Evaluation of Postoperative Analgesia Using Clonidine as an Adjuvant with Caudal Bupivacaine in Paediatric Patients Posted for Infraumbilical Surgery

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ABSTRACT

Introduction: Caudal block epidurally is a highly popular means of administering pain relief to children undergoing infra-umbilical surgeries. Addition of clonidine, a centrally acting alpha 2 agonist as an adjuvant to caudal Bupivacaine has added advantages of providing prolonged postoperative analgesia and also, thus reducing the no. of doses of postoperative rescue pain relief agents.

Objective: To compare the efficacy and safety of caudally administered clonidine as an adjuvant to bupivacaine.

Methods: The study will be carried out with 40 patients in each group randomly allocated using computer-generated software, posted for infraumbilical surgeries between the age group 2 years to 7 years, ASA grade I and II. Children less than 2 yrs or more than 7 yrs, ASA grade III-IV, in case of any allergy to drugs involved in this study, serious cardiac or respiratory disease, history of developmental delay or mental retardation, caudal block site infection if present, then it will be excluded from the study. Group B (control group) Caudal epidural with 0.25% bupivacaine 1 ml/kg + 1 ml Normal saline (NS) Group C (study group) Caudal epidural with 0.25% bupivacaine 1ml/kg with clonidine 1 ug/kg+1ml

Results: It is expected that the duration and quality of postoperative analgesia in group C will be prolonged as compared to that in group B. Haemodynamic changes with no significant difference between the 2 groups are expected. Also minimal or no adverse effects are anticipated.

Conclusion: We expect to conclude that caudally administered clonidine, in a dose of one microgram /kg as an adjuvant to 0.25% bupivacaine 1 ml/kg, will prove to be efficacious in providing prolonged analgesia both intraoperatively and postoperatively. Also, we hope that this addition reduces the requirement of postoperative rescue analgesia and its associated side effects.

Key Words: Caudal block, Neuraxial block, Caudal epidural

INTRODUCTION

Pain can be defined as "An unpleasant sensory and emotional experience related with actual or potential tissue damage, or described in terms of such damage." (International Association for the study of pain).¹ Pain that children and infants feel often goes unnoticed and is also neglected because they are unable to complain about it.²⁻⁴ Surgery not only causes post-operative pain but also causes bodily responses to stress. The stress response is carried by hypothalamic-pituitary-adrenal and sympathoadrenal system. This causes an increase in the

release of catecholamines and catabolic hormones while the decrease in the secretion of anabolic hormones. Children get significantly less analgesic agent irrespective of the degree of pain because continuous administration of opioid analgesics agents will put them at increased risk for respiratory depression and sedation.^{4,5} Pain management, postoperatively is necessary for paediatric age group because if it is not managed properly it may lead to increased morbid conditions and also mortality.⁵ Anaesthesiologists must be very cautious and must use pain killers very carefully for infants and children.^{6,7} A multimodal method must be followed to

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manage acute postoperative pain in paediatric patients. Neuraxial blocks are almost devoid of significant side effects and can be endured by young children without much difficulty. Thus, they have come to be used routinely in surgeries below the umbilicus in children.

Caudal block is the most common method of neuraxial block that is used in lower abdominal and urological surgeries.^{7,8} It is very easy and safe to perform. Caudal anaesthesia can also be combined with general anaesthesia to decrease the need for inhalational and opioid agents. This method also allows for rapid recovery with very few incidences of nausea and vomiting postoperatively. Also patients need not follow NBM for a longer duration. Complications rarely occur. But, giving bupivacaine alone, provides the short duration of pain relief postoperatively. So to extend the duration of pain relief post operatively Bupivacaine can be combined with various adjuvants.

Clonidine is a centrally acting α_2 agonist drug,⁸ and acts in a similar way to local anaesthetics. There are 3 possible mechanisms by which it can act. First, clonidine blocks Ad and C fibres due to an increase in K^+ conductance in neurones, thus blockade due to Local Anaesthesia(LA) increases.⁹ Second, local vasoconstriction caused by clonidine, which might decrease LA spread and its elimination around neural structures. This is caused due to local anaesthetic agents' action on post-synaptic α_2 receptors.¹⁰ Third, clonidine when added as an adjuvant to LA for a neuraxial blockade or used in peripheral blockade deepens and increases analgesia.¹¹ Clonidine is an agonist at α_2 adrenergic site in spinal also produce an analgesic effect by stimulating cholinergic neurones in the spinal cord which results in Ach discharge.¹²

A caudal epidural block is the utmost common type of regional anaesthesia used in paediatric patients.⁷ It yields strong relief from pain perioperatively. Further, if it is added along with analgesics, it gives tremendous analgesia with least adverse reaction. This makes it very appropriate for ambulatory surgery. This procedure is considered simple and safe. The duration of the block can be easily increased by inserting epidural catheters.

