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Original Research Article

A Study of the Effect of Caudal Epidural Neostigmine for Relief of Post Operative Pain in Children Undergoing Lower Abdominal General Surgical Procedures

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Abstract

Background: Pain has become the fifth vital sign and is now a critical focus of the patient. The relief of pain has always been part of anaesthesiologist's role. In the immediate postoperative period and extending beyond post anaesthesia care unit. Materials and methods: The study population consisted of 60ASA I and II Children in the age group of 2 years to 8 years admitted to undergoing elective lower abdominal general surgical procedure at our hospital.

Conclusion: We conclude that caudal epidural analgesia using a combination of 0.25% bupivacaine 0.5ml/kg and neostigmine (2µg/kg) significantly prolong the postoperative analgesia when compared to 0.25% bupivacaine alone in children undergoing lower abdominal general surgical procedures without any significant increase in side effects.

Keywords: Epidural Analgesia, Neostigmine.

Introduction

Pain has become the fifth vital sign and is now a critical focus of the patient. The relief of pain has always been part of anaesthesiologist's role. In the immediate post operative period and extending beyond post anaesthesia care unit. There is also increasing evidence that optimal pain management can impact outcome beyond the intra operative period. Alleviation of post operative pain may continue to improve clinical outcomes, hasten recovery, facilitate early mobilization and return to daily living. The treatment and alleviation of pain is a basic human right. Children suffer pain in the same way as adults though they may be unable to describe the pain or their subjective experiences. Unfortunately even when their pain is obvious children frequently receive no treatment or inadequate treatment. PAIN is a perception that is far more complex than simple transmission of information along nerve pathways to brain. It consists of component of transmission of pain sensation, a component of processing and evaluation by higher centers of brain and a component of reaction to sensation. The response to PAIN in children consists of behavioral, psychological and social changes. The cognitive ability, child's trust of caregivers and previous painful experiences will influence this response.

The manner in which the family reacts to the stress of a child's pain will also influence the response to pain. Appropriate pain management is of great importance when dealing with children, because the way the child is treated may influence the way he/she deals with pain for rest of his /her life. Untreated Pain can lead to physiologic complications, psychological distress, and personality changes in developing children, family disruption, interruption of hospital routine and prolongation of hospitalization with resultant increased costs. In addition social withdrawal, temper tantrums and demanding behaviour are also seen in these children. Children withdraw from their environment and stop participating in interpersonal interactions. Various pharmacological agents and analgesic delivery systems have been employed to avoid under-treatment of pain in children. Many children will withdraw or deny their pain in an attempt to avoid yet another terrifying and painful experience-the intramuscular injection or "shot". Genito urinary surgery is generally associated with considerable pain of long duration. Caudal extradural block with bupivacaine ensures satisfactory analgesia in the initial post operative period only, and becomes ineffective once the block wears off. Various methods have been devised to extend the duration of regional analgesia with local anaesthetics. Like placement of a catheter and using adjuvants like, clonidine, tramadol, ketamine and opioids. The placement of a catheter possess an inherent risk of infection and delays mobilization. The use of ketamine, clonidine and opioids is limited because of potential side effects such as sedation, respiratory depression, nausea and vomiting. The role of neostigmine as an analgesic administered by the extra dural route is now well established in children and adults. Co administration of caudal neostigmine in a dosage of 2µg/kg with bupivacaine or ropivacaine has been found to prolong analgesia without any adverse effect.

Objectives

A study of the effect of caudal epidural neostigmine for relief of post operative pain in children undergoing lower abdominal general surgical procedures.

Material and Methods

The study population consisted of 60ASA I and II Children in the age group of 2 years to 8 years admitted to undergo elective lower abdominal general surgical procedure at our hospital, RIMS Ranchi, Jharkhand. Study duration of Two years.

Exclusion criteria consisted of local infection in the caudal region, bleeding diathesis, preexisting neurological or spinal diseases and congenital anomaly of the lower back. The study was approved by the institutional ethics committee.

A written consent was obtained from the parents after they were informed about the procedure to be performed, to give postoperative analgesia to their child. All Children were kept fasting (NPO for 6 hours) and unpremeditated. They were received by an anaesthesiologist inside the operating room half an hour before surgery. Thereafter, baseline cardiorespiratory parameters such as pulse rate, systolic blood pressure, ECG, respiratory rate and (SpO_2) were recorded and monitored continuouslyuntil extubation.

