

COMPARATIVE STUDY TO EVALUATE ANALGESIC EFFICACY OF CAUDAL MIDAZOLAM AND CLONIDINE POSTOPERATIVE ANALGESIA IN CHILDREN

Ramalinga Raju A.V.S¹, Kalyan Chakrawarthy Y², Ravikant S³

¹Associate Professor, Department of Anaesthesiology, Malla Reddy Institute of Medical Sciences, Hyderabad.

²Associate Professor, Department of Anaesthesiology, Konaseema Institute of Medical Sciences, Amalapuram, Andhra Pradesh.

³Assistant Professor, Department of Anaesthesiology, Konaseema Institute of Medical Sciences, Amalapuram, Andhra Pradesh.

ABSTRACT

BACKGROUND

Caudal epidural analgesia is one of the most popular regional techniques used in paediatric patients undergoing lower limb, anoperineal and abdominal surgical procedures for postoperative pain relief. The aim of postoperative pain relief is to provide subjective comfort and inhibit trauma-induced nociceptive impulses to blunt autonomic and reflex responses to pain and subsequently to enhance the restoration of function. Caudal epidural analgesia though practiced widely is of short duration even when used with long-acting local anaesthetics.

MATERIALS AND METHODS

Children of either sex undergoing elective hernia or hydrocele surgery within in the age group of 2-8 years belonging to ASA I and II were included in the study. Informed consent was obtained from the parents before procedure.

RESULTS

The duration of analgesia in the study group was 10.14 ± 4.69 hrs. and 6.83 ± 0.79 hrs. in the clonidine group and midazolam group. Duration of analgesia in clonidine group was significantly longer when compared to with midazolam group with a p value of <0.05 .

Sedation Score- There was decrease in heart rate and mean arterial pressure from baseline, but these were under allowable limits of 20%. The patient had pain scores of less than 8 for first 6-8 hrs. The patients were well sedated and were easily arousable.

CONCLUSION

We conclude that in our study we found that clonidine 8 µg/kg provided good analgesia for a longer duration when compared with midazolam.

Clonidine also provided good sedation with minimal haemodynamic variations.

This is in agreement with studies conducted to know haemodynamic stability with higher doses of clonidine.

KEYWORDS

Caudal Midazolam, Clonidine, Children.

HOW TO CITE THIS ARTICLE: Ramalinga Raju AVS, Chakrawarthy KY, Ravikant S. Comparative study to evaluate analgesic efficacy of caudal midazolam and clonidine postoperative analgesia in children. J. Evid. Based Med. Healthc. 2017; 4(25), 1447-1450. DOI: 10.18410/jebmh/2017/281

BACKGROUND

Caudal epidural analgesia is one of the most popular regional techniques used in paediatric patients undergoing lower limb, anoperineal and abdominal surgical procedures for postoperative pain relief.¹ The aim of postoperative pain relief is to provide subjective comfort and inhibit trauma-induced nociceptive impulses to blunt autonomic and reflex responses to pain and subsequently to enhance the restoration of function. Caudal epidural analgesia though practiced widely is of short duration even when used with long-acting local anaesthetics.

Bupivacaine is a local anaesthetic used for caudal anaesthesia. The major limitation with the use of this drug is cardiotoxicity and during postoperative period motor weakness and urinary retention. Prolongation of analgesia has been achieved by various adjuvants.² Although, the adjuvants have prolonged the duration of analgesia and improved the quality of pain relief. All these agents have its own advantages and disadvantages.²

Opioids may cause pruritus, nausea, vomiting, urinary retention and late respiratory depression. Clonidine, an α_2 agonist, produces analgesia by acting directly on spinal cord by interacting with α_2 adrenergic receptors. Midazolam is a benzodiazepines acts on GABA minergic receptor present in spinal cord and peripheral nerves.

AIMS AND OBJECTIVES

The objective of the study was to compare the analgesic efficacy of caudal administration of midazolam and clonidine for postoperative analgesia and to observe for side effects if any.

Financial or Other, Competing Interest: None.

Submission 08-03-2017, Peer Review 15-03-2017,

Acceptance 23-03-2017, Published 24-03-2017.

Corresponding Author:

Dr. Ramalinga Raju A.V.S,

No. 49, Vessella Villa, Opp. Chirac Public School,

Botanical Garden Road, Kondapur, Hyderabad - 500084.

E-mail: dravsrlr@gmail.com

DOI: 10.18410/jebmh/2017/281



MATERIALS AND METHODS

Prospective randomised controlled double-blind study. 50 patients were allocated randomly into 2 groups- All patients received standardised general anaesthesia.

