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A PROSPECTIVE DOUBLE-BLIND COMPARATIVE CLINICAL STUDY BETWEEN CAUDAL LEVOBUPIVACAINE (0.125%) WITH CLONIDINE AND ROPIVACAINE (0.125%) WITH CLONIDINE ON POST-OPERATIVE ANALGESIA IN PAEDIATRIC PATIENTS UNDERGOING INFRA-UMBILICAL SURGERY

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Abstract

Introduction: *Caudal epidural block is a reliable technique in paediatric patients but associated with various complications especially with higher concentration of drugs. We proposed a comparative study between levobupivacaine and ropivacaine at low concentration (0.125%) with clonidine at low dose (1 mcg/kg) taken as adjuvant. We aimed to see duration of post-operative analgesia, degree of motor blockade and other associated complications.* ***Materials and Methods:*** *Eighty paediatric patients (1–6 years), American society of anaesthesiologists grade I and II, undergoing infra-umbilical surgery under general anaesthesia were randomly allocated into two groups of 40 each. Group A patients were given caudal levobupivacaine (0.125%) and Group B patients were given caudal ropivacaine (0.125%). Clonidine (1 mcg/kg) was taken as adjuvant in both the groups. Post-operative pain, sedation and motor blockade were assessed at 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12 hours, 18 hours and 24 hours using Observational Pain Scale, modified Bromage Scale and four-point sedation score, respectively. Any other complications were also noted.* ***Results:*** *Motor blockade was not associated with any of the patients. Duration of post-operative sedation was similar in both the groups. Duration of post-operative analgesia was significantly higher in Group A ($p < 0.0001$). Adverse effects and complications were negligible in both the groups.* ***Conclusion:*** *Both levobupivacaine and ropivacaine can be used safely at low concentration (0.125%) taking clonidine at low dose (1 mcg/kg) as adjuvant in paediatric caudal epidural block without significant motor blockade and other complications, duration of post-operative analgesia being significantly higher in the levobupivacaine group.*

Keywords

caudal • levobupivacaine • ropivacaine • clonidine • paediatric • infra-umbilical

INTRODUCTION

It is now established that paediatric patients can appreciate pain and react to it with tachycardia, hypertension, increased neuroendocrine response and intracranial pressure. So post-operative pain relief in a child is an important concern to the anaesthesiologist not only for the patients but also to reduce anxiety in the parents.

Several methods have been employed for paediatric pain relief with different degrees of success. Regional anaesthesia technique like caudal epidural blockade is a good option, which reduces the overall intraoperative requirement of anaesthetic agents and allows more rapid return of the consciousness while providing effective post-operative pain relief with minimal sedation [1].

Various long-acting local anaesthetics have been used for paediatric caudal block with various advantages, disadvantages and adverse effects. Levobupivacaine and ropivacaine are long-acting amide local anaesthetics used for paediatric caudal block with various concentrations [2]. Profound motor block and systemic toxicity are the problems encountered with higher concentrations and volumes of local anaesthetics, which can be minimised by not only reducing the concentration and dosage of the drugs but also decreasing the duration of post-operative analgesia.

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To prolong the duration and improve the quality of intraoperative and post-operative analgesia of local anaesthetics, various drugs like opioid [3,4,5], midazolam [6], ketamine [7], neostigmine [8] and clonidine [8,9] have been used as adjuvants with various results. Clonidine, an alpha-2 adrenergic agonist, is known to produce analgesia of variable intensity and duration, which is dose dependent [10]. It has been used as an adjuvant with different dosages ranging from 1 µg/kg to 3 µg/kg in paediatric caudal block.

In this study we assessed the safety, efficacy and duration of analgesia of low volumes and concentrations of local anaesthetics with a low dose of clonidine as an adjuvant for caudal block. We undertook a comparative study between levobupivacaine (0.125%) combined with 1 µg/kg of clonidine and ropivacaine (0.125%) combined with 1 µg/kg of clonidine at a volume of 1 ml/kg in children undergoing infra-umbilical surgeries.

