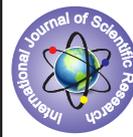


**A COMPARISON OF POST OPERATIVE ANALGESIC EFFICACY OF BUPIVACAINE FENTANYL COMBINATION VERSUS ROPIVACAINE FENTANYL COMBINATION IN CAUDAL BLOCKADE IN PEDIATRIC PATIENTS UNDERGOING INFRAUMBILICAL SURGERY**



**Anaesthesiology**

**KEYWORDS:**

<b>Dr. Pabitra Das.</b>	MD. Anaesthesiologist. WBHS. Govt of WB.
<b>Dr. Haripada Das.</b>	Assistant Professor, Department of Anaesthesiology / Cardiac Anaesthesiology. NRS Medical college. Kolkata.
<b>Dr. Sampa Dutta Gupta.</b>	Professor, Head Department of Cardiac Anaesthesiology, Nil Ratan Sirker Medical College. Kolkata, India.
<b>Dr. Saikat Majumdar.</b>	DM PDT Department of Cardiac Anaesthesiology., Nil Ratan Sirker Medical College. Kolkata,
<b>Dr. A K Singh.</b>	Prof & Director. Directorate General Medical Services (Army) Adjuvant General's Branch. Integrated HQ of MOD(Army).
<b>Dr. Aritra Bhattacharya.</b>	House staff. Department of Radiology. Central Hospital South Eastern Railway. Garden Reach. Kolkata.

**ABSTRACT**

A total of 80 children of either sex, aged between 1-8 years, belong to ASA grade I and II, scheduled to undergo infra-umbilical surgeries were included in a prospective, randomized, controlled, double-blind paralleled group study with an aim to compare the postoperative analgesic efficacy between single dose caudal epidural bupivacaine-fentanyl and caudal epidural ropivacaine –fentanyl combination.

The children of Group A- (N=40) received inj bupivacaine (0.125%)+ inj fentanyl (1mcg/Kg /Body wt) with total volume of 1ml/kg and Group B- (n=40) and children received inj. ropivacaine ( 0.125% ) + inj fentanyl (1mcg/Kg /Body wt) with total volume of 1ml/kg after induction of general anaesthesia and endotracheal intubation. Demographic characteristics were comparable. Group A patients had no significant increase of heart rate, systolic, diastolic and mean blood pressure, respiratory rate, oxygen saturation and pain scores compared to Group B patients. The requirement of rescue analgesics in Group B patients were earlier than Group A patients.

**INTRODUCTION**

Caudal blocks result in lower postoperative pain scores compared with scores of patients after general anaesthesia alone. They can be combined with general anaesthesia to reduce the requirement for volatile agents and opioids, allowing rapid, pain-free recovery with minimal postoperative vomiting and an early resumption of oral intake.<sup>1,2,3</sup> Due to residual motor block and cardiac toxicity of bupivacaine, ropivacaine, a pure S(-) enantiomer has been developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles<sup>4</sup>. Many investigators<sup>5, 6</sup> have evaluated the use of fentanyl as an adjuvant to caudal analgesia.

**AIM** to compare between bupivacaine-fentanyl combination and ropivacaine-fentanyl combination in caudal epidural analgesia of postoperative pain management of paediatric patients in infra-umbilical abdominal surgeries. Objectives to compare observation pain score (OPS) immediately after extubation in the both groups, time of first rescue analgesic in both groups, and adverse reaction if any.

**METHODOLOGY**-After obtaining IEC and consent from parents, this prospective, randomized, double-blind controlled paralleled group study was carried out in patients with ASA grade I and II, age between 1 to 8 years of either sex put for infra-umbilical surgeries were included in the study.

Parental refusal, children with bleeding diathesis, Pre-existing neurological or spinal diseases, neurological abnormalities, infection at injection site, history of seizures were excluded from the study.

Children thus enlisted for the study were randomly allocated into two groups as follows

Group A- ( n =40) children received inj bupivacaine (0.125% )+ inj fentanyl (1mcg/Kg /Body wt) with total volume of 1ml/kg.

