 0.25% Bupivacaine (group B) and 1.5 mg/kg of Clonidine hydrochloride (group C). Vital monitoring was done intraoperatively as per institutional protocol. Post-operative monitoring was done in the post-anesthesia care unit (PACU) for 2–3 hours and in the ward for next 24 hours. Data with respect to duration of surgery, duration of pain-free period, time to void and any other complications was compiled. The final results of the study were tabulated and analyzed for significance using standard statistical techniques (unpaired t-test).

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Results

This study was undertaken to evaluate the efficacy of Clonidine in prolonging post-operative analgesia of Bupivacaine when given caudally in 60 children undergoing lower abdominal surgeries. The duration of pain-free period with caudal Bupivacaine with Clonidine (group C) is significantly longer than caudal Bupivacaine (group B). The duration of pain relief was 20.4 hours in group C as compared to 14.2 hours in group B. This is statistically significant ($p < 0.05$).

Conclusion

We conclude that adding Clonidine 1.5 mg/kg to Bupivacaine 0.25% for caudal anesthesia in children undergoing lower abdominal surgeries enhances and prolongs postoperative analgesia compared to caudal Bupivacaine 0.25% alone. Clonidine may be the drug of choice to prolong the duration of caudal anesthesia provided by a single injection in children.

Keywords: Caudal epidural block, Bupivacaine Clonidine

Introduction

Pain is a protective mechanism designed to alert the body to potentially injurious stimuli. The International Association for the Study of Pain has defined pain as 'an unpleasant sensory and emotional experience, associated with actual or potential tissue damage'.¹

The alleviation of pain has been the focus of continuing human effort. However, it has been recognized for some time that the management of acute pain, especially post-operative pain, has been consistently inadequate. The situation in children has been even worse; children have long been under-medicated for acute pain.²

Caudal block is one of the most common regional anesthetic techniques in children being used to supplement general anesthesia for a wide variety of sacral-segment surgery. During the second half of the 1980s, neuroaxial administration of opioids became en-vogue in adult anesthesia and Krane and colleagues in 1988 published dose-response data for morphine as an adjunct to caudal anaesthesia in children.³ Soon after this, the successful use of both racemic ketamine and Clonidine was described.⁴ During the following years, a large number of studies on the adjunct use of these drugs in caudal anaesthesia have been published and this literature has recently been the focus of a number of review articles.⁵⁻⁷

The use of adjuvants in caudal block has several advantages. Several studies have demonstrated that Clonidine added to the local anesthetic in caudal block both enhances and prolongs the analgesia produced by the block without the unpleasant or hazardous side-effects.^{8,9}

Aims and Objectives

The aims of this study were:

- To clinically evaluate the efficacy of caudal epidural

Clonidine in prolonging the post-operative analgesia when mixed with Bupivacaine in children;

- To compare the post-operative pain-free duration and side effects of Bupivacaine with or without Clonidine.

Materials and Methods

After institutional ethical committee approval and written informed consent from the patients, sixty children of ASA I and ASA II physical status, between 1 and 12 years of age, posted for elective lower abdominal surgery were included in the study.

Study Design: Prospective randomized double blind.

Sample Size: 60

Exclusion Criteria

- Children with known allergy to local anesthetics
- Bleeding diathesis
- Aspirin ingestion in the preceding one week
- Presence of septic focus on the skin over the caudal region
- Any bony abnormality of the sacrum
- Pre-existing neurological disease or ASA III

The children were randomly divided into two groups of 30 each.

Group B (n=30) received only 0.75 mL/kg of 0.25% Bupivacaine.

Group C (n=30) received Inj. Clonidine 1.5 µg/kg in addition to 0.75 mL/kg of 0.25% Bupivacaine.

Procedure Methodology

After careful pre-anesthetic checkup and routine investigations, and informed consent, the patients were pre-medicated inj. Glycopyrrolate 5–10 µg/kg intramuscularly

and an intravenous line was started inside the operating room. Thereafter, the patients were induced with inj. Thiopentone 5–6 mg/kg IV+inj. Vecurenium 0.1 mg/kg and ventilated for 3 min. Patients not having intravenous access were induced with inhalational agent Sevoflorane+O₂+N₂O and intravenous line was taken. Inj. Vecuronium 0.1 mg/kg was used to facilitate intubation. Endotracheal tube was used to maintain the airway. Maintenance of anesthesia was done with Oxygen+Nitrous oxide+Isoflurane. Inj. Vecuronium was used for muscle relaxation. Caudal block was performed after induction and before the start of surgery, using standard techniques. The children were randomly divided into two groups of 30 each with regards to drug used for caudal block.

Group B (n=30) received only 0.75 mL/kg of 0.25% Bupivacaine.

