ISSN: 0975-1556

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(1);247-253
Original Research Article

Prospective, Randomized, Controlled, Double Blinded Comparative Assessment of Ropivacaine with Dexmedetomidine, Clonidine and Magnesium Sulphate as Adjuvant in Caudal Epidural Block

Shatrughan Kumar[1], Narendra Kumar[2]

[1]Senior Resident, Department of Anaesthesiology, Sri Krishna medical college & Hospital, Muzaffarpur, Bihar, India
[2]Associate Professor, Department of Anaesthesiology, Sri Krishna medical college & Hospital, Muzaffarpur, Bihar, India

Received: 08-11-2021 / Revised: 19-12-2021 / Accepted: 24-12-2021
Corresponding author: Dr Shatrughan Kumar
Conflict of interest: Nil

Abstract

Aim: Controlled comparison of ropivacaine with dexmedetomidine, clonidine and magnesium sulphate as adjuvant in caudal epidural block in paediatric population for infra-umbilical surgeries

Material and methods: This prospective, randomized, controlled, double blinded study was carried out in the Department of Anaesthesiology, Sri Krishna medical college& hospital, Muzaffarpur, Bihar, India for 1 year.100 children belonging to age group of 2-8 years, weighing 8-20 kilograms(kgs), falling into American Society of Anesthesiologists' (ASA) physical status I- II and undergoing elective below umbilical surgeries, were enrolled for the study.

Results: The mean duration of analgesia in group R, D, C and M were 260.75±10.94, 388.6±10.90, 440±10.8 and 330.75±13.1 minutes(mins) respectively and the difference was statistically significant in all four groups (F=855.4778 and P<0.0001). The inter group differences were highly significant. The mean duration of analgesia was highest in group D followed by C, M and finally least in group R (Table 2). The time to onset of blockade in group D, C, M and R were 10.80±0.82, 10.10±0.70, 7.35±0.85 and 7.20±0.86 mins respectively and the difference was statistically not significant. No significant difference was seen in all four groups regarding haemodynamic parameters intraoperatively and postoperatively till 180 mins. The comparison of HR between four Groups showed highly significant difference at 240 mins, 300 mins and 360 mins, whereas of MAP showed similar findings at 240 mins, 300 mins and 360 mins.

Conclusion: It can be concluded there is a definitive increase in post-operative analgesia when any of three adjuvants namely dexmedetomidine, clonidine or magnesium are added to Ropivacaine for caudal epidural block than control group.

Keywords: Dexmedetomidine, Clonidine, Epidural Block.

Introduction

Pediatric anesthesia has evolved a long way in making surgical procedures much safer, anesthesia-induced neurotoxicity lesser, and postoperative analgesia much longer. In the pursuit of achieving these goals, regional blocks supplementing anesthesia evolved, and they remain one of the most reliable and efficient means. Caudal blocks are time tested for infraumbilical surgeries [1]. Single-shot blocks may not last long and would still depend on the dose, volume, and concentration. An excess of any of this could lead to unintended motor blocks, hemodynamic disturbances, and systemic side effects. To strike a balance between the analgesic efficacy and safety, it has always been a challenge. It may not always be feasible to prolong the duration by placing continuous catheters.

Adjuvant to local anesthetics, bridge the gap by prolonging the duration of single shot blocks. However, it is still a dilemma whether additives improve the outcome and outweigh the potential harm or not. Opioids used as adjuvant carry the disadvantage of occasional delayed respiratory depression, especially when combined with systemic administration. Other adverse effects could be nausea and vomiting, pruritus, urinary retention, and postoperative ileus [2,4]. Dexmedetomidine a novel selective α-2 agonist with a favorable pharmacokinetic profile and versatility with slight concern of bradycardia, has shown promise as an adjuvant in neuraxial use as shown by many recent trials [5,9]. Dexamethasone with its analgesic, anti-inflammatory, and antiemetic properties has been safely used perineurally with good outcome in prolonging the analgesia as agreed with a number of studies [9].