Group B- ( n =40) children received inj. ropivacaine ( 0.125% ) + inj.

fentanyl (1mcg/Kg /Body wt) with total volume of 1ml/kg (All the injected were sealed with white envelop) injectables.

On the morning of surgery the following data were obtained: body weight, heart rate /minute, respiratory rate /min, non-invasive blood pressure (NIBP) in mm of Hg, temperature in °F, SpO<sub>2</sub>%. All the patients were premeditated 30 minutes before surgery with syrup midazolam 0.5 mg/Kg body weight orally.

With proper pre-oxygenation all the patients were induced with halothane (0.4-2%) along with 60% N<sub>2</sub>O in 40% O<sub>2</sub>, I.V access secured with Ringer Lactate. Inj. glycopyrrolate 0.01mg/Kg, inj fentanyl 2µg/Kg body weight and inj. thiopental 3-5 mg/Kg body weight. Patients were intubated with atracurium 0.5mg/kg. Anaesthesia was maintained with 60% N<sub>2</sub>O in O<sub>2</sub> and (0.5-1%) in halothane using controlled ventilation. Then the child was turned to left lateral position to institute caudal block. At the end of surgery, patients were reversed with injection neostigmine 0.05mg/kg body wt and injection glycopyrrolate 0.01 mg/kg & shifted to PACU. During the post-operative period, moist oxygen was administered for 2 hours. The parameters were assessed. Analgesic efficacy was documented by using the Children's Hospital of Eastern Ontario Pain Scale which is based on behavioural objectives. A score of 4 signifies excellent analgesia and a score of 13 signifies that the analgesia was ineffective. When score was exceeding 6, rescue analgesic was administered.

Statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 10.0.1 and Graph Pad Prism version 5. Data have been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Student's independent sample's t-test was applied to compare normally distributed numerical variables; Mann Whitney U-test was employed for intergroup comparison of non-parametric numerical variables. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

**RESULTS AND ANALYSIS.**

**Table 1.**

Heart rate		Group	N	Mean	Std Dev	Median	p- value
Pre	op	A	40	91.0000	11.1032	88.0000	0.59
		B	40	92.4000	12.1461	89.0000	
Intra	OP	A	40	97.6000	12.2387	95.0000	0.5735
		B	40	99.2000	13.0624	97.0000	
Intra	OP	A	40	95.1000	11.8620	91.0000	0.5564
		B	40	96.7500	13.0929	95.0000	
HR15min	Post	A	40	96.0500	12.1401	95.0000	0.2092
		B	40	92.6000	12.2303	89.0000	
HR1 hr	Post	A	40	95.0000	12.0767	93.0000	0.2693
		B	40	91.9500	12.4405	89.0000	
HR 2 hr	Post	A	40	94.7000	11.9017	93.0000	0.6108
		B	40	93.3000	12.5967	90.0000	
HR 3 hr	Post	A	40	97.1000	11.8534	94.0000	0.6746
		B	40	95.9500	12.5472	92.0000	
HR 5 hr	Post	A	40	99.2000	11.7826	96.0000	0.3166
		B	40	96.4500	12.6043	94.0000	
HR 8 hr	Post	A	40	100.0000	12.0341	98.0000	0.2651
		B	40	95.4500	12.1105	93.0000	
HR 12 hr	Post	A	40	96.1500	11.7791	95.0000	0.4651
		B	40	94.2000	11.9812	91.0000	

Table 1. shows comparison of pre, intra and post operative heart rate (beats/minute) of patients at various time points. This correlation was not statistically significant.

**Table 2.**

	Group	Mean	p-value
Pre-op SBP	A	100.3000	0.62
	B	101.4000	
Intra OP SBP 30	A	103.5294	0.3266
	B	106.0714	
Intra OP SBP 60	A	101.4545	0.5193
	B	97.6000	
Post OP SBP 1 hr	A	104.1500	0.5657
	B	102.8500	
Post OP SBP 5 hr	A	103.7500	0.9489
	B	103.6000	
Post OP SBP 8 hr	A	102.1500	0.2166
	B	101.8000	
Post OP SBP 12 hr	A	105.6000	0.6781
	B	104.6500	
Post OP SBP 24 hr	A	103.8000	0.7750
	B	103.1500	

Table 2. shows the comparison of pre, intra and post operative systolic blood pressure (mm of Hg) of patients at various time points. This was not statistically significant.