Indications

In children less than 20 kg approximately six years of age Caudal blocks can be used to block dermatomes T10-S5 making it acceptable for infra umbilical surgeries like hypospadias repair, herniotomy, orchidopexy. But, in case of older children, it can reliably block only sacral dermatomes.¹³

Complications

The caudal blockade is relatively safe. Serious complications like accidental intravenous injection (1:10 000), abscess, hematoma are very rare. Minor complications like retention of urine, leg weakness, and unsteady gait due to loss of propri-

ception are common. The failure rate is very low and may due to unusual anatomy, if the operator is not having enough experience or if the choice of block was inappropriate.

In our study, we have compared the efficacy of Bupivacaine and bupivacaine combined with clonidine for postoperative analgesia in paediatric population undergoing infraumbilical surgeries.

SAMPLE SIZE CALCULATION AND STATISTICAL ANALYSIS:

Sample size has been derived using the formula:

$$n = \frac{2(Z_{\alpha} + Z_{1-\beta})^2 \sigma^2}{\Delta^2}$$

$Z_{\alpha} = 1.96$ (Z table) 5% type I error

$Z_{1-\beta} = 0.8416$ (Z table) at the power of 80%

σ = Standard Deviation

Δ^2 = Effective Size

By adding clonidine at extubation, 45 % patients didn't require rescue analgesia.

$$n = \frac{2(1.96 + 0.8416)^2 (0.72)^2}{(0.45)^2}$$

= 40.6/arm

n=40.6

There will be 80 patients for the study and they will be randomly distributed into two Groups; Group B And Group C. Each Group will have 40 patients.

Group B(control group) – Caudal epidural with 25% bupivacaine 1 ml/kg + ONE ml NS

Group C (study group)- Caudal epidural with 25% bupivacaine 1 ml/kg with clonidine 1 μ g/kg+1ml NS

STATISTICAL ANALYSIS

Descriptive and inferential statistics will be used for data analysis, with the use of student's paired t-test, chi-square test, and unpaired t-test. The analysis will be done by software SPSS 22.0 version and Graph Pad Prism 6.0 version and $p < .05$ will be considered as the level of significance

MATERIALS AND METHODS

This is a prospective, observational study and will be conducted in the department of Anaesthesia at JNMC, Sawangi (M) Wardha following the guidelines and permission of the institutional ethical review board. The study will be carried out with 40 patients in each group randomly allocated using computer-generated software, posted for infra umbilical surgeries between the

age group 2 years to 7 years, ASA grade I and II. Children less than 2 years or more than 7 years, ASA grade III-IV, with any drug allergy involved in the study, serious cardiac or respiratory disease, any history of delay in mental development, any caudal block site infection will be excluded from the study.

Group B (control group) –caudal epidural with 0.25% bupivacaine 1 ml/kg +1 ml Normal saline (NS)

Group C (study group)–caudal epidural with 0.25% bupivacaine 1ml/kg with clonidine 1µg/kg+1ml

Procedure

A pre-anaesthetic check-up will be done for all the patients a day before surgery. They will be kept nil by mouth for 6 hours. Written informed consent will be taken from the patients. An intravenous catheter attached with a venoline will be secured in the preoperative room itself. Inj. Glycopyrrolate 0.005mg/kg will be given and the patients will be sedated using 0.5mg /kg Midazolam in the pre-operative room itself. This is done for their co-operation. In the operation theatre, patients will be monitored with five lead electrocardiography, Oxygen saturation(SpO₂), End tidal carbon dioxide (ETCO₂), Non invasive blood pressure(NIBP) and Temperature, if the probe can be available. Patients will be anaesthetized using standard inhalational induction with sevoflurane in oxygen, the neuromuscular agent will be given following that to simplify endotracheal intubation. After that left lateral decubitus position will be given and using 22 G needle single dose caudal block will be given using 22G needle. Group B will receive .25% (1 ml/kg) of bupivacaine and Group C will receive bupivacaine. 25 % (one ml / kg) with clonidine one µ / kg in Normal Saline one ml. **Analgesia will be purposefully avoided.**