Group C (n=30) received inj. Clonidine 1.5 µg/kg in addition to 0.75 mL/kg of 0.25% Bupivacaine.

Intraoperatively, the patient was monitored using standard monitoring, i.e., systolic blood pressure (non-invasive), pulse-oximetry, heart rate and ECG during the course of surgery. Intravenous fluids were given as per requirement. The neuromuscular blockade was reversed with inj. neostigmine 50 µg/kg and inj. Glycopyrrolate at the end of surgery. Post-operative monitoring was done in the post-anesthesia care unit (PACU) for 2–3 hours and in the ward using a standard proforma for next 24 hours.

The assessment of pain relief was done by using an objective pain score (Hannallah-Broadman). In addition, the following parameters were noted:

- Duration of surgery
- Duration of pain-free period
- Time to void
- Any other complications namely – nausea, vomiting, motor weakness, respiratory depression, sedation, hypotension, and bradycardia

At the onset of pain, rescue analgesia was given as appropriate and the total duration of analgesia was noted. The final results of the study were tabulated and analyzed for significance, using standard statistical techniques (unpaired t-test).

Results

There was no significant difference between the two groups with respect to age (years), weight and duration of surgery. Two independent sample t-tests were used for comparison of Bupivacaine group and Bupivacaine plus Clonidine group with respect to systolic blood pressure (SBP) (mmHg), diastolic blood pressure (DBP), heart rate, and pain score. There was significant difference between Bupivacaine group and Clonidine group with respect to systolic blood pressure (SBP) at post-caudal 10th min, 20th min, p-value <0.05, 30th min, 60th min and 90th min (Table 1). There was significant difference between Bupivacaine group and Clonidine group with respect to diastolic blood pressure (DBP) at post-caudal 10th min, 20th min, 30th min, 60th min, 90th min, 120th min and post-op 1st hour, 2nd hour, 3rd hour, 6th hour, 9th hour to 24th hour except 21st hour, p-value <0.05 (Table 2). There was significant difference between Bupivacaine group and Clonidine group with respect to heart rate at post caudal 10th min, 20th min, 30th min, 60th min, 90th min, 120th min, after extubation and post-op 1st hour, 2nd hour, 3rd hour, 6th hour, 9th hour to 24th hour, p-value < 0.05 (Table 3). There was significant difference between Bupivacaine group and Clonidine group with respect to objective pain score at after extubation and post op 3rd hour, 6th hour, 9 hour to 21st hour. p-value <0.05 (Table 4). Mann-whitney test (Table 5) p-value <0.05 showed there was significant difference between the Bupivacaine group and Clonidine group with respect to sedation score at after extubation, post-op 1st hour to 9th hour and post-op 15th hour, 18th hour and 24th hour. Two independent sample t-test p-values <0.05 showed there was significant difference between the two groups with respect to time at analgesia required (Table 6).

Table 1. Comparison of Bupivacaine Group and Bupivacaine Plus Clonidine Group with respect to Systolic Blood Pressure (SBP) (mmHg)

SBP at	SBP (Mean±SD)		p-value
	Bupivacaine	Clonidine	
Baseline	93.53±5.19	93.73±4.83	0.878
After induction	87.53±3.10	88.33±3.37	0.342
Post caudal at 10th min	87.73±5.24	84.40±3.98	0.007*
at 20th min	84.67±2.99	78.60±3.11	<0.001*
at 30th min	88.67±6.04	85.33±5.36	0.027*
at 60th min	85.67±1.97	80.33±4.24	<0.001*
at 90th min	85.60±1.98	82.40±5.29	0.003*
at 120th min	88.29±6.46	86.14±4.87	0.331
after extubation	88.73±6.38	90.20±3.42	0.273
Post-op 1st hour	91.20±5.03	89.20±5.70	0.155
2nd hour	88.53±4.73	90.80±4.69	0.067
3rd hour	90.20±5.29	89.60±4.88	0.650
6th hour	89.93±5.84	90.27±4.16	0.800
9th hour	90.87±6.00	89.53±4.69	0.342
12th hour	90.87±5.53	88.47±5.30	0.091
15th hour	88.67±5.05	90.53±6.12	0.203
18th hour	90.07±5.13	89.07±3.59	0.386
21st hour	90.33±5.51	89.60±4.15	0.563
24th hour	88.27±5.58	87.80±6.24	0.761

Table 2. Comparison of Bupivacaine Group and Bupivacaine Plus Clonidine Group with respect to Diastolic Blood Pressure (DBP) (mmHg)