Anaesthesia was induced by inhalation of halothane at increasing concentrations in N_2O and oxygen mixture. Intravenous line secured after achieving adequate depth of anaesthesia. Thiopentone was used as the induction agent. Orotracheal intubation was performed with an appropriate size uncuffed endotracheal tube. No opioids or benzodiazepines were used intraoperatively. The patients were placed in left lateral position with hips and knees flexed. The children were allocated into two groups of each 30 patients, A 22G hypodermic needle was inserted in the hiatus at 45° angle to the skin. Once the

sacrococcygeal membrane was penetrated and loss of resistance obtained, the angle of the needle was changed and directed up the canal for further 0.5 cm. The injection was made after gentle aspiration to rule out any intrathecal and intravascular placement. General anaesthesia was maintained with halothane and 60% nitrous oxide in 40% oxygen. The surgical incision was made 20 min after administering caudal block during which time the children were surgically prepared and draped. Adequate caudal analgesia was defined as haemodynamic stability as indicated by absence of increase in heart rate and systolic BP of more than 15% compared with basal values obtained just before surgical incision with halothane concentration maintained at 1%. If systolic BP >15% increase occurred analgesia was considered inadequate and rescue opioids fentanyl given at the dosage of 2µg/kg. Intraoperative fluid managementwas taken care by using HOLIDAY AND SEGAR formula. postoperatively the Children were shifted to the recovery room for continuous monitoring. Postoperative sedation score was done using RAMSAY SCALE every one hour for first 6 hours and then every 2 hours The recovery was assessed using Modified Aldrete Score the children were shifted to a dedicated postoperative ward where monitoring of respiratory rate, (SpO_2), pulse rate and systolic blood pressure were continued. The quality of analgesia was assessed hourly for first 6 hours and then every 2 hours. The intensity of pain was measured using the Objective Pain Scale Score devised by Hannallah RS**.** Each parameter was awarded a score of 0-2 accordingly. The sum total of the awarded score was taken at each time interval. A log was kept at the bedside for noting the occurrence of possible complications including, hypotension, urinary retention, nausea and vomiting. Patients were administered rescue analgesia with syrup paracetamol 10 mg/Kg on evidence of pain that is if the OPS reached a value of 5. The time of first analgesia (TFA) was calculated from the time of injection of the drug in the epidural space to the time when OPS reached 5. Respiratory depression was defined as decrease of (SpO_2) < 93% or a decrease in RR < 10 /min. Excessive sedation was defined as a ramsay sedation score of v or vi.

Results

Sixty patients posted for elective lower abdominal general surgical procedure who were admitted in the Department of paediatric surgery, RIMS Ranchi, of physical status ASA I and II were taken up for the study. They were randomly divided into two groups of 30 patients each to receive caudal block as mentioned below. One group (group BN) received a mixture of Bupivacaine 0.25% and neostigmineat 2µg/kg, 20 minutes before surgery. Other group (group B) received 0.25% Bupivacaine alone 20 minutes before surgery. The patients were assessed by a blinded observer in the postoperative period. The age distribution in both groups ranged from 2 – 8 years. The age and sex distribution is as follows, From this table it is clear that the number of children in 24-48, 48-72, and 72-96 month interval are not much different between the two groups. This shows age was not a confounding factor.

Age in yrs age bn

	Frequency	Percent	Valid percent	Cumulative percent
Valid <4	11	36.7	36.7	36.7
5-6	15	50	50	86.7
7-8	4	13.3	13.3	100
Total	30	100	100	

AGE B

	Frequency	Percent	Valid percent	Cumulative percent
Valid <4	17	56.7	56.7	56.7
5-6	8	26.7	26.7	83.3
7-8	5	16.7	16.7	100
Total	30	100	100	

Although there are more children in the (1-4yrs)in B group the distribution among the two study group is almost the same.

SEX B

	Frequency	Percent	Valid percent	Cumulative percent
Valid				
Male	20	66.7	66.7	66.7
Female	10	33.3	33.3	100
Total	30	100	100	

SEX BN

	Frequency	Percent	Valid percent	Cumulative percent
Valid				
Male	22	73.3	73.3	73.3
Female	8	26.7	26.7	100
Total	30	100	100	

In group B 66.7% are male and 33.3% are female and in group BN 73.3% are male and 26.7 % are female. The sex distribution in boththe group is also not much different. Hence there is no bias in the age and sex distribution .

Surgical Procedures	Group B	Group Bn
Herniotomy	15	15
PV sac ligation	8	5
Hypospadias	7	10
Total	30	30

From this table it is clear that the type of surgical procedures between the two groups isnot much different. Hence there is no bias in the type of surgical procedures.

Duration of Analgesia

Duration of analgesia in group B (0.25% bupivacaine) range from 3. to 5 hours with amean duration of 4.3 hours. In group BN (0.25 % Bupivacaine + 2 µg/Kg Neostigmine) the duration of analgesia ranged from 10 to 16 hours with a mean duration of 14.6 hours.

