Original research article

Clinical Comparative Study Between Caudal Levobupivacaine-Clonidine and Ropivacaine- Clonidine for Post-Operative Analgesia in Paediatric Subumbilical Surgery

Kumar Akash[1], Garima Gaurav[2]

[1]Senior Resident, Department of General Surgery DMCH Darbhanga

[2]Senior Resident, Department of Anaesthesia DMCH Darbhanga

Corresponding Author: Garima Gaurav

Abstract

Background and objectives: The provision of adequate analgesia is necessary after any surgery and is all the more important in children. Pain after surgery is inevitable. It has been recognized for some time that management of acute pain, especially postoperative pain, has been consistently and systematically inadequate, situation being worse in children. Bupivacaine has been for long used in caudal for post-operative analgesia but had back drop considerations of toxicity in large doses thus making it necessary to be able to use an alternative drug like Ropivacaine and levobupivacaine with lower toxicity but similar analgesic capability.

Methodology: After careful pre-anaesthetic check-up children posted for elective sub-umbilical surgeries between age groups of 3-8yrs of ASA I & II were randomly divided into 2 equal groups. Group L received levobupivacaine 0.25% 1ml/kg + 2mcg/kg clonidine and Group R received ropivacaine 0.25% 1ml/kg + 2mcg/kg clonidine. Following intrathecal administration of these drugs, intraoperative hemodynamic changes, postoperative pain relieving quality and rescue analgesia were studied. Hemodynamic parameters were monitored in the intraoperative and postoperative period. Incidence of side effects were also noted. **Conclusion:** we noted that Addition of clonidine as an adjuvant to both the groups were significantly increase in Post-operative analgesic quality with perioperative hemodynamic stability with minimum side effects. Thus making it evident the clonidine as an adjuvant to Ropivacaine and levobupivacaine can be safely used for single shot caudal block in children undergoing elective subumbilical surgeries.

Keywords: Levobupivacaine; Ropivacaine; Caudal; clonidine; adjuvant; Analgesia.

Introduction

The provision of adequate analgesia is necessary during peri-operative period and it is all the more important in children.[1] There is a well-defined pathway for sensation in the new-born infant. Nociception is associated with signs of distress even in new-born.[2]The density of nociceptive nerve endings in the skin of new-born infants is similar to or greater than that in adults.[3,4] Pain is an enigma to the whole of mankind and it has been defined by the International Association for the Study of Pain (IASP) as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."[5] Pain after surgery is inevitable. Relieving pain has been the focus of continuing human effort. However, it has been recognized for some time that the management of acute pain, especially postoperative pain, has been consistently and systematically inadequate. If anything, the situation in children has been even worse, who

have long been under-medicated for acute pain.[3]Caudal anaesthesia was first described at the turn of last century by Fernand Cathelin and Jean Anthanase Sicard in year 1895. It was predated by lumbar approach to epidural block by almost a decade. Since its first description in 1933 for paediatric urological interventions, it has evolved to become the most popular regional anaesthetic technique for use in children.[6]It prides great analgesia during surgery as well as postoperatively in subumbilical surgeries in children.[7]It is a simple technique to perform and remains corner stone in paediatric regional anaesthesia. These positive properties favor the use of Ropivacaine for caudal epidural analgesia for lower abdominal surgery in children. Levobupivacaine, a pure S-enantiomer of Bupivacaine has recently been introduced with a potentially reduced toxic profile compared to Bupivacaine. Various pharmacokinetic, animal and clinical studies not only confirm the cardiac toxicity of racemic bupivacaine but experimental studies with levobupivacaine also indicate lower cardiovascular depressant effect and central nervous toxicity. The rationale for replacing racemic bupivacaine with the s-enantiomers levobupivacaine and ropivacaine is to provide a wider margin of safety with the same analgesic efficacy and less postoperative motor block[9] Levobupivacaine and ropivacaine are associated with less risk for cardiac and central nervous system toxicity and are also less likely to results in unwanted postoperative motor blockade.[10,11] Clonidine is an alpha-2-adrenergic agonist and stimulation of presynaptic alpha-2 adrenergic receptors cause the inhibition of release of norepinephrine from the sympathetic terminals at periphery and noradrenergic neurons in CNS. These alpha 2 receptors are located on the superficial laminae of spinal cord and brainstem nuclei responsible for pain. So, analgesia may be produced at spinal and brainstem level. Clonidine like local anaesthetics also causes the blockade of conduction of nerve fibers. At spinal cord level, it also decreases the noxious afferent inputs through interaction with the alpha-2 adrenoreceptors. It also reduces the release of substance P and excitatory amino acid in spinal cord from peripheral nerve stimulation by noxious stimuli, suggesting presynaptic inhibitory mechanism. It also hyperpolarizes the neurons in the dorsal horn and render them less responsible to afferent stimuli. In addition to brainstem and peripheral site of action, neuraxial administration of clonidine inhibits the sympathetic preganglionic neurons in spinal cord resulting in hypotension. The sedative property of clonidine also reduces the requirement of hypnotics and is often a desirable feature[8]. With these background, the study was carried out to evaluate and to compare ropivacaine-clonidine and levobupivacaine-clonidine for duration of post-operative analgesia, Hemodynamic parameters and complications in caudal epidural block for lower abdominal surgery in pediatric patients