MATERIALS AND METHODS

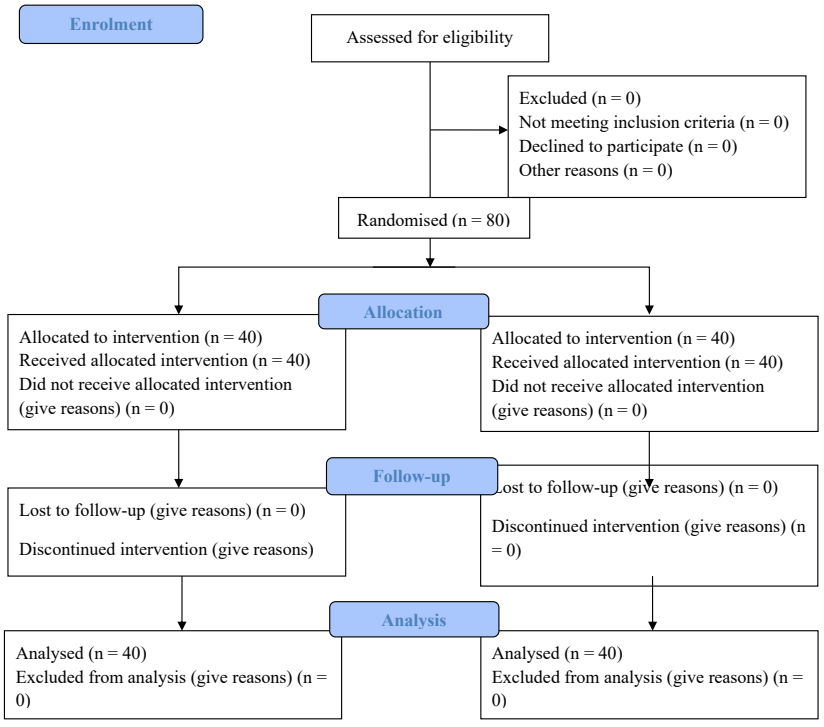
This study was conducted at Indira Gandhi Institute of Medical Sciences, Patna, after taking approval from the institutional ethical committee and getting it registered with Central Trial Registry of India (reg. no CTRI/2014/11/005193). Written informed consent was taken from parents. Study was prospective randomised one and was done from November 2014 to October 2016.

We included paediatric patients of ASA grade I and II, aged 1–06 years, undergoing infra-umbilical surgery under general anaesthesia. Children having body weight > 20 kg with pre-existing neurological or spinal disease, cardiovascular, respiratory, renal, hepatic or any other systemic disease, bleeding diathesis, infection at the site of block or allergy to local anaesthetics were excluded from the study.

Eighty patients were randomly allocated by computer-generated random number method into two groups having 40 in each. Group A patients were given 0.125% levobupivacaine (1 ml/kg) with 1 µg/kg of clonidine, whereas Group B patients received 0.125% ropivacaine (1 ml/kg) with 1 µg/kg of clonidine. Sample size was calculated using the data of a previous study done by Locatelli et al (2005) keeping alpha error 0.5 and power of study 80%.

All the patients were premedicated with atropine (0.01 mg/kg) and midazolam (0.03 mg/kg) 30 minutes before induction. After taking baseline vitals using multi-para cardiac monitor patients were induced with fentanyl (2 µg/kg) and propofol (2 mg/kg). Atracurium (0.5 mg/kg) was used for endotracheal intubation. Caudal epidural block was given in left lateral position under all aseptic precaution using 23G needle.

CONSORT Flow Diagram



The person administering drug was kept unknown to the drugs preserving the blindness of the study. Anaesthesia was maintained with oxygen (FiO_2 0.5), nitrous oxide, sevoflurane and atracurium boluses. Post-operatively neuromuscular block was reversed with the usual reversal agent (neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg)).

Vitals [eart rate (HR), mean arterial pressure (MAP) and oxygen saturation (SpO_2)] were recorded every 5 minutes intra-operatively and every 30 minutes post-operatively. Post-operative pain, sedation and motor blockade were assessed at 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12 hours, 18 hours and 24 hours using Observational Pain Scale, modified Bromage Scale and four-point sedation score, respectively. Any other complications like bradycardia, hypotension, xerostomia, retention of urine, respiratory depression, nausea or vomiting were also noted.