General anaesthesia will be maintained with 50% Oxygen(O₂)50% Nitrous oxide(N₂O) and inhalational anaesthetic agents like sevoflurane. Oxygen saturation (SpO₂), Heart Rate(HR) and Mean arterial Pressure(MAP) will be marked before the surgery and then for the 1st 30 minutes and after that each 5 min and then each 15 min until the surgery ends. The time of anaesthesia (from the time of induction of anaesthesia), time of emergence (the period since the completion of operation till the opening of the eyes on shouting the patient's forename), late recovery from anaesthesia (after the surgery if 20 min elapsing time is present to shift patient out of OT), paediatric observational Face, legs, Activity, Cry and Consolability(FLACC)¹⁴ pain scale was used with its score ranging from 0–10 (Table 1), each study patient's intensity of pain will be assessed upon arrival in the preoperative room and during discharge from the postoperative room. Then every 4 hours for the first 12 hours after the surgery is over, heart rate, respiratory rate, FLACC score will be monitored at an interval of 30 minutes till 4 hours then every 4 hours for the 12 hours and then at 24 hours. If the FLACC

pain scale score was noted at any time to be 4 or more, injection paracetamol 10 mg/kg will be given intravenously as rescue analgesia. Total doses of rescue analgesics will be noted in both the groups at the end of 24 hours. Side effects during the study period like bradycardia, hypotension, urinary retention will be monitored. Bradycardia will be treated with injection Atropine and hypotension with Phenylephrine (Table 1).

Table 1: Flacc Pain Scale ¹⁴

CATEGORY	SCORE		
	0	1	2
Face	Smile No specific expression	grimace or frown, withdrawn, disinterested	Recurrent frown, gritted jaw, trembling chin
Leg	calm and comfortable	Anxious, agitated, apprehensive	Legs are drawn up
Activity	Quiet in the supine position, easily moving.	Struggling, moving here and there, apprehensive	Rounded, stiff, or jolting
Cry	Not crying	Sighs or cries intermittently	progressively cries shrieks or snuffles complains repeatedly
Controllability	Satisfied, peaceful	Calmed by intermittent touches, hugs, or speaking to, easily distracted	Hard to comfort

*Manickam A, Vakamudi M, Parameswari A, Chetan C. Efficacy of clonidine as an adjuvant to ropivacaine for caudal analgesia in children undergoing sub umbilical surgery. J Anaesthesiol Clin Pharmacol. 2012;28:185-89

Assessment of the scale:

0 = calm and contented

1 - 3 = slight uneasiness

4 - 6 = moderate ache

7 - 10 = severe distress / ache

TECHNIQUE

The caudal epidural regional block will be performed in a complete aseptic manner. By palpating PSIS, sacral hiatus will be identified. The thumb and middle fingers of the anaesthesiologists will be placed on the PSIS. Then an equilateral triangle will be formed using the index finger and hence, the sacral cornua and hiatus will be identified. A twenty-two Gauge intricate will be used because the intricate will act

like a blocker and prevent the spilling of skin in the epidural space, it will produce a better give away on going through the sacrococcygeal membrane and the proceeding of the cannula above the needle will help to check correct placement, the easy cannula will be less probable to puncture artery, vein or dura and, because of the size of the intricate is smaller, it will be easier to check intravenous placement or location in the subarachnoid place. placement, any resistance that will be encountered during injection of the local anaesthetic will indicate that the cannula is not properly placed;

Caudal epidural analgesia will be confirmed by either the WHOOSH TEST or Nerve stimulation test.

EXPECTED RESULT

We expect that caudal clonidine as an addition caudal bupivacaine will result in haemodynamic changes which will be clinically insignificant and with lesser adverse effects. It is also expected to have better quality and longer duration of pain relief after the surgery with a substantial decrease in the total no. of rescue analgesic agents requirement in comparison with bupivacaine alone group.

DISCUSSION

Postoperative pain in children can often go unnoticed. Clonidine when used via epidural route can have significant analgesic action. Thus, we have chosen 1 µg/kg of clonidine combines with 0.25% bupivacaine (1 ml/kg) for prolongation of the caudal epidural block in paediatric age group going through infra umbilical surgeries. It is expected that caudally administered clonidine as an additive to bupivacaine may prolong the period of analgesia postoperatively with a lesser chance of hypotension, bradycardia and respiratory depression and less of other side effects. Even though the exact mechanism for the analgesic effect of clonidine is not known, a few theories have been postulated. Clonidine is a centrally acting α-2 agonist which after crossing the BBB combines with α-2 adrenoreceptors in spinal and supraspinal sites, thus producing analgesia. It also suppresses peripheral sensory A-delta and C nerve fibre neurotransmission and spinal cord nociceptive neurons. Clonidine 1 microgram/kg in combination with 0.1% ropivacaine as compared to plain. Ropivacaine provides increased periods of analgesia with no motor blockade and sedation. We expect a similar result after finishing our study. Our study also agrees with a study conducted by Aruna et al.¹⁵ were in the period of pain relief in the group which received clonidine was ten hours while the group that received bupivacaine alone had analgesia only for 4.5 hours.