Objectives

The aim of this study is to compare the following factors in 2 groups: Group L: Levobupivacaine 0.25% 1ml/kg+ Clonidine 2mcg/kg
Group R: Ropivacaine 0.25% 1ml/kg+ clonidine 2mcg/kg, with respect to:

1. Post-operative pain relieving quality.
2. To study the intra-operative hemodynamics.
3. To record the side effects, if any

Material and Methods

Patients undergoing subumbilical surgeries at Darbhanga Medical College and Hospital Laheriasarai, Bihar. Study duration of Two years. were included in the study after obtaining written informed consent from the parents. Study was done on 60 children of physical status ASA1 and 2, aged between 3-8years, undergoing subumbilical surgeries .They were randomly included in groups having equal numbers by using a closed envelope technique

and they received caudal epidural block with the following drugs:
Group L (Levobupivacaine-Clonidine)-Levobupivacaine 0.25%1ml/kg-2mcg/kg clonidine.
Group R (Ropivacaine-Clonidine)-Ropivacaine 0.25% 1ml/kg 2mcg/kg clonidine.
After pre anesthetic evaluation on the previous day of surgery. Basic laboratory investigations was carried out. The entire procedure was explained to the patient and parents. All patients were evaluated one day prior to the surgery with a detailed general physical examination, systemic examination including airway and spine examination. Baseline parameters were recorded. Routine laboratory investigations like complete blood picture, urine routine, bleeding and clotting time, HIV, HBs Ag status and chest x-ray if needed. Informed consent for the procedure was acquired from the parent with clear fasting guidelines (solid foods stopped 6hrs before, milk 4 hours and water 2 -3 hours prior to surgery).

Premedication: (45 min. before Induction)
Oral midazolam: 0.5 mg/ kg Oral glycopyrrolate: 20 mcg/kg
EMLA cream was applied on the dorsum of hand, intravenous (i.v) line was secured with appropriate gauge iv cannula. After 45 min, patient was taken to the OT. Preoxygenation was done with 100% O2 through Jackson-Rees circuit for 3-5 min, followed by induction with intravenous injection of propofol 2mg/kg, fentanyl 2mcg/kg, injection atracurium 0.5mg/kg.
During intra-operative period adequacy of analgesia assessed by hemodynamic stability. An increase or decrease in heart rate >15% from the baseline values considered as tachycardia or bradycardia. Similarly, an increase or decrease in mean arterial pressure >15% from baseline considered as hypertension or hypotension.
The assessment was done within 15s in the postoperative period, score between 0-3- pain free situation4 and above- analgesic requirement with increasing urgency as scores increase.

Inclusion criteria
Patients of either sex
Patients of age between 3-8 yearsPatients of ASA status I & II
Patients scheduled for lower abdominal surgeries with written informed consent.