The duration of analgesia was defined as the time of administration of studied drug to the time of appreciation of pain. Rescue analgesic was given when observational pain score was greater than or equal to 3, with paracetamol suppository (15 mg/kg). Parameters included in Observational Pain Scale (maximum score 6) were heart rate variation from baseline (0- 10% to 20% variations, 1- 20–% to 30% variations and 2- >30% variations), mean arterial pressure variation from baseline (0- 10% to 20% variations, 1- 20% to 30% variations and 2- >30% variations) and crying (0 – not crying, 1 – crying but responds to tender loving care, 2 – crying and does not respond to tender loving care).

Statistical analysis was done using SPSS for Windows 21 (IBM, Chicago, IL, USA). Continuous variables were analysed with the unpaired t-test and categorical variables were analysed with the chi-square test and Fisher's exact test. Statistical significance was taken as $p < 0.05$.

RESULTS

Demographic profile and mean duration of surgery were comparable in both the groups (Table 1). There was no significant difference in intraoperative and post-operative heart rate and mean arterial pressure (Figures 1–4). Motor blockade was not associated with any of the patients. Duration of post-operative sedation was statistically similar in both the groups (Table 2). Duration of post-operative analgesia was found to be more in Group A, which was statistically significant ($p < 0.0001$) (Table 2 and Figure 5). Adverse effects and complications were negligible in both the groups.

Table 1. Demographic profile of both the groups

	Group A	Group B	p-value
Age, (years), mean +/- SD	3.673 ± 1.515	3.438 ± 1.503	0.497
Weight, (kg), mean +/- SD	13.495 ± 3.355	13.352 ± 3.612	0.855
Sex (M/F)	37/3	38/2	0.739
Mean duration of surgery (minutes)	55.8 ± 2.794	55.15 ± 2.675	0.788

Table 2. Duration of post-operative sedation and analgesia in both the groups

	Group A	Group B	p-value
Sedation (mins)	139.125 ± 8.312	138.375 ± 9.295	0.705
Analgesia (mins)	471.75 ± 43.494	421.5 ± 26.047	<0.0001