Material and methods

This prospective, randomized, controlled, double blinded study was carried out in the Department of Anaesthesiology, Sri Krishna medical college& hospital, Muzaffarpur,Bihar, India for 1 year.

Methodology

100 children belonging to age group of 2-8 years, weighing 8-20 kilograms(kgs), falling into American Society of Anesthesiologists' (ASA) physical status I-II and undergoing elective below umbilical surgeries, were enrolled for the study. Children with bleeding diathesis, active respiratory infection, fever, spinal deformity, neurological diseases, developmental delays, local site infections and allergies to local anesthetics, were excluded from the study.

In pre-anesthetic assessment child's age, sex, weight and baseline parameters were recorded, detailed history was taken followed by general and systemic examination. Investigations including complete blood count, kidney function tests and coagulation profile were done preoperatively. Parents were taught the use of Wong- Baker Faces Pain Score (WBFPS) for participation in the study and explained about the procedure after which written informed consent was taken.

On the day of surgery children were kept fasted according to standard fasting protocols. After arriving in preoperative area, children were accompanied by their parents inside the operating room where multipara monitor was attached and baseline heart rate (HR), mean arterial pressure (MAP), oxygen saturation (spo2) recorded. Induction of anaesthesia done with oxygen and nitrous oxide (50/50) and 8% sevoflurane with spontaneous ventilation. After loss of consciousness, peripheral venous access taken and inj. glycopyrrolate 4µg/kgs, inj. ondansetron 80 µg/kgs and inj. ketamine 0.5 mg/kgs administered after which sevoflurane was switched off. All children then placed in lateral decubitus position and single dose caudal epidural block performed with 23-gauge needle by loss of resistance technique under all aseptic and antiseptic precautions by an experienced anaesthesiologist who was blinded to the

group allocations. Caudal anaesthesia given with inj. Ropivacaine 0.25% in group R and with added adjuvant inj. dexmedetomidine

0.5 µg/kg in group D, inj. clonidine 1µg/kgs in group C, inj. magnesium sulphate 50 mg in group M. The drug volume was calculated according to modified Armitage formula (0.75-1ml/kg). Patients were made supine after the procedure and onset of block was checked by absence of rise in HR and Systolic blood pressure (SBP) of more than 20% from the baseline and by pinching with toothed forceps at the incision site and time for onset of block was noted. Children were administered oxygen with Hudson mask and Inj. dexmedetomidine started at rate 0.5 µg/kg/hr and Inj. Isolyte-P started at the rate of 6ml/kg/hour.

Haemodynamic parameters like ECG, HR, MAP and oxygen saturation recorded before and after induction of anaesthesia, after caudal blockade administration, every 10 minutes till completion of surgery and thereafter every 30 minutes postoperatively.

Children were assessed intraoperatively by Children's Hospital of Eastern Ontario Pain Scale [8] (CHEOPS) for effectiveness of blockade every 10 minutes till completion of surgery. Ten minutes before completion of surgery dexmedetomidine infusion stopped and total duration of surgery noted.

Children were shifted to PACU for continuous monitoring and assessed using WBFPS and Face Leg Activity Cry Consolability scale [9] (FLACC) every 30 minutes till both FLACC and WBFPS were ≥4 then inj. Paracetamol 20 mg/kg was administered intravenously as rescue analgesia.

Primary objective of the study was to calculate duration of block (time interval between onset of caudal block to first recording of pain scores 4) and time to onset of block. Secondary objective was to study haemodynamic stability and adverse effects such as nausea, vomiting, hypotension, bradycardia and urinary retention monitored.

Study of continuous variables from independent controls and experimental subjects with 1 control per experimental subject planned. We recruited 25 subjects for each group anticipating any dropouts. Results were recorded as mean (standard deviation), median (IQR) and ratios. Normally distributed data (age, weight, HR, MAP, duration of analgesia and onset of block) were analysed with One-Way Analysis of Variance Test (ANOVA) to compare all the four groups together and within pairs of group comparisons and finding the better group done with unpaired t test. The non- normal data distributions (FLACC, WBFPS and CHEOPS) were analysed with Kruskal Wallis Test and inter group comparison done with Mann Whitney U test. Qualitative data (gender) was analysed using chi-square ($\chi 2$) test. P-value of < 0.05 was considered statistically significant. The data was analysed using institutional SPSS statistical software (version 24.0, IBM corporation NY, USA).