Exclusion criteria
Patients with known hypersensitivity to local anesthetics. Grossly abnormal sacrum anatomy, Bleeding diathesis, Pre-existing neurological, neuromuscular disease. Local sepsis. ASA > II. Mentally retarded child

All values were expressed as mean the standard deviation and a p value less than 0.05 will be considered as statistically significant

Results

Table 1: Distribution of study group based on their age

GROUPS	N	Mean age	Std. Deviation	Minimum age	Maximum Age
ROPIVACAINE AND CLONIDINE	30	5.47	1.46	3	8
LEVOBUPIVACAIN EAND CLONIDINE	30	5.23	1.30	3	8

TOTAL	60	5.35	1.38	3	8

The age distribution of patients among the 2 groups. The men age is 1.46 years in ropivacaine and clonidine and 1.30 years in levobupivacaine and clonidine.
There is no significant difference in age of patients in both the groups (p>0.05). Both the groups are similar with respect to age distribution.

Table 2: Difference in mean age between the two groups

GROUPS	N	Mean age	Std. Deviation	t value	p value
ROPIVACAINE AND CLONIDINE	30	5.47	1.46	0.6724	0.5040
LEVOBUPIVACAINE AND CLONIDINE	30	5.23	1.30		

gender distribution in both the groups. There is no significant difference in gender distribution in both the groups (p>0.05).

Table 3: Difference in mean weight of the patients between the two groups

GROUPS	MEAN	STANDARD DEVIATION	t VALUE	p VALUE
ROPIVACAINE AND CLONIDINE	13.73	2.48	0.0484	0.9616
LEVOBUPIVACAINE AND CLONIDINE	13.70	2.32		

weight distribution of patients. The mean weight is 13.73kg in Ropivacaine and clonidine group and 13.70kg in levobupivacaine and clonidine group. There is no significant difference in body weight of patients in both the groups (P>0.05). the mean duration of analgesia in both the groups. The mean of caudal analgesia was 661.17 minutes in ropivacaine and clonidine group and 662.83 minutes in levobupivacaine and clonidine group. There is no statistically significant difference between the two Groups were observed (P>0.05). intraoperative mean arterial pressure changes in both the groups. The mean arterial pressure was 66.66, 65.27, 62.67, 62.3, 62.25 mmHg in ropivacaine and clonidine group and 66.8, 63.97, 62.4, 61.47, 59.71mmHg in levobupivacaine and clonidine group. There is no statistically significant difference in mean arterial pressure in both the groups (p>0.05) postoperative systolic blood pressure in both the groups. The mean systolic blood pressure was 87.27, 90.07, 91.13, 93.73, 94.33, 95.43, 95.67, 90.07, 91.13, 93.73, 94.33, 95.43, 95.67mmHg in ropivacaine and clonidine group and 88.9, 0.1, 92.07, 94.1, 95.87, 96.23, 95.57, 90.1, 92.07, 94.1, 95.87, 96.23, 95.57 mmHg in levobupivacaine and clonidine group. There is no statistically significant difference in mean diastolic blood pressure in both the groups (p>0.05) shows postoperative SpO2 in both the groups. There is no statistically significant difference in mean diastolic blood pressure in both the groups (p>0.05) incidence of side effects in both the groups. Only 2 children in each group had sedation. Other side effects like pruritus, urinary retention, respiratory depression, hypotension, bradycardia were not observed in both the groups.

Discussion

The study population was randomly divided into 2 groups by closed envelop method of 30 each who received caudal epidural block with the following drugs: Group L (Levobupivacaine-clonidine)-Levobupivacaine 0.25% 1 ml/kg with 2mcg/kg clonidine. Group R (Ropivacaine-clonidine)-Ropivacaine 0.25%1ml/kg with 2mcg/kg clonidine. The