- Group C - Clonidine 8 µg/kg in saline as 15 µg/mL dilution.
- Group M - Midazolam 50 µg/kg with normal saline 1 mL/kg.

Children of either sex undergoing elective hernia or hydrocele surgery within the age group of 2-8 yrs. belonging to ASA I and II were included in the study. Informed consent was obtained from the parents before procedure.

Exclusion Criteria

- Parent’s refusal.
- Children with contraindication to caudal block.
- Children with any cardiovascular diseases, neurological disorders and obvious skeletal abnormalities.

Anaesthesia Procedure

Premedication- All patients were premedicated with syrup - promethazine 0.5 mg/kg orally previous night and 2 hrs. before surgery.

Induction was done with Inj. Atropine 20 µg/kgs, Inj. Fentanyl 2 µg/kg, Inj. Thiopental 5 mg/kg and Atracurium 0.5 mg/kg to facilitate endotracheal intubation.

Anaesthesia was maintained with oxygen in 66% nitrous oxide and halothane 0.2-0.6% under controlled mode ventilation to maintain an EtCO2 in-between 30-35 mmHg. Caudal block was performed just before extubation. The caudal block was performed in left lateral position using 23 GZ needle.

The patients did not receive any other analgesics till pain was noticed in postoperative period.

Neuromuscular blockade was reversed with Inj. Neostigmine and Inj. Glycopyrrolate before extubation.

After completion of surgery, the patients were extubated and transferred to the recovery room. All the vital was monitored every 15 mins.

In the surgical ward, assessments were done every 2-hour interval for next 12 hours. and then at 24 hours. from recovery from anaesthesia.

Intraoperative Monitoring-

- ECG.
- Pulse oximetry.
- NIBP.
- Temperature.
- Capnography.

Haemodynamic parameters, EtCO2 and temperature were recorded during intraoperative period.

Postoperative Monitoring

1. Haemodynamic monitoring- Every 15 mins. during 1st hour, then at 2nd hourly for next 12 hours and then at 24 hrs.

2. Level of sedation using 4-point sedation score.
3. Point sedation score.³
 - 1 = Asleep, not arousable by verbal commands.
 - 2 = Asleep, arousable by verbal commands.
 - 3 = Drowsy/Not sleeping.
 - 4 = Alert/Awake.
4. Pain was evaluated by using FLACC scale.

Duration of analgesia was noted. It was the duration from the time of caudal block till patient had a pain score >8.

Pain score of 5 - Excellent analgesia.

Pain score of 5 - Poor analgesia.

Rescue analgesia when pain score >8.

Syrup paracetamol 10 mg/kg given.

Complications

- Fall in HR by more than 20% was considered as bradycardia and was treatment Inj. Atropine 20 µg/kg.
- Fall in BP by more than 20% was treated as hypotension with IV fluids and Inj. Ephedrine.
- Patients were also observed for nausea, vomiting, dryness of mouth, pruritus, etc.

Analysis

- Student’s t-test (two-tailed, independent), Mann-Whitney U test, Chi-square/Fisher exact test has been used to find the significance of study.
- Statistical software- The statistical software namely SAS 9.2, SPSS 15.0 stata 10.1, Medcalc 9.0.1, Systat 12.0 and Renvironment ver.211.1 were used for the analysis of the data.

RESULTS

Age in Years	Clonidine Group		Midazolam Group	
	Number	%	Number	%
2-5 years	20	80	20	80
5-8 years	5	20	5	20
Total	25	100.0	25	100.0
Mean ± SD	3.90 ± 1.76		3.74 ± 1.38	

Table 1. Age Distribution

Gender	Study Group		Control Group	
	Number	%	Number	%
Male	19	76.0	19	76.0
Female	6	24.0	6	24.0
Total	25	100.0	25	100.0

Table 2. Gender Distribution

	Clonidine	Midazolam Group
Weight (kg)	12.57 ± 2.82	11.97 ± 1.98
Duration of surgery (mins.)	60.23 ± 29.24	56.67 ± 34.50

Table 3. Weight of Patients and Duration of Surgery

In our study with the age of the patients, sex weight of patients and duration of surgery were statistically comparable.

The vital parameters were also comparable during intraoperative period.

	Clonidine Group	Midazolam Group	P value
Duration of postop analgesia (hrs.)	10.14 ± 4.69	6.83 ± 0.79	<0.05

Table 4. Duration of Post Analgesia

P value of <0.05 is significant.