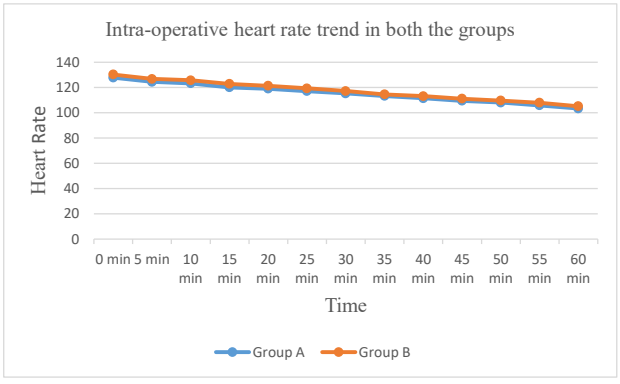


Figure 1. Comparison of intraoperative heart rate in both the groups

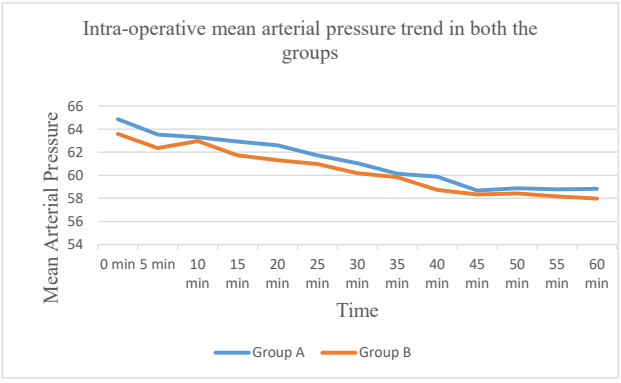


Figure 2. Comparison of intraoperative mean arterial pressure in both the groups

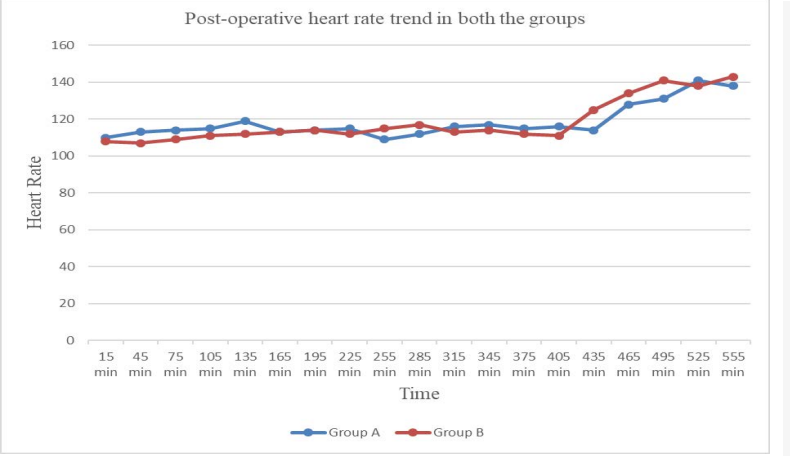


Figure 3. Comparison of post-operative heart rate in both the groups

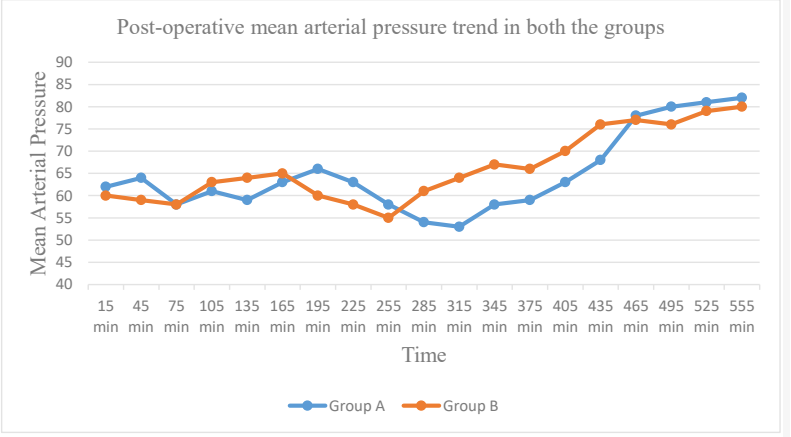


Figure 4. Comparison of post-operative mean arterial pressure in both the groups

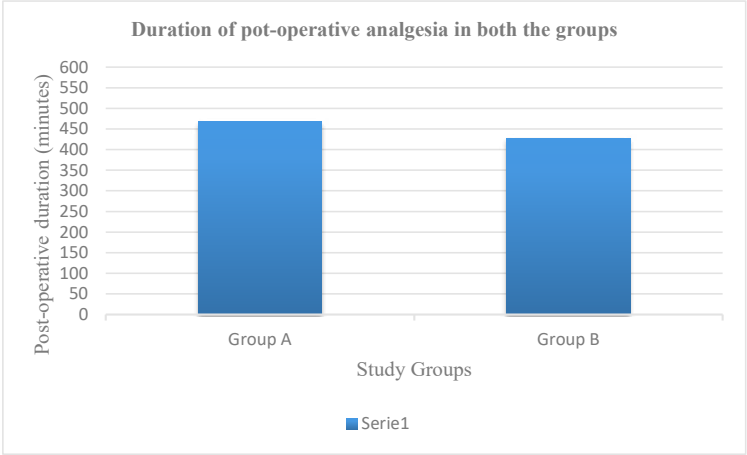


Figure 5. Comparison of post-operative analgesia in both the groups

DISCUSSION

There have been remarkable advancements in the understanding and treatment of pain in paediatric patients in the past decades. It has now been accepted that children including neonates also appreciate pain like adults. So good peri-operative analgesia is a major concern in them.