**Table 3:**

	Group	Diastolic BP	p-value	Resp. rate Mean	p-value
Pre-op MAP	A	75.4250	0.80	29.8250	0.5756
	B	75.8000		30.2750	
Intra OP MAP 30	A	77.6471	0.8763	24.3750	0.3504
	B	77.9286		24.9000	
Intra OP MAP 60	A	75.8000	0.4003	22.3250	0.2118
	B	72.0000		23.0750	
Post OP MAP 0	A	81.6250	0.2350	25.2250	0.0592
	B	79.7500		26.4750	
Post OP MAP 1 hr	A	78.6750	0.2008	25.3000	91.0000
	B	76.6750		63.0000	
Post OP MAP 8 hr	A	80.0750	0.2908	68.0000	91.0000
	B	78.4250		65.0000	

Post OP MAP 12 hr	A	80.1000	0.1026	69.0000	91.0000
	B	77.5500		65.0000	
Post OP MAP 24 hr	A	78.2250	0.4268	65.0000	91.0000
	B	76.9750		64.0000	

Table 3 shows show comparison of pre, intra and post operative Mean Arterial Pressure (mm Hg), respiratory rates, of patients at various time points. This was not statistically significant.

Table 4. show comparison of post operative CHEOPS-Scale of patients at various time points. This was not statistically significant.

**Table 4. CHEOPS-Scale of patients at various time points.**

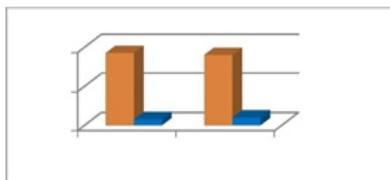
	Group	N	Mean	p-value
PostOP CHEOPS 0	A	40	5.2750	0.5831
	B	40	5.3750	
Post OP CHEOPS 30m	A	40	5.0500	0.4521
	B	40	4.9250	
Post OP CHEOPS 1 hr	A	40	4.9231	0.8707
	B	40	4.9000	
Post OP CHEOPS2 hr	A	40	4.9750	0.2035
	B	40	4.7750	
Post OP CHEOPS 6 hr	A	40	5.8250	0.6460
	B	40	5.7500	
Post OP CHEOPS 12 hr	A	40	6.4250	0.6848
	B	40	6.3500	
Post OP CHEOPS 24 hr	A	40	6.0000	0.2114
	B	40	5.5000	

**Table 5: Comparison of time to first rescue analgesic ( in minutes) between two groups.**

Group	Mean	p-value
A	545.1500	0.0024
B	501.0000	

Table 5 summarizes the descriptive statistics of times to first rescue analgesic between two groups. It was significantly earlier in Group-B compare to Group-A (p=0.0024), (2-tail unpaired t- test).

**Table 6. shows comparison of sedative score between two groups.**



**Table 6 , shows the comparison of sedation immediate post operative period. This was not statistically significant (p=0.692).**

**DISCUSSION**

This prospective, randomized, double-blind controlled parallel group study was conducted in the paediatric operation theatre of different surgical department of SSKM Hospital, Kolkata, from January 2013 to September 2014. 80 children 1-8 years of age, of either sex ASA physical status I or II undergoing elective infraumbilical surgery under general anesthesia were included in this study.

The haemodynamic profiles of the patients were monitored as an indirect indicator of postoperative pain management. However there was no clinically significant bradycardia, hypotension or respiratory depression in any patients in present studies. The maintenance of haemodynamic parameters may be attributed to the diminished sympathetic tone due to better postoperative analgesia achieved by both the combinations. The findings are corroborative with those of previously mentioned clinical studies by Gentili A and coworkers<sup>7</sup>, Shukla Uand coworkers<sup>6</sup> and the study of Pandya M and coworkers<sup>8</sup> for postoperative pain relief in children. Egashira T and coworkers<sup>9</sup> studied on comparative efficacy of levobupivacaine and ropivacaine

for epidural block in outpatients with degenerative spinal disease. There were no significant differences in arterial blood pressure and heart rate.