Further, in our study, it is anticipated that the group receiving a combination of clonidine and bupivacaine will require less-

er no. of postoperative rescue analgesic agent as compared to the group receiving bupivacaine alone similar to previous study.¹⁶ In their study too, no. of doses of postoperative rescue pain relief agents required were considerably lower in the group that received both bupivacaine and clonidine than Palin bupivacaine group similar to study by Parmeshwari et al.¹⁵ The efficacy of caudally administered clonidine (1 µg/kg), as an adjuvant to caudal bupivacaine for postoperative pain relief in paediatric patients undergoing infafrumbilical surgeries was successfully proved.¹⁷ We also expect to obtain similar results in our study. Moreover, in our study, we are using the caudal epidural block as the means of providing pain relief intraoperatively as well as postoperatively. Caudal analgesia is one of the most appropriate and safest methods of providing analgesia to children undergoing infafrumbilical surgeries.⁷

CONCLUSION

From the above study, we expect to conclude that caudally administered clonidine, (1 µ/kg) as an adjuvant to 0.25% bupivacaine 1 ml/kg, will prove to be efficacious in providing prsolonged analgesia both intraoperatively and postoperatively. Also, we hope that this addition reduces the requirement of postoperative rescue analgesia and its associated side effects.

REFERENCES

1. International Association for the study of pain, subcommittee on taxonomy. Pain terms: a list with definitions and notes on usage. Pain 1979;6:249-252.
2. Anand KJ, Craig KD. New perspectives on the definition of pain. Pain. J Int Asso Study Pain 1996;67(1):3-6.
3. Walco GA, Cassidy RC, Schechter NL. Pain, hurt, and harm-the ethics of pain control in infants and children. N Engl J Med 1994;331(8):541-4.
4. Cummings EA, Reid GJ, Finley GA, McGrath PJ, Ritchie JA. Prevalence and source of pain in pediatric inpatients. Pain 1996 ;68(1):25-31.
5. Anand KJ, Hickey PR. Halothane-morphine compared with high-dose sufentanil for anaesthesia and postoperative analgesia in neonatal cardiac surgery. N Engl J Med 1992;326(1):1-9.
6. Taksande K. Comparative study between caudal bupivacaine and caudal midazolam for postoperative analgesia in paediatric patients. J Datta Meghe Inst Med Sci Uni 2018; 4(3): 15.
7. Rajan R, Gosavi SN, Dhakate V, Ninave S. A comparative study of equipotent doses of intrathecal clonidine and dexmedetomidine on characteristics of bupivacaine spinal anaesthesia. J Datta Meghe Inst Med Sci Uni 2018;13(1):4.
8. Butterworth JF, Strichartz GR. The α2-adrenergic agonists clonidine and guanfacine produce tonic and phasic block of conduction in rat sciatic nerve fibres. Anesth Analge 1993;76(2):295-301.
9. Gaumann DM, Brunet PC, Jirounek P. Clonidine enhances the effects of lidocaine on C-fiber action potential. Anesth Analge 1992;74(5):719-25.

10. Nagurib M, Yaksh TL. Antinoceptive effects of spinal cholinesterase inhibition and isobolographic analysis of the interaction with mu and alpha 2 receptor systems. *Anesthesiology* 1994;80:1338-48.
11. Krane EJ, Dalens BJ, Murat I, Murrell D. The safety of epidurals placed during general anaesthesia. *Regional anaesthesia Pain Med* 1998;23(5):433.
12. Giaufre E, Dalens B, Gombert A. Epidemiology and morbidity of regional anaesthesia in children: a one-year prospective survey of the French-Language Society of Pediatric Anesthesiologists. *Anesth Analg* 1996;83(5):904-12.
13. Willis MH, Merkel SI, Voepel-Lewis T, Malviya S. FLACC Behavioral Pain Assessment Scale: a comparison with the child's self-report. *Pediatric Nurs* 2003;29(3):195.
14. Manickam A, Vakamudi M, Parameswari A, Chetan C. Efficacy of clonidine as an adjuvant to ropivacaine for caudal analgesia in children undergoing subumbilical surgery. *J Anaesthesiol Clin Pharmacol* 2012;28:185-9.
15. Cook B, Grubb DJ, Aldridge LA, Doyle E. Comparison of the effects of adrenaline, clonidine and ketamine on the duration of caudal analgesia produced by bupivacaine in children. *Br J Anaesthe* 1995;75(6):698-701.
16. Priolkar S, D'Souza SA. Efficacy and safety of clonidine as an adjuvant to bupivacaine for caudal analgesia in paediatric infra-umbilical surgeries. *J Clin Diagn Res* 2016;10(9):UC13.
17. Nishikawa T, Dohi S. Clinical evaluation of clonidine added to lidocaine solution for epidural anaesthesia. *Anesthesiology* 1990;73(5):853-9.