hypothesis made before starting the study was that the addition of clonidine to ropivacaine and levobupivacaine will prolong the duration of analgesia when compared to plain drugs and to compare duration of analgesia and side-effects of the study drugs. Caudal anaesthesia is one of the most popular regional block in children. This technique is a useful adjuvant to general anesthesia and for providing post-operative analgesia after infra-umbilical surgeries. The quality and level of caudal blockade is dependent on the dose, volume and concentration of the injected drug. Bupivacaine, levobupivacaine and ropivacaine are widely utilised in caudal block. As established by several authors, metameric spread depends on volume of the injected mixture, while the desired density of the block depends on the concentration of the anaesthetic. However, concentration must be established in order to avoid anaesthetic toxicity. The Levobupivacaine and ropivacaine are associated with less risk for cardiac and central nervous system toxicity and are also less likely to results in unwanted postoperative motor blockade.[10,11] The rationale for replacing racemic bupivacaine with the s-enantiomers levobupivacaine and ropivacaine is to provide a wider margin of safety with the same analgesic efficacy and less postoperative motor block.[9] The main disadvantage of caudal anesthesia is shorter duration of action after a single injection of local anesthetic solution. The use of caudal catheters to administer repeated doses or infusion of local anaesthetic solution is not popular, partly because of concern about infection. Prolongation of caudal analgesia using single shot technique has also been achieved by the addition of various adjuvants. The additives can be divided as non-opioids (clonidine, ketamine, s-ketamine, midazolam, neostigmine) and opioids (morphine, fentanyl, buprenorphine, tramadol). The use of opioids significantly prolongs the duration of analgesia but carries with it a number of unpleasant side-effects (nausea, vomiting, pruritus, urinary retention) as well as the risk of late respiratory depression. In a retrospective review of 138 children given caudal morphine 0.07mg/kg, there were 11 cases of clinically important hypoventilation (8%). Schnabel et al in there meta-analysis of 13 Randomised Clinical Trials on the efficacy and adverse effects of ketamine as an additive for paediatric caudal anaesthesia found an increased incidence of PONV. They also found sedation and hallucination as adverse effects though they were rare. Locatelli et al. found that addition of 0.5mg/kg of s-neostigmine to caudal levobupivacaine 0.175% significantly decreases the need for rescue analgesia in children undergoing abdominal and urological surgery compared with levobupivacaine 0.2% alone. Ingelmo P et al. in there study about relative analgesic potencies of levobupivacaine and ropivacaine for caudal anaesthesia in children found that in children receiving 1 MAC of sevoflurane, there were no significant difference in the ED for caudal levobupivacaine and ropivacaine. The potency ratio at ED was 0.92 and 0.89 at ED, indicating that caudal levobupivacaine and ropivacaine have a similar potency. Klimscha et al., had studied the effectiveness of caudal clonidine in potentiating the post-operative analgesic effect and found that in small children (mean age group 3 years) who underwent an elective lower abdominal day care surgeries, the addition of clonidine 1-2mcg/kg to ropivacaine 0.25% significantly prolonged the median duration of analgesia and reduced the total dose of post-operative analgesic compared with ropivacaine alone or ropivacaine plus epinephrine 5mcg/ml ($p<0.05$). There is no statistically significant difference in heart rates in both the groups of our study both intra-operatively and post-operatively. This consistent with studies conducted by Parameshwari A et al., Koul A et al., Shulka U et al., where they found no significant changes in heart rate both intra-operatively and post-operatively.

Mean arterial pressure: There is no statistically significant difference in the mean arterial pressure in both the groups of our study both intra-operatively and post- operatively. This consistent with studies conducted by Parameshwari A et al., Koul A et al., Shulka U et al.[14],

where they found no significant changes in mean arterial pressure both intra-operatively and post-operatively. The mean sedation scores in the postoperative period between the groups were comparable and not statistically significant ($P > 0.05$). There was no incidence of sedation in group L which coincides with studies conducted by PottiL Ret al., There was no incidence of sedation in group R which coincides with Laha A et al.[12], Manickam A et al.[13], Parameswari A et al., Epidural clonidine has been associated with sedation reflecting systemic absorption and action on higher centers. A delayed sedation might as well as be due to the cephalad migration of the drug in the cerebrospinal fluid. Sedation is a desired effect in most children, thus reducing the requirement of sedatives and anxiolytics in the postoperative period. However, in our study, the mean sedation scores in both the groups were comparable. We used clonidine in a dose of 2 μg/kg and this might explain the sedation in our study groups. Adverse effects related to clonidine like hypotension and bradycardia were not observed in our study which is again consistent with the study conducted by Koul et al, parameshwari A et al[16], Potti R L et al, Bajwa SJ et al[15], Ivani G et al[17].