DBP at	DBP (Mean±SD)		p-value
	Bupivacaine	Clonidine	
Baseline	48.47±5.42	46.93±3.05	0.184
After induction	43.20±3.43	43.73±2.86	0.516
Post caudal at 10th min	42.93±4.60	40.73±2.43	0.025*
at 20th min	37.87 ±6.85	34.87±2.34	0.029*
at 30th min	46.07±4.56	42.67±3.50	0.002*
at 60th min	40.93±3.14	43.67±2.88	0.001*
at 90th min	41.00±3.18	38.47±3.75	0.006*
120th min	43.43±5.05	40.29±2.02	0.045*
After extubation	43.13±4.83	43.67±2.68	0.600
Post-op 1st hour	46.33±4.84	43.33±3.50	0.008*
2nd hour	46.67±5.74	44.33±2.63	0.045*
3rd hour	48.13±5.48	43.53±2.96	< 0.001*
6th hour	45.60±4.05	43.53±2.56	0.022*
9th hour	46.60±5.44	43.20±3.51	0.006*
12th hour	48.40±5.95	42.93±3.43	< 0.001*
15th hour	45.47±4.55	42.87±3.59	0.017*
18th hour	47.13±4.89	43.67±2.47	< 0.001*
21st hour	45.13±4.32	43.93±2.70	0.203
24th hour	45.00±5.40	42.13±3.82	0.021*

Table 3. Comparison of Bupivacaine Group and Bupivacaine Plus Clonidine Group with respect to Heart Rate (HR)

HR at	HR (Mean±SD)		p-value
	Bupivacaine	Clonidine	
Baseline	137.53±9.13	141.33±7.78	0.088
After induction	134.73±5.74	137.40±5.54	0.072
Post caudal at 10th min	122.73±5.50	117.33±6.35	0.001*
at 20th min	121.47±6.06	104.53±7.08	< 0.001*
at 30th min	120.33±5.46	94.60±8.52	< 0.001*
at 60th min	123.13±5.27	92.60±8.73	< 0.001*
at 90th min	124.60±5.88	89.43±14.47	< 0.001*
120th min	123.14±4.20	88.14±3.46	< 0.001*
After extubation	137.07±6.43	113.73±8.59	< 0.001*
Post op 1st hour	128.40±3.54	104.47±4.97	< 0.001*
2nd hour	129.60±5.29	111.27±8.57	< 0.001*
3rd hour	130.27±5.06	112.87±7.57	< 0.001*
6th hour	131.13±3.66	114.13±6.89	< 0.001*
9th hour	132.07±6.31	115.80±6.92	< 0.001*
12th hour	131.13±3.66	121.00±5.32	< 0.001*
15th hour	129.13±4.66	116.87±7.57	< 0.001*
18th hour	129.53±4.35	123.27±5.37	< 0.001*
21st hour	130.47±5.19	122.07±6.29	< 0.001*
24th hour	132.53±5.33	126.40±4.53	< 0.001*

Table 4. Comparison of Objective Pain Score in Plain Bupivacaine Group and Bupivacaine Plus Clonidine Group

Objective Pain Score at	Pain Score (Mean±SD)		p-value
	Bupivacaine	Clonidine	
After extubation	1.93±0.37	0.43±0.50	<0.001*
Post-op 1st hour	0.23±0.43	0.20±0.41	0.759
2nd hour	0.60±0.62	0.43±0.68	0.325
3rd hour	0.70±0.70	0.13±0.43	<0.001*
6th hour	3.90±1.09	0.30±0.53	<0.001*
9th hour	2.77±0.73	0.17±0.46	<0.001*
12th hour	2.87±1.01	0.90±0.61	<0.001*
15th hour	2.43±0.86	3.70±0.70	<0.001*
18th hour	0.90±0.66	2.03±0.81	<0.001*
21st hour	1.20±0.89	0.57±0.63	0.002*
24th hour	0.60±0.72	0.60±0.72	0.996

Table 5. Comparison of Sedation Score in Plain Bupivacaine Group and Bupivacaine Plus Clonidine Group

Sedation Score	Mean Rank		p-value
	Bupevacaine	Clonidine	
After extubation	21.00	40.00	<0.001
Post-op 1st hour	22.35	38.65	<0.001
2nd hour	17.50	43.50	<0.001
3rd hour	20.05	40.95	<0.001
6th hour	21.50	39.50	<0.001
9th hour	21.50	39.50	<0.001
12th hour	32.43	28.57	0.395
15th hour	43.52	17.48	<0.001
18th hour	32.82	28.18	0.295
21st hour	15.50	45.50	<0.001
24th hour	25.50	35.50	0.001

Table 6. Comparison of Time at Analgesia Required (hour) in Plain Bupivacaine and Bupivacaine Plus Clonidine Group

Group	Number of Patients	Time at Analgesia Required (Mean±SD)	p-value
Bupivacaine	30	6.20±0.76	<0.001
Bupivacaine plus Clonidine	30	15.00±0.00	

Discussion

This study demonstrates a marked synergistic effect of the combined caudal injection of Clonidine and Bupivacaine in children, resulting in prolongation and enhancement of caudal analgesia post-operatively.