Comparison of post-operative pain scores in terms of Children's Hospital of Eastern

Ontario Pain Scale (CHEOPS)<sup>10-12</sup> of patients at various time points revealed no statistically significance (Mann Whitney U-test). Postoperative CHEOPS ( Post op CHEOPS 0mins-P=0.5831; Post op CHEOPS 30mins-p=0.4521; Post op CHEOPS 1hr-p=0.8707; Post op CHEOPS 2hrs-p=0.2035; Post op CHEOPS 3hrs-p=0.7767; Post op CHEOPS 5hrs-p=0.6460; Post op CHEOPS 8hrs-p=0.1054; Post op CHEOPS 12hrs-p=0.6848; Post op CHEOPS 24hrs-p=0.2114)

Comparison of time to first rescue analgesic (in minutes) distribution of two groups revealed was significantly needed earlier in Group-B compare to Group-A (p=0.0024). But there was no statistically significant (p=0.2450) difference between the two groups in terms of required total number of rescue analgesic doses. Comparison of sedation in immediate post-operative period shows no statistically significant difference between the groups (p=0.692).

Chipde S and coworkers<sup>13</sup> conducted a prospective randomized controlled comparison of caudal bupivacaine and ropivacaine in pediatric patients. They examined 50 consecutive patients in the age group of 1-10 years, undergoing urogenital surgeries under general anesthesia. Caudal block was given with either bupivacaine (0.25%) 1 ml/kg (Group I) or ropivacaine (0.25%) 1 ml/kg (Group II). They found no significant differences in terms of hemodynamic variable, pain score and duration of analgesia. Only significant difference was the motor-block score at 2, 3 and 4 h after surgery, although the score was same 1 h post-operatively.

Bhowmick DK and coworkers<sup>14</sup> evaluated the effect of caudal bupivacaine(I) and bupivacaine-clonidine(II) in postoperative pain relief in children after subumbilical surgeries. They found significantly longer (p=0.000) duration of analgesia in Group II (712 ± 15.30 minutes) as compared with Group I (246 ± 8.74 minutes) as well as significantly lower requirement of rescue analgesic in group II.

Shrestha SK, Bhattarai B<sup>15</sup> observed that, the mean duration of pain relief was significantly longer bupivacaine + tramadol than bupivacaine (8.8 hrs Vs 7 hrs).

Seyedhejazi M, Azerfarin R, Kazemi F, Amiri M<sup>16</sup> recommended caudal analgesia as the best choice in children under 6 years old (or 25 kg) for hypospadias repair. Bilgen S, and coworkers<sup>17</sup> studied between two different doses of bupivacaine in caudal anesthesia for neonatal circumcision, to compare the analgesia quality of caudal block of low volume, high concentration bupivacaine to the conventionally used volumes and concentrations of the drug in neonates undergoing circumcision with sole caudal anesthesia. None of the neonates required additional analgesic for the first 24 hours following the surgery; therefore postoperative analgesic requirement was similar among the groups (p>0.1).

Fyneyface-Ogan S, and coworkers<sup>18</sup> recorded pain scores and time to first analgesic request and, total dose of analgesics administered in the first 24 hours. The mean duration of effective analgesia in bupivacaine group was 286.4 ± 47.8 minutes, (p < 0.001).

The result of this study corroborate with the above studies in terms of postoperative pain management in infra-umbilical surgery using ropivacaine fentanyl and bupivacaine fentanyl as pre-emptive caudal analgesia was effective and comparable outcome. Comparison of Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) immediately after extubation in the both groups was comparable. Times to first rescue analgesic was statistically significantly earlier in Group-B compare to Group-A (p=0.0024). This study is consistent with the study of Bilgen S, Koner O, Menda F, Karacay S, Kaspar EC,

Sozubir S though bupivacaine 0.25% (2.5 mg/kg) was used for that study.