Results

The demographic data distribution in all four groups showed no statistically significant difference (Table 1). The mean duration of analgesia in group R, D, C and M were 260.75±10.94, 388.6±10.90, 440±10.8 and 330.75±13.1 minutes(mins) respectively and the difference was statistically significant in all four groups (F=855.4778 and P<0.0001) (Table 1). The inter group differences were highly significant. The mean duration of analgesia was highest in group D followed by C, M and finally least in group R (Table 2). The time to onset of blockade in group D, C, M and R were 10.80±0.82, 10.10±0.70, 7.35±0.85 and 7.20±0.86 mins respectively and the difference was statistically not significant. (Table 1) The intraoperative CHEOPS scores showed no statistically significant difference between the four groups. Postoperatively there was no statistically significant difference in

FLACC and WBFPS for four groups till 180 minutes. The comparison of FLACC between four Groups showed highly significant difference at 240 mins, 300 mins and 360 mins. The comparison of WBFPS showed similar findings at 240 mins, 300 mins and 360 mins. (Table 3) No significant difference was seen in all four groups regarding haemodynamic parameters intraoperatively and postoperatively till 180 mins. The comparison of HR between four Groups showed highly significant difference at 240 mins, 300 mins and 360 mins, whereas of MAP showed similar findings at 240 mins, 300 mins and 360 mins. No respiratory depression, haemodynamic instability, neurological deficit or any other adverse effect was noted in any study group.

Table 1: Demographic profile, surgeries, duration and onset of block

Characteristics	Group R	Group C	Group D	Group M	p
Age (years)	4.2±2.40	5.32±2.68	5.5±2.79	3.8±1.93	0.126(NS)
Weight(kg)	14.4±3.30	16±3.8	3.87±2.30	13.3±3.90	0.315(NS)
Gender (M: F)	18:01	18:01	0.7104166	19:00	0.775(NS)
Surgical procedures High ligation	14	20	17	16	-
Circumcision	4	5	5	9	-
Orchidopexy	7	-	3	-	-
Duration of block	260.75±10.94	388.6±10.90	440±10.8	330.75±13.1	<0.0001(S)
Onset of block	7.20±0.86	10.10±0.70	10.80±0.82	7.35±0.85	8.77(NS)

Table 2: Intergroup comparison of duration of block

Groups		Mean	Std. Deviation	p (2-tailed)
Group C Vs Group D	**C** **D**	**375.60** **431.00**	**10.878** **10.808**	**.000(S)**
Group C Vs Group M	**C** **M**	**375.60** **324.75**	**10.878** **13.105**	**.000(S)**
Group C Vs Group R	**C** **R**	**375.60** **254.75**	**10.878** **10.914**	**.000(S)**
Group D Vs Group R	**D** **R**	**431.00** **254.75**	**10.808** **10.914**	**0.000(S)**
Group D Vs Group M	**D** **M**	**431.00** **321.75**	**10.808** **13.105**	**0.000(S)**
Group M Vs Group R	**M** **R**	**324.75** **254.75**	**13.105** **10.914**	**0.000(S)**

unpaired t test. $p < 0.05$ is considered statistically significant. NS means not significant, S means significant.

