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Original Research Article

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

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ABSTRACT

Background and Aims: Caudal analgesia and anaesthesia is one of the safest and widely used methods for pain relief in paediatric population. Aim of this study is to compare the efficacy of dexmedetomidine, clonidine, magnesium sulphate as adjuvants to 0.25% ropivacaine in caudal anaesthesia for enhancement of duration of analgesia as well as to determine safety of the blockade in paediatric population.
Materials and Methods: It is prospective, randomised, double-blinded study in which eighty children (2–8 years), belonging to American society of Anesthesiologists physical status I and II scheduled for infra-umbilical surgeries were randomised into four groups namely: group R; Inj. Ropivacaine 0.25%, Group D; inj.ropivacaine 0.25% with adjuvant dexmedetomidine 0.5 μg/kg, Group C; inj.ropivacaine 0.25% with clonidine 1 μg /kgs, group M; inj.ropivacaine 0.25% with magnesium sulphate 50 mgs. The primary outcomes of study were time to onset of block and duration of analgesia. The secondary outcome was to study haemodynamic stability and adverse effects.
Results: Duration of analgesia was significantly longer (f=855.4778 and p<0.0001) in adjuvant groups as compared to control group and was statistically significant (p = 0.0001 and 0.0411 respectively). No significant difference was observed in the incidence of haemodynamic changes or side effects.
Conclusion: Addition of above-mentioned drugs as adjuvants to 0.25% ropivacaine in caudal block significantly prolonged the duration of post-operative analgesia with least effect on haemodynamic profile or any other significant adverse effects.

1. Introduction

Caudal anaesthesia and analgesia are most widely used regional block in children for post-operative pain management in below umbilicus surgeries. It is simple to perform, reliable and safe.[1] The main limitation is duration of block is short after single administration which can be prolonged by adding various adjuvants.[2]

Ropivacaine is long acting amide local anaesthetic providing selective sensory blockade. Lower incidence of cardiovascular side effects, neurotoxicity and ability to produce less motor blockade has made it local anaesthetic of choice for regional blocks.[2]

Clonidine and Dexmedetomidine are alpha-2 adrenergic agonists with the later having eight times more affinity for alpha-2 adrenergic receptors than former and negligible alpha-1 effects.[3] Both provide a substantial anti-nociceptive effect by acting on the alpha-2 receptors in the dorsal horn of spinal cord and brain stem nuclei dealing with pain

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sensations at spinal cord level.[4]

Magnesium's anti-nociceptive effects are primarily based upon the regulation of calcium influx into the cell. It blocks NMDA receptors and also acts as an agonist on central alpha-2 receptors desensitising the nociceptive stimulation.[5,6]

This study compares the effects of these drugs as adjuvants in caudal epidural block, using it as primary mode of anaesthesia.

2. Materials and Methods

This prospective, randomized, controlled, double blinded study was conducted following principles of Declaration of Helsinki.It was approved by Institutional ethical committee. This study was conducted in a teaching institute over a period of 1.5 years from June 2018 to November 2019 and 90 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.[Figure 1] 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. Out of 90 patients, eight patients did not consent and two had fever on the day of surgery hence dropped from the study.

In pre-anaesthetic 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[7] (WBFPS) for participation in the study and explained about the procedure after which written informed consent was taken.

Computer randomisation with sealed envelopes method was used and twenty patients were allocated in each group. Table of random allocation was kept with anesthesiologist who prepared drugs and was not part of the study. The drugs were given in prefilled unlabeled syringes while performing the block.

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. The primary endpoint being FLACC and WBFPS score ≥4 after study drug administration, 16 patients in each group would be needed to detect an intergroup difference in the meantime to first rescue analgesia of at least 20% with α = 0.05, β= 0.10 and power of 90% based on the pilot study demonstrating mean (standard deviation) time of 256 (31.78) mins in children who received caudal analgesia using ropivacaine 0.25%.We recruited 20 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 21.0, IBM corporation NY, USA).

3. 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 256.75±10.91, 433±10.81, 377.6±10.91 and 326.75±13.10 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 10.78±0.80, 10.7±0.66, 7.33±0.83 and 7.18±0.85 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. (Table 4)

No respiratory depression, haemodynamic instability, neurological deficit or any other adverse effect was noted in any study group.

4. 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[6] 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

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

Characteristics	Group R	Group C	Group D	Group M	F value Ď	p Ě
Age (years)	4.3±2.40	5.33±2.67	5.5±2.80	3.9±1.94	1.976	0.125(NS)
Weight(kg)	14.3±3.27	15±3.7	13.85±2.27	13.2±3.86	1.205	0.314(NS)
Gender (M: F)	18:02	18:02	0.7104167	19:01	1.11*	0.774(NS)
Surgical procedures						
High ligation	13	14	15	11	-	-
Circumcision	2	6	4	9	-	-
Orchidopexy	5	-	1	-	-	-
Duration of block	256.75±10.91	377.6±10.87	433±10.8	326.75±13.1	855.47	<0.0001(S)
Onset of block	7.18±0.84	10.7±0.66	10.78±0.80	7.33±0.83	129.41	8.77(NS)

Data are expressed as mean ± SD, ratios or numbers. *chi square(χ2) value. †F value and ‡P value calculated by ANOVA test applied in four groups. F value 1 and p < 0.05 is considered statistically significant. NS means not significant, S means significant.