To assess the effects of drugs injected in the caudal epidural space via the sacrococcygeal ligament, it is essential to ensure that no technical failure occurs with the establishment of the caudal block. Caudal block is the most popular neuraxial procedure being used with general anesthesia for analgesia during and after operative procedures involving the lower limbs, perineal region, genitourinary and abdominal surgeries below the umbilicus.^{10,11}

As a measure of effectiveness of the caudal block in our study, the inspired isoflurane concentration could be reduced markedly 15 min after skin incision, and throughout the entire operative procedure, no further increase in the concentration of isoflurane was necessary. As with lipophilic opioids, it is possible to achieve analgesia from systemic, epidural or intrathecal administration of Clonidine. However, Clonidine is more potent after neuraxial than systemic administration, indicating a spinal site of action and favoring neuraxial administration.¹²

Clonidine produces analgesia by actions on alpha-2 adrenoreceptors, as shown by partial reversal in humans of epidural Clonidine analgesia and sedation, by the alpha-2 adrenergic antagonist, Yohimbine, although Clonidine's

effects on blood pressure and heart rate were not reversed.¹³

The addition of Clonidine (1 mg/kg) to a caudal epidural solution of Bupivacaine, improved the duration of postoperative analgesia without compromising ventilation.¹⁴

In our study, caudal Bupivacaine 0.25% with addition of Clonidine 1.5 mg/kg provided post-operative analgesia for 15 hours (mean) compared to 6.20 hours with Bupivacaine 0.25%. When adding Clonidine 2 mg/kg to Bupivacaine 0.25% for caudal analgesia in children undergoing orthopedic surgery, postoperative analgesia lasted for 9.8±2.1 hours compared to 5.2±1.2 hours when plain Bupivacaine was used.⁸

We observed a lower incidence of vomiting in the Clonidine group, as compared to Lee and Rubin.⁸ Also no adverse effects of Clonidine administration in the caudal space were observed. There was no incidence of excessive sedation or hypotension, as seen with higher doses of caudally administered Clonidine. One case had bradycardia in the Clonidine group, which was managed with injection Atropine 0.12 mg IV. However, the addition of Clonidine to caudal Bupivacaine did not result in a higher incidence of side-effects compared to caudal Bupivacaine alone.

In the present study, there was no significant motor or sensory blockade 4 hours post-operatively. The number of children in group C requiring rescue analgesia in the first 24 hours was only six which is significantly less, when compared to group B in which as many as 12 children needed rescue analgesia within the first 24 hours.

In our study, a dose of 1.5 mg/kg Clonidine was used, but the significant difference in the sedation scores occurred during the first to ninth hours post-operatively. In another study, addition of 1 mg/kg of Clonidine with 1 mL/kg of .25% Bupivacaine had a higher sedation score up to 2 in immediate post-operative period for 1 hour compared with addition of 0.2 mg/kg of Dexamethason in 1 mL/kg of .25% Bupivacaine in the caudal block.⁹

Although the direct ventilatory effects of epidural Clonidine are minor, a decreased slope of the ventilatory response to CO₂ may detect mild respiratory depression. In addition, obstructive apnea and arterial oxygen desaturation might occur with marked sedation. Penon et al. studied the effects of epidural Clonidine (300 µg) on circulation and ventilatory control in seven healthy unpremedicated subjects. After Clonidine injection, arterial blood pressure decreased significantly in all subjects. Heart rate decreased significantly by 10%–16% between 75 and 105 min after injection. The slope of the ventilatory response to CO₂ decreased significantly from 2.06±0.70 (baseline) to 1.37±68, 1.25±0.65, and ±1.330.67 L/min/mm Hg (mean±SD, P less than 0.05) at 15, 60, and 120 min.¹⁵

In this study, we did not find any effects on respiratory rate and SpO₂, although sedation was more pronounced in the Clonidine group for the first 2 hours post-operatively.

Based on the findings of our study, adding Clonidine 1.5 mg/kg to Bupivacaine 0.25% for caudal anesthesia in children undergoing lower abdominal surgeries prolongs duration of analgesia.

Conclusion

We conclude that adding Clonidine 1.5 mg/kg to Bupivacaine 0.25% for caudal anesthesia in children undergoing lower abdominal surgeries enhances and prolongs post-operative analgesia compared to caudal Bupivacaine 0.25% alone. This could be a safe and cost-effective alternative to extradural catheter placement for surgical procedures of intermediate duration. Caudal Clonidine also prevents the sympathoadrenergic response during emergence from anesthesia, but may have hemodynamic and sedative effects in the early postoperative period. Clonidine may be the drug of choice to prolong the duration of caudal anesthesia provided by a single injection in children.

Conflict of Interest: None

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