Caudal epidural block is a safe and reliable regional block technique that is used very commonly in paediatric patients, also as a part of multi-modal analgesia. Many long-acting local anaesthetics in various concentrations have been studied earlier. Levobupivacaine and ropivacaine have been studied in concentrations more than or equal to 0.25% and 0.20%, respectively [2,11,12]. Higher concentration of local anaesthetics has been found to be associated with significant post-operative motor blockade and other adverse effects. We proposed to study in infra-umbilical urological surgeries where motor blockade was not required. So we planned to study lower concentrations, that is 0.125% for both agents. Anticipating lower duration of post-operative analgesia we added clonidine, that too in lower dose (1 µg/kg), as adjuvant in both the groups, which has been used earlier in many studies [13,14,15]. Total volume of drug has been kept 1 ml/kg keeping in mind the volume of caudal space, which remains 9.5–26.6 ml [16].

Duration of analgesia was found to be 471 minutes in the levobupivacaine group, which was significantly higher than that in the ropivacaine group, 421 minutes ($p < 0.0001$). Astuto and colleagues (2003) found duration of analgesia to be 302 minutes with levobupivacaine 0.25% and 230 minutes with ropivacaine 0.25%, volume of both the agents being 1 ml/kg [12]. Arpita and co-researchers (2012) observed analgesia of 466 minutes with ropivacaine 0.2% and 975 minutes on adding clonidine (2 µg/kg) to ropivacaine 0.2%, volume of drug in both the groups being 1 ml/kg [11]. Potty and co-workers (2017) derived pain-free period of 4.24 hours with levobupivacaine 0.25% (1 ml/kg) and of 16.68 hours when clonidine (1 µg/kg) was added as adjuvant [17]. So it can be derived from our study that both the agents can be used at concentrations as low as 0.125% with clonidine as adjuvant, that too at a low dose of 1 µg/kg, to get duration of analgesia at least comparable to same agents at higher concentration without adjuvant.

Sedation was assessed using a four-point sedation score (1 – asleep, not arousable by verbal command, 2 – asleep, arousable by verbal command, 3 – drowsy or not sleeping and 4 – alert or aware. Duration of sedation was found to be 139 minutes in the levobupivacaine group and 138 minutes in the ropivacaine group, which was statistically insignificant, and results were comparable to that of Bajwa and colleagues (2010) [14]. Clonidine causes sedation due to its action on the locus coeruleus [17].

We did not find post-operative motor blockade in any of the patient, which can be taken as the benefit of using local anaesthetics at low concentration.

Intraoperative and post-operative haemodynamic parameters were statistically comparable in both the groups. Hypotension, bradycardia, dryness of mouth and retention of urine were the anticipated adverse effects. We found only one case of urinary retention in the levobupivacaine group and no other adverse effect in rest of patients. So the studied drug combination was found to be safe to use in paediatric caudal block.

Small sample size and single-centre study can be taken as limitations to this study.

CONCLUSION

We conclude from this study that both levobupivacaine and ropivacaine can be used safely at low concentration (0.125%) with low-dose clonidine (1 µg/kg) as adjuvant in paediatric caudal epidural block without significant motor blockade and other complications, duration of post-operative analgesia being significantly higher in the levobupivacaine group.

Conflict of Interest: The authors declare that there is no conflict of interest.

Acknowledgement:

Contribution Details

Contributor 1: Concepts, design, definition of intellectual content, literature search, clinical studies, experimental studies, data acquisition, statistical analysis, manuscript preparation, manuscript editing, guarantor

Contributor 2: Concepts, definition of intellectual content, literature search, clinical studies, data acquisition, statistical analysis, manuscript preparation, manuscript editing, guarantor

Contributor 3: Concepts, design, definition of intellectual content, literature search, clinical studies, data analysis, statistical analysis, manuscript preparation, manuscript editing, guarantor

Contributor 4: Literature search, clinical studies, data analysis, statistical analysis, manuscript preparation, manuscript editing, guarantor

Contributor 5: Data analysis, statistical analysis, manuscript preparation, manuscript editing, guarantor

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