Table 2: Intergroup comparison of duration of block

Groups		Mean	Std. Deviation	Std. Error Mean	t	df	p (2-tailed)
Group C Vs Group D	C	377.60	10.879	2.433	-16.155	38	.000(S)
	D	433.00	10.809	2.417			
Group C Vs Group M	C	377.60	10.879	2.433	13.351	38	.000(S)
	M	326.75	13.106	2.931			
Group C Vs Group R	C	377.60	10.879	2.433	35.069	38.000	.000(S)
	R	256.75	10.915	2.441			
Group D Vs Group R	D	433.00	10.809	2.417	51.310	38.000	0.000(S)
	R	256.75	10.915	2.441			
Group D Vs Group M	D	433.00	10.809	2.417	27.969	38.000	0.000(S)
	M	326.75	13.106	2.931			
Group M Vs Group R	M	326.75	13.106	2.931	18.354	38.000	0.000(S)
	R	256.75	10.915	2.441			

t: T value, df: degree of freedom calculated from 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=20)		Group C (n=20)		Group D (n=20)		Group M (n=20)		p
		Median	IQR	Median	IQR	Median	IQR	Median	IQR	
240 Min	WBFPS	4	3.25-4	1	1-2	1	1-2	1	1-2	0.000*
	FLACC	4	3-4	3	2-3	2.5	2-3	3	2-3	0.000*
300 Min	WBFPS			1	1-2	1	1-2	4	3-4	0.000*
	FLACC			3	2-3	3	2-3	4	3-4	0.000*
360 Min	WBFPS			4	3.25-4	1	1-2			0.000‡
	FLACC			4	4-4	3	2-3			0.000‡
420 Min	WBFPS					4	3-4			
	FLACC					4	4-4			

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.

Table 4: Postoperative haemodynamic parameters

Time	Parameter	Group R (mean ±SD)	Group C (mean ±SD)	Group D (mean ±SD)	Group M (mean ±SD)	f value*	p
240 MIN	HR	124.4±3.97	113.1±5.99	112.8 ±5.78	111.5±5.53	24.46	0.000†
	MAP	75.13± 2.76	106.36±3.85	105.73± 3.50	106.36± 3.85	401	0.000†
300 MIN	HR	-	113.1±5.99	112.4±5.49	123.5±4.44	27	0.000†
	MAP	-	106.36±3.85	105.56± 4.33	73.4 ±2.57	541	0.000†
360 MIN	HR	-	124.6 ±4.63	112.5±5.65	-	-	0.000‡
	MAP	-	74.23±2.40	105.9±3.40	-	-	0.000‡
420 MIN	HR	-	-	124.3 ±4.41	-	-	-
	MAP	-	-	74 ±2.80	-	-	-

This table represents only statistically significant values among all the analysed ones. SD: standard deviation. * F value and ^{Ď} P value calculated by ANOVA test and ^{Ě}p value calculated from unpaired t test applied. F value 1 and $p < 0.05$ is considered statistically significant. monitoring stopped at 300 min (group R), 360 min (group M &R), 420 min (group C, M & R) so scores unavailable.

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.

The limitations of study are it does not analyze the further administration of rescue analgesia and time of administering them.

5. 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.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

References

1. Wiegele M, Marhofer P, Lönnqvist P. Caudal epidural blocks in paediatric patients: a review and practical considerations. *Br J Anaesth*. 2019;122(4):509–17.
2. Veeravalli S, Sunil B, Shenoy T. Comparing the Anaesthetic and Analgesic Efficacy of Caudal Levobupivacaine and Ropivacaine in Paediatric Patients. *J Clin Diagn Res*. 2018;12(6):UC05–9.
3. Triptu P, Parmar J, Thomas S, Elder J. Clonidine increases duration of bupivacaine caudal analgesia for ureteroneocystostomy: A double-blind prospective trial. *J Urol*. 2005;174(3):1081–3.
4. Joshi W, Connelly N, Freeman K, Reuben S. Analgesic effect of clonidine added to bupivacaine 0.125% in paediatric caudal blockade. *Pediatr Anesth*. 2004;14:483–6.
5. Do SH. Magnesium: a versatile drug for anesthesiologists. *Korean J Anesthesiol*. 2013;65(1):4–8.
6. 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.
7. Oliveira A, Batalha L, Fernandes A, Gonçalves J, Viegas R. A functional analysis of the Wong-Baker Faces Pain Rating Scale: linearity, discriminability and amplitude. *Revista de Enfermagem Referência*. 2014;IV(3):121–30.
8. Barrier G, Attia J, Mayer M, Amiel-Tison C, Shnider S. Measurement of post-operative pain and narcotic administration in infants using a new clinical scoring system. *Intensive Care Med*. 1989;15(S1):37–9.
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.

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