Duration of Analgesia	Group B	Group BN
Range	3-5	10-16
Mean	4.3	14.6
Standard Deviation	0.75	1.52

This duration of analgesia is also statistically significant as detected by using One sample T test by which the probability value is less than 0.05 (P value < 0.0005). This P value means that it is highly significant. One patient in group B had

nausea and vomiting (3.3%) when compared with twopatients in group BN (6.6 %). There was no significant difference in the incidence of urinary retention between the twogroups. No side effects like hypotension, respiratory depression or apnea was seen in anypatient. Overall side effects did not differ between the two groups.

Side effects	Group B	Group BN
Nausea and vomiting	1	2
Urinary retention	1	1
Hypotension	0	0

Duration of Analgesia B

	Frequency	Percent	Valid percent	Cumulative percent
Valid 3	5	16.7	16.7	16.7
4	11	36.7	36.7	53.3
5	14	46.7	46.7	100
Total	13	100	100	

Age B Sex B Cross tabulationCount

	Sex B		Total
	Male	Female	
Age Group B <4	11	6	17
5-6	5	3	8
7-8	4	1	5
Total	20	10	30

Age BN Sex BN Cross tabulationCount

	Sex BN		Total
	Male	Female	
Age Group BN <4	9	2	11
5-6	11	4	15
7-8	2	2	4
Total	22	8	30

The one sample T test procedure test whether the mean of a single variable differs from a specified constant. A low significant value typically below 0.05 indicates that there is a significant difference between the test value and the observed mean. (Sig 2 tailed-4th column) If the confidence interval for the mean difference does not contain the zero, this also indicates that the difference is significant. (99% CI Between 9.53-11.07 there is no zero hence the difference observed is significant) (If the significant value is high and the confidence interval for the mean difference contain zero then you can't conclude that there is a significant difference between thetest value and the observed mean), This is not the case in this study hence the result observed is significant.

Discussion

The present study demonstrated that caudal neostigmine in a dose of 2 µg/kg co-administered with bupivacaine 0.25% markedly prolonged postoperative analgesia and reduced the need for oral paracetamol in children undergoing lower abdominal surgeries.The study conducted by Mahajan [1] and coworkers which reported a mean duration of 16.6 ± 4.9 hours, was well correlated with our study. The mean duration of postoperative

analgesia in our study Group BN is (14.6 hours). This value is statisticallysignificant as detected by one sample T- Test by which the probability value is less than 0.05 (P <0.0005), which means that it is highly significant. In the present study, we have confirmed the analgesic efficacy of caudal neostigmine when co-administered with bupivacaine. The neuraxial administration of neostigmine is known to produce analgesia in animals, human volunteers and patients with acute postoperative and chronic pain. Spinal delivery of the cholinesterase inhibitor neostigmine inhibits the breakdown of the endogenous spinal neurotransmitter acetylcholine which has been shown to produce analgesia. Eisenach et al [2] Neuraxial administration of neostigmine increases the concentration of acetylcholine in cerebrospinal fluid and produces antinociception in animals which is blocked by the intrathecal administration of a muscarinic antagonist. The analgesic effect is thought to be mediated via spinal muscarinic M_1 receptors and supraspinal muscarinic M_1 and M_2 and nicotinic cholinergic receptors. Various investigators have reported a dose-independent effect of the neuraxial administration of neostigmine on postoperative pain relief and analgesic requirements. In pregnant patients Krukowski *et al*. [3] have demonstrated that varying doses of intrathecal (10, 30 and 100 µg) provided dose independent analgesia lasting approximately ten hours in all three groups. Similarly Lauretti *et al*. [4] have shown dose independent analgesia in patients undergoing vaginal hysterectomy in a dose range of 25 to 75 µg intrathecal neostigmine. The same authors have also demonstrated dose independent analgesia with the combination of 20 mg intrathecal bupivacaine plus 85 mg epidural lidocaine with neostigmine (1, 2 or 4 µg·kg–1) in patients undergoing knee surgery Lauretti et al. [5]. The lowest dose of neostigmine may have maximally potentiated the analgesic effect of caudal bupivacaine, making higher doses of caudal neostigmine no more effective. Considering the lack of efficacy of neostigmine alone in doses < 10 $\mu g \cdot kg^{-1}$, Batra YK, et al [6]. It is not surprising that lower doses combined with bupivacaine may have uniformly potentiated the effect of caudal bupivacaine. Although the use of neuraxial neostigmine has been associated with gastrointestinal side effects such as nausea and vomiting, these were encountered very minimally in the present study. Lauretti *et al* [7] and Roelants *et al*. [9] have also reported the extradural administration of neostigmine to be devoid of these undesirable side effects. [8] Further, these side effects have been found to be statistically insignificant (Abdullatif and EL-Sanabary [10]- and independent of the dose of neuraxialneostigmine. The use of caudal bupivacaine alone has been found to be associated with nausea and vomiting to the extent of 25 to 45%, Wolf AR, [11] an incidence similar to that seen with caudal morphine, fentanyl and tramadol. Senel AC [12], It seems that caudal neostigmine in such low doses contributes minimally to nausea and vomiting. Caudal neostigmine is effective as a sole analgesic with duration of analgesia comparable to that reported with caudal bupivacaine 0.25%. In line with the findings of the present study, co-administration of neostigmine with bupivacaine significantly extended the duration of postoperative analgesia. The duration of analgesia in Group BN ranged from 10-16 hours was comparable to results obtained by Rudra et al [13] ranged between 19±4.2 hours. These results were also correlated well with the study results obtained by Abdullatif and EL-Sanabary[10]. That combination of bupivacaine and neostigmine provides superior analgesia than to bupivacaine alone with the mean duration of 22.8±2.9 hours. In their study they had used 1 ml/kg of bupivacaine, but in our study, we used only 0.5ml/kg of bupivacaine, so that might be a reason for difference in theduration of analgesia. The incidence of nausea and vomiting in Group BN is 6.6%. this was