Table 3: Postoperative pain score

Time	Pain score	Group R(n=25)		Group C(n=25)		Group D(n=25)		Group M(n=25)		p
		Median	IQR	Median	IQR	Median	IQR	Median	IQR	
240 Min	WBFPS	5	3.30-5	2	2-3	2	2-3	2	2-3	0.000*
	FLACC	5	4-5	4	3-4	3.5	3-4	4	3-4	0.000*
	WBFPS			2	2-3	2	2-3	5	4-5	0.000*

300 Min	FLACC			4	3-4	4	3-4	5	4-5	0.000*
360 Min	WBFPS			5	3-5	2	2-3			0.000*
	FLACC			5	5	4	3-4			0.000*
420 Min	WBFPS					5	4-5			
	FLACC					5	5-5			

This table represents only statistically significant values among all the analysed ones. Data expressed as median (IQR), SD: standard deviation, IQR: inter quartile range. *Kruskal Wallis test and ‡Mann -Witney U test applied. P<0.05 considered statistically significant. Monitoring stopped at 300 min (group R),360 min (group M &R), 420 min (group C, M & R) so scores unavailable.

Discussion

Caudal block has good recovery profile, better post- operative analgesia and early restoration of function. Anand VG et al [10]. Gupta S et al [11]. studied 60 children divided in two groups for caudal block with Ropicavaine 0.25% with Dexmedetomidine 1µg/kgs and Ropicavaine 0.25% in former study while 0.25% ropivacaine with 2 mg/kg of tramadol (RT) and 2 µg/kg dexmedetomidine (RD) as adjuvant in later. They observed lower FLACC scores in dexmedetomidine group similar to results of our study where Group D showed longest duration of analgesia and lowest FLACC and WBFPS.

A Parmeshwari et al [12] compared three groups, consisting of hundred patients of 1-3 years each where namely: Group A 1 ml/kg 0.25% bupivacaine, group B 1 ml/kg 0.25% bupivacaine with clonidine 1 µg/kg. The mean duration of analgesia was prolonged with lower FLACC scores in group B concluding clonidine-bupivacaine mixture provided longer duration of analgesia similar to our study, where group C had longer duration of analgesia compared to Group R.

H. Birbicer et al [13] Studied 60 children assigned in two groups with ropivacaine 0.25% administered in Group R and ropivacaine 0.25% plus 50 mg magnesium to Group RM. Paediatric observation priority score, CHEOPS, Bromage Motor Scales, analgesia duration and adverse effects were similar in both groups showing that addition of magnesium as an adjuvant agent to local anaesthetics for caudal analgesia has no effect on postoperative pain and analgesic need, which was in contrast to our study where adding magnesium sulphate as adjuvant results in longer duration of analgesia as compared to control group similar to study by Kim E et al [14]. who studied 80 children administered caudal block with magnesium 50 mg added to ropivacaine 0.1% compared with ropivacaine 0.1% alone.

In our study the duration of analgesia showed statistically significant difference between Group C and D with better analgesia in Group D, results are congruent with study done by S. Gupta et al [15]where 60 children were administered caudal block with ropivacaine 0.2% and clonidine 2 µg/kg as adjuvant in group A and dexmedetomidine 2 µg/kg in group B concluding that there was a significant increase in duration of analgesia in dexmedetomidine over clonidine group without increase in incidence of side-effects. Jehan Ahmed Sayed et al [16] allocated 120 children into four groups: group C (saline), group MG (50 mg magnesium sulphate), group D (1 µg/kg dexmedetomidine), and group MGD (same doses dexmedetomidine and magnesium sulphate) added to bupivacaine as adjuvants. When all groups were compared it showed dexmedetomidine as adjuvants to bupivacaine in caudal block had higher duration of analgesia and lower FLACC scores as compared to magnesium sulphate group, a finding similar to our study where duration of analgesia was longer in group D

when compared to group M. Duration of analgesia was longer in group C compared to group M and is found to be statistically significant and These two groups were never compared before in any other study.

The onset of block when compared in all four groups showed no statistically significant difference but time to onset of block was faster in group M and R. All studies quoted above used general anaesthesia with or without muscle relaxants while securing the airway either with laryngeal mask airway or endotracheal tube facilitating caudal epidural block unlike our study where induction agents were used to make children unaware of caudal block administration, afterwards no supplementation with anaesthetic agents were done and inj. dexmedetomidine was only used for sedation at maintenance dose along with oxygen support. The groups compared in our study have never been compared before in our knowledge. Addition of control group to the study makes it more sensitive.