Conclusion

In conclusion, this study suggests that addition of clonidine (2mcg/kg) as an adjuvant to 0.25% ropivacaine (1ml/kg) and 0.25% levobupivacaine (1ml/kg) through caudal route increased duration and quality of analgesia without perioperative hemodynamic instability and any significant side-effects.

References

1. Duggan J, Drummond GB. Activity of lower intercostal and abdominal muscles after upper abdominal surgery. AnesthAnalg 1987; 66: 852.
2. M Fitzgerald, N McIntosh Pain and analgesia in the newborn Arch Dis Child 1989;64:4 Spec No 441-443doi:10.1136/adc.64.4_Spec_No.441
3. Choonara, I.A. Pain relief. Arch Dis Child. 1989; 64:1101 –1102.
4. Anand KJ1, Hickey PR Pain and its effects in the human neonate and fetus. N Engl J Med. 1987 Nov 19; 317(21):1321-9.
5. IASP Subcommitte on Taxonomy. Pain terms; a list of definition & notes on usage. Pain 1980; 8:249-52
6. Campbell MF. Caudal anesthesia in children. J Urol. 1933; 30:245–9.
7. Wolf AR1, Hughes D, Wade A, Mather SJ, Prys -Roberts C. Postoperative analgesia after paediatricorchidopexy: evaluation of a bupivacaine -morphine mixture. Br J Anaesth. 1990 Apr; 64(4):430-5.
8. Ankith Agarwal, R.K.Verma, ShivikaShrivastava. Ropivacaine the latest local anaesthtic in Indian market: J Anaesthclinpharmacol: 2010: 26 (2);223-228.
9. Eisenach JC, De Kock M, Klimscha W. Alpha (2)-adrenergic agonist for regional anesthesia: A clinical review of clonidine (1984-1995) Anesthesiology.1996;85:655-74.
10. Bonnet F, Boico O, Rostaing S, Loriferne JE, Saada M. Clonidine- induced analgesia in postoperative patients: epidural versus intramuscular administration. Anesthsiology. 1990; 72:423-7
11. Eisenach J, Detweiter D, Hood D. Haemodynamic and analgesic action of epidurally administered clonidine. Anesthesiology.1993;78:277-87.
12. Laha A, Ghosh S, Das H. Comparison of caudal analgesia between ropivacaine and ropivacaine with clonidine in chidren: A randomized controlled trial. Saudi J Anaesth.2012;6(3):197-200
13. Manikam A, Vakamudi M, Parameswari A ,Chetan C .Efficacy of clonidine as an adjuvant to ropivacaine for caudal analgesia in children undergoing subumbilical surgery.

J AnaesthesiolClinPharmacol.2012;28(2):185-189.
14. Shukla U ,Prabhakar T, Malhotra K .Postoperative analgesia in children when using clonidine or fentanyl with ropivacaine given caudally . J Anaesthesiol Clin Pharmacol. 2011;27(2):205-210.
15. Bajwa SJS, Kaur J, Bajwa SK, Bakshi G , Singh K, Panda A. Caudal ropivacaine-clonidine: A better post-operative analgesic approach. Indian J Anaesth 2010;54:226-30.
16. ParameswariA ,Dhev AM , Vakamudi M. Efficacy of clonidine as an adjuvant to bupivacaine for caudal analgesia in children undergoing sub-umbilical surgery. Indian J Anaesth.2010; 54(5):458-463.35.
17. Ivani G, DeNegri P, Conio A, Grossetti R, Vitale P, Vercellino C, et al. Comparison of racemic bupivacaine, ropivacaine, and levo-bupivacaine for pediatric caudal anesthesia: Effects on postoperative analgesia and motor block. Reg Anesth Pain Med. 2002;27:157–61.