comparable to the results obtained by Rudra et al [13] and Mahajan [1] coworkers who reported theincidence was less than 20%. In this study, in spite of using a smaller dose of neostigmine (2μg/kg) the mean duration of analgesia was 14.6 hours, which could due to synergistic effect of bupivacaine and neostigmine. [14]

Conclusion

We conclude that caudal epidural analgesia using a combination of 0.25% bupivacaine 0.5ml/kg and neostigmine (2μg/kg) significantly prolong the postoperative analgesia when compared to 0.25% bupivacaine alone in children undergoing lower abdominal general surgical procedures without any significant increase in side effects.

References

1. Rajesh Mahajan et al Caudal neostigmine with bupivacaine produces a dose- independent analgesic effect in children Canadian Journal of Anaesthesia. 2004; 51:702-706.
2. Lauretti GR, Hood DD, Eisenach JC, Pfeifer BL. A multi-center study of intrathecal neostigmine for analgesia following vaginal hysterectomy. Anaesthesiology. 1998; 89:913–8.
3. Krukowski JA, Hood DD, Eisenach JC, Mallak KA, Parker RL. Intrathecal neostigmine for post-cesarean section analgesia: dose response. Anaesth Analg. 1997;84: 1269–75.
4. Lauretti GR, Reis MP, Lima ICPR. Association of intrathecal fentanyl and intrathecal neostigmine: an effective postoperative analgesic for abdominal hysterectomy. Reg Anaesth. 1996; 21(2S): 77 (abstract).
5. Lauretti GR, Mattos AL, Reis MP, Prado WA. Intrathecal neostigmine for postoperative analgesia after orthopedic surgery. JClin Anaesth. 1997; 9: 473–7.
6. Batra YK, Arya VK, Mahajan R, Chari P. Dose response study of caudal neostigmine for postoperative analgesia in paediatric patients undergoing genitourinary surgery. Paediatr Anaesth. 2003; 13: 515–21.
7. Hood DD, Eisenach JC, Tuttle R. Phase I safety assessment of intrathecal neostigmine methylsulfate in humans. Anaesthesiology. 1995; 82: 331–43.
8. Lauretti GR, de Oliveira RD, Reis MP, Juliao MC, Pereira NL. Study ofthree different doses of epidural neostigmine coadministered with lidocaine for postoperative analgesia. Anaesthesiology. 1999; 90: 1534–8.
9. Roelants F, Rizzo M, Lavand'homme P. The effect of epidural neostigmine combined with ropivacaine and sufentanil on neuraxial analgesia during labor. Anesth Analg. 2003; 96:1161–6.
10. Abdulatif M, El-Sanabary M. Caudal neostigmine, bupivacaine, and their injected cholinomimetic drugs in the rat and cat. Eur J Pharmacol. 1985; 117: 81–8.
11. Wolf AR, Hughes D, Wade A, Mather SJ, Prys-Roberts C. Postoperative analgesia after paediatric orchidopexy: evaluation of a bupivacaine morphine mixture.Br J Anaesth. 1990; 64: 430–5.
12. Senel AC, Akyol A, Dohman D, Solak M. Caudal bupivacaine-tramadol combination for postoperative analgesia in pediatric hernioraphy. Acta Anaesthesiol Scand. 2001; 45:78 6–9.
13. RUDRA et al scope of caudal neostigmine with bupivacaine for post operative analgesia in children: comparison with bupivacaine Indian j. anaesth. 2005; 49 (3): 191 – 194.
14. Chakdoufi S., Mamoune E. M., Brahim E. M., & Anas G. A. Postoperative (Pressure) Alopecia on Head Rest Fixation Pointes Area, Following Intracranial Removal of Meningioma. A Rare but Disturbing Complication to Consider. Journal of Medical Research and Health Sciences. 2023; 6(3): 2480–208