Conclusion

It can be concluded there is a definitive increase in post-operative analgesia when any of three adjuvants namely dexmedetomidine, clonidine or magnesium are added to Ropivacaine for caudal epidural block than control group. Maximum duration of analgesia seen with dexmedetomidine followed by clonidine and magnesium group while least in control group. The study also showed more rapid onset of blockade in magnesium and control group.

References

1. Beyaz SG, Tokgöz O, Tüfek A. Caudal epidural block in children and infants: Retrospective analysis of 2088 cases. Ann Saudi Med 2011; 31:494-7.
2. Vetter TR, Carvallo D, Johnson JL, Mazurek MS, Presson RG Jr. A comparison of single-dose caudal clonidine, morphine, or hydromorphone combined with ropivacaine in pediatric patients undergoing ureteral reimplantation. Anesth Analg 2007; 104:1356-63.
3. de Beer DA, Thomas ML. Caudal additives in children – Solutions or problems? Br J Anaesth 2003; 90:487-98.
4. Lönnqvist PA, Ivani G, Moriarty T. Use of caudal-epidural opioids in children: Still state of the art or the beginning of the end? Paediatr Anaesth 2002; 12:747-9.
5. Wu HH, Wang HT, Jin JJ, Cui GB, Zhou KC, Chen Y, et al. Does dexmedetomidine as a neuraxial adjuvant facilitate better anesthesia and analgesia? A systematic review and meta-analysis. PLoS One 2014;9:e93114.
6. Saadawy I, Boker A, Elshahawy MA, Almazrooa A, Melibary S, Abdellatif AA, et al. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. Acta Anaesthesiol Scand 2009; 53:251-6
7. Anand VG, Kannan M, Thavamani A, Bridgit MJ. Effects of dexmedetomidine added to caudal ropivacaine in paediatric lower abdominal surgeries. Indian J Anaesth 2011; 55:340-6.
8. Xiang Q, Huang DY, Zhao YL, Wang GH, Liu YX, Zhong L, et al. Caudal dexmedetomidine combined with bupivacaine inhibit the response to hernial sac traction in children undergoing inguinal hernia repair. Br J Anaesth 2013; 110:420-4
9. Merkel S, Voepel-Lewis T, Malviya S. Pain Assessment in Infants and Young Children: The FLACC Scale. Am J Nurs. 2002;102(10):55–8.
10. Gupta S, Sharma R. Comparison of analgesic efficacy of caudal dexmedetomidine versus caudal tramadol with ropivacaine in paediatric infraumbilical surgeries: A prospective, randomised, double-blinded clinical study. Indian J Anaesth. 2017;61(6):499–504.

11. Anand VG, Kannan M, Thavamani A, Bridgit MJ. Effects of dexmedetomidine added to caudal ropivacaine in paediatric lower abdominal surgeries. Indian J Anaesth. 2011; 55:340–6.
12. Parameswari A, Anand M, Mahesh V. Efficacy of Clonidine as an Adjuvant to Bupivacaine for Caudal Analgesia in Children Undergoing Sub-Umbilical Surgery. Indian J Anaesth. 2010; 54:458– 63.
13. Birbicer H, Doruk N, Cinel I, Atici S, Avlan D, Bilgin E. Could adding magnesium as adjuvant to ropivacaine in caudal anaesthesia improve postoperative pain control. Pediatr Surg Int. 2006;23(2):195–203.
14. Kim E, Kim M, Han S, Moon B, Choi E, Kim E. Magnesium as an adjuvant for caudal analgesia in children. Pediatr Anesth. 2014;24(12):1231–9.
15. Gupta S, Pratap V. Addition of Clonidine or Dexmedetomidine to Ropivacaine prolongs caudal analgesia in children. Indian J Pain. 2014;28(1):36.
16. Sayed J, Kamel E, Riad M, Abd-Elshafy S, Hanna R. Dexmedetomidine with magnesium sulphate as adjuvants in caudal block to augment anaesthesia and analgesia in paediatric lower abdominal surgeries. Egyp J Anaesth. 2018;34(4):114–22.