Regarding adverse reaction of this study, nausea and vomiting was observed in 25% of the patients in group B and 20 % of the patients in group A. Postoperative vomiting was compared between two groups. It was not statistically significant.(p=0.7454). There was no respiratory depression between two groups. Comparison of urinary retention reveal of two groups (Table 23, Figure 30). It was not statistically significant (p=0.3049026010). No hypotension and no incidence of pruritus found. None of the patients in both the groups had complication like motor weakness in the postoperative period. Unlike the study of Lynch C<sup>19</sup>, this study did not revealed the systemic toxicity of local anesthetics leading to impair myocardial performance and conduction system. Y. Kawaraguchi , and coworkers<sup>20</sup> showed that, ropivacaine is less cardiotoxic and there is a greater separation of sensory and motor effects than with bupivacaine. But in this study no such difference happened as an untoward event.

Similar to the conclusion of study of Gentili A, and coworkers , Shukla U and coworkers this study may conclude that paediatric caudal anaesthesia is an effective method with a very infrequent complication rate. Moeller R, Covino BG<sup>21</sup> also showed that, clinical effect of ropivacaine is difficult to separate from a similar effect from bupivacaine, although it appears to produce less motor block and has a slightly shorter duration of action than bupivacaine does. , but similar to the study of Ray M<sup>22</sup> studied for caudal analgesia in paediatric patients for comparison between bupivacaine and ropivacaine and found a safe and effective local anaesthetic agent which provides prolonged postoperative analgesia following caudal block.

This study revealed consistent with the study of Moeller R and Covino BG<sup>23</sup> in relieving post operative pain in children which was almost difficult to separate the effect of ropivacaine from the effect of bupivacaine, though it appears to produce slightly shorter duration of action than bupivacaine does. Moreover similar to the study of Shukla U and co-workers and Egashira T, co-workers hemodynamic, changes were comparable and stable throughout the study duration . Similar result was also revealed in the study of Pandya M, and co-workers.

The most frequently used measure of motor block is the Bromage scale<sup>24</sup>, by the patient's ability to move their lower extremities. All patients found free movement of legs and feet at the end of extubation. The concentration of local anaesthetic used in this study did not alter motor activity even with the addition of fentanyl in any patients.

Chipde S,<sup>7</sup> performed a prospective randomized controlled comparison of caudal bupivacaine and ropivacaine in paediatric patients. Caudal block was given with either bupivacaine (0.25%) 1 ml/kg (Group I) or ropivacaine (0.25%) 1 ml/kg (Group II). HR and SBP showed no significant difference. All the patients had adequate intra-operative analgesia. Mean OPS were comparable between two groups. Duration of absolute analgesia was 276.8 (11) min in Group I and 284.8 (12) min for Group II. The present study is consistent with the of study of Chipde S, and co-workers.

Conclusion: Hence, it can be concluded from the study that though bupivacaine – fentanyl combination has slight prolonged analgesic action than ropivacaine – fentanyl combination.

#### Reference-

1. International association for study of pain. Subcommittee on Taxonomy. Pain terms: a list with definition and notes on usage. Pain 1979;6:249-52.
2. Giaufre E, Dalens B, Gombert A. Epidemiology and morbidity of regional anaesthesia: A one year prospective survey of the French Language society of Paediatric anaesthesiologists (ADARPEF). Anesth Analg 1996;83:904.
3. Dalens B, Hasnoui A. Caudal anesthesia in pediatric surgery: success rate and adverse effects of 750 consecutive patients. Anesth Analg 1989;68:83-9.
4. Hansen TG. Ropivacaine: A pharmacological review. Expert Rev Neurother. 2004; 4:78-91.