- The duration of analgesia in the study group was 10.14 ± 4.69 hrs. and 6.83 ± 0.79 hrs. in the control group.
- Duration of analgesia in clonidine group was significantly longer when compared with midazolam group with a P value of <0.05.

Pain Score

Comparison of sedation in two groups of patients studied.

15 mins.	2.25 ± 0.61	1.58 ± 0.50	<0.001**
30 mins.	2.25 ± 0.44	2.21 ± 0.41	0.738
45 mins.	2.25 ± 0.61	2.67 ± 0.48	0.012*
1 hours	2.71 ± 0.91	2.83 ± 0.38	0.537
2 hours	2.54 ± 0.93	3.42 ± 0.50	<0.001**
4 hours	2.38 ± 0.77	3.42 ± 0.65	<0.001**
8 hours	2.71 ± 0.91	3.50 ± 0.51	0.001**
12 hours	2.92 ± 0.65	3.79 ± 0.41	<0.001**

Sedation Score

- There was decrease in heart rate and mean arterial pressure from baseline, but these were under allowable limits of 20%.
- The patient had pain scores of less than 8 for first 6-8 hrs.
- The patients were well sedated and were easily arousable.

DISCUSSION

This study group included patients of age groups 2-8 years as caudal block is easier to perform in younger children. In a retrospective study of 750 consecutive caudal blocks in children, dalens and Hasnaoui noted a failure rate of only 1% in children less than 7 yrs. old compared with a 14.5% failure rate in older children.⁴ Extradural administration of midazolam to postoperative adult patients and individuals with chronic pain has shown to result in significant analgesia.^{5,6} Nishiyama et al evaluated four doses (25, 50, 75 and 100 ug/kg) of epidural midazolam mixed with saline in patients undergoing upper abdominal surgery. 50 ug/kg was found to be the optimal dose. Higher doses were associated with prolonged and deep sleep.⁷

The principal mechanism by which epidural midazolam provides analgesia is through the GABA benzodiazepine system in the spinal cord. At all levels, the highest density of binding sites was found within lamina II of the dorsal horn

region, which plays a prominent role in the processing of nociceptive information.

Midazolam has been used in the epidural space and as a spinal anaesthetic and has been shown to have no neurological deficits.^{5,8}

The analgesic action of epidural clonidine is due to stimulation of descending noradrenergic pathways and inhibiting the release of nociceptive neurotransmitters in dorsal horn of spinal cord.

Clonidine has been shown to potentiate postoperative analgesia when used in combination with local anaesthetics. Although, the addition of clonidine to bupivacaine improved the efficacy of caudal analgesia, it was associated with prolonged sedation in children.^{9,10}

Clonidine in a dose of 8 ug/kg provides good analgesia for a longer duration.

Assessing pain scale in children, it is difficult as they cannot actually express their feeling. Assessment of pain in children was done by FLACC scale. It is a valid and reliable method of assessing pain in children and has been used by other groups also.

We wanted to assess the analgesic effect of clonidine when used alone and compare the efficacy with midazolam.

We noted that total pain relief for initial 4 hrs. and good analgesia for next 6-10 hrs., which is in agreement with results of various studies.^{11,12}

We noted haemodynamic stability in all the patients.

This is in agreement with studies conducted to know haemodynamic stability with higher doses of clonidine.

De Negri et al study have found that there was not much haemodynamic variation in patients after administering higher doses of clonidine by epidural infusion.^{12,13}

In our study, there are no side effects noted. This is in concurrence with observations done by other workers.^{4,5} Duration of recovery to first analgesic time was found to be longer in clonidine group (mean 10.14 hrs.) than in midazolam group (mean 6.8 hrs.).

No other complications like respiratory depression, prolonged sedation, motor weakness, urinary retention were observed in either of the group.

Duration of recovery to first analgesic time was found to be longer in clonidine group than in midazolam group, however, it is not statistically significant (P value 0.9).

In this study, there was no incidence of motor weakness in any patients in any of groups. This study has shown that caudal administration of midazolam is equipotent to clonidine for postoperative analgesia without any added side effects. Hence, caudal midazolam is safe and maybe used as an effective alternative to clonidine for postoperative analgesia via caudal route.

CONCLUSION

We conclude that in our study we found that clonidine 8 ug/kg provided good analgesia for a longer duration when compared with midazolam.

Clonidine also provided good sedation with minimal haemodynamic variations.

The caudal administration of midazolam in a dose of 50 µg/kg provides equipotent analgesia to clonidine with no side effects.

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