5. Lonnqvist PA, Ivani G, Moriarty T. Use of caudal epidural opioids in children: Still state of the art or beginning of the end? *Paediatr Anaesth* 2002;12:747.
6. Shukla U, Pravakar T, Malhotra K. Postoperative analgesia in children when using clonidine or fentanyl with ropivacaine given caudally. *J Anaesth Clin Pharmacol*. 2011;27(2):205-10.
7. Gentili A, Pasini L, Bachiocco V, Landuzzi V, Giuntoli L, Lima M, et al. Cardiocirculatory intraoperative assessment during single-shot caudal anaesthesia in children: comparison between levobupivacaine and ropivacaine. *Pediatr Med Chir*. 2012;34(3):133-42.
8. Pandya M, Tailor K, Vachhrajani P. Caudal block using Ropivacaine with or without Tramadol in children for lower abdominal and lower limb surgery. *Int J Med Sci Public Health*. 2014;3(4):461-464.
9. Egashira T, Fukasaki M, Araki H, Sakai A, Okada M, Terao Y, et al. Comparative efficacy of levobupivacaine and ropivacaine for epidural block in outpatients with degenerative spinal disease. *Pain Physician*. 2014;17(6):525-9.
10. Beyer JE, McGrath PJ, Berde CB. Discordance between self-report and behavioral pain measures in children aged 3-7 years after surgery. *J Pain Symptom Manage*. 1990;5:350-56.
11. Jacobson SJ, Kopecky EA. Randomised trial of oral morphine for painful episodes of sickle-cell disease in children. *Lancet*. 1997;350:1358-61.
12. Mitchell P. Understanding a young child's pain. *Lancet*. 1999;354:170.
13. Chipde S, Banjare M, Arora K, Saraswat M. Prospective randomized controlled comparison of caudal bupivacaine and ropivacaine in pediatric patients. *Ann Med Health Sci Res*. 2014;4(Suppl2):S115-8.
14. Bhowmick DK, Akhtaruzaman KM, Ahmed N, Islam MS, Hossain MM, Islam MM. Postoperative pain relief in children after infra-umbilical surgeries—a comparison between caudal bupivacaine and bupivacaine-clonidine. *Mymensingh Med J*. 2011;20(1):93-7.
15. Shrestha SK, Bhattarai B. Caudal bupivacaine vs bupivacaine plus tramadol in postoperative analgesia in children. *J Nepal Health Res Counc*. 2010;8(2):99-10.
16. Seydehjezi M, Azerfarin R, Kazemi F, Amiri M. Comparing caudal and penile nerve blockade using bupivacaine in hypospadias repair surgeries in children. *Afr J Paediatr Surg*. 2011;8(3):294-7.
17. Bilgen S, Koner O, Menda F, Karacay S, Kaspar EC, Sozubir S. A comparison of two different doses of bupivacaine in caudal anesthesia for neonatal circumcision: A randomized clinical trial. *Middle East J Anaesth*. 2013;22(1):93-8.
18. Fyeface-Ogan S, Mato CN, Tobin M. A comparative study between caudal bupivacaine and bupivacaine co-administered with neostigmine for postoperative analgesia in children. *Niger Postgrad Med J*. 2014;21(1):51-6.
19. Lynch C. Depression of myocardial contractility in vitro by bupivacaine, etidocaine, and lidocaine. *Anesth Analg* 1986; 65:551
20. Constant I, Gall O, Gouyet L, Chauvin M, Murat I. Addition of clonidine or fentanyl to local anaesthetics prolongs the duration of surgical analgesia after single shot caudal block in children. *Br J Anaesth*. 1998;80(3):294-8.
21. Moeller R, Covino BG. Cardiac electrophysiologic properties of bupivacaine and lidocaine compared with those of ropivacaine, a new amide local anesthetic. *Anesth* 1990;72:322.
22. Ray M, Mondal SK, Biswas A. Caudal analgesia in paediatric patients, comparison between bupivacaine and ropivacaine. *IRnAdYa, nMJO, NADnaAeLs, tBh, IS2W00A3S; 4:7C A(4U)D: A2L75B-U2P78I bupivacaine and ropivacaine* 275.
23. Moeller R, Covino BG. Cardiac electrophysiologic properties of bupivacaine and lidocaine compared with those of ropivacaine, a new amide local anesthetic. *Anesth* 1990;72:322.
24. Bromage PR. *Epidural Analgesia*. 1st ed: WB Saunders editor. Philadelphia, 1978:p.144.