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Evaluation of efficacy of caudal dexmedetomidine with ropivacaine for postoperative analgesia in paediatric lower abdominal surgeries.

KEYWORDS: Dexedetomidine, ropivacaine, caudal analgesia, paediatric lower abdominal surgeries.

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ABSTRACT *Background: Caudal epidural analgesia is reliable, safe and has become most popular and commonly performed regional blocks in paediatric anaesthesia. Dexmedetomine is a potent adjuvant which apart from its analgesic effects has concomitant benefits like sedation and sympatholysis. In this study we determined the efficacy of Dexmedetomidine as an adjuvant to caudal anaesthesia for postoperative analgesia in paediatric patients undergoing lower abdominal surgeries.*

Methods: The study consisted of 60 infants and children (1yr–6yr) of ASA physical status I, of either sex, undergoing lower abdominal surgery who were randomised into two groups of 30 each namely Group R and group RD. After induction of anaesthesia caudal block was performed on all patients. Depending on results of randomisation, drug used for caudal anaesthesia in R Group was 0.5ml/kg 0.25% ropivacaine whereas in Group RD it was 0.5ml/kg 0.25% ropivacaine with Dexmeditomidine 1 mcg/kg. Heart rate (HR), mean arterial pressure (MAP) and oxygen saturation (SpO2) were recorded before surgery and every 5 min till 20 minutes after skin incision and at the end of surgeries. The time from caudal block to end of surgery, time for first rescue analgesia, total consumption of rescue analgesia in the period of 24 hours were recorded. In the postanaesthesia care unit, FLACC and ramsay sedation scores were assessed on arrival (0) and at 4, 8,12,16, 20 and 24 hours.

Results: There was a significant reduction in FLACC score in group RD at 4,8 and 12 hours postoperatively compared to group R. At the 16 ,20 and 24 hours there was no significant difference.The mean duration of postoperative analgesia(time of first rescue analgesia) was significantly prolonged in group RD compared to group R.The mean total consumption of rescue analgesia in 24 hours postoperatively was significantly decreased in group RD (217±65.054) mg when compared with the group R(464±1.456) mg. Mean sedation score using Ramsay Sedation Scores was very significant ($p \leq 0.001$) at 4 and 8 hrs. Perioperative haemodynamic changes between the groups were comparable and were not statistically significant and required no treatment.

Conclusion: We find dexmedetomidine is an effective adjuvant for caudal analgesia in paediatrics age group with lower abdominal surgeries.

INTRODUCTION

Pain is a subjective feeling that can only be experienced .Children are totally dependent on their parents for their well-being and cannot express their feelings, so the concept of postoperative pain relief and its utilization in the paediatric age group has improved dramatically over few years. Various methods for providing postoperative pain relief like narcotics, oral and preventable analgesics are not being used in children due to the risks of respiratory depression, chances of aspiration and needle stick injuries.

Caudal epidural analgesia is reliable, safe and has become most popular and commonly performed regional block in paediatric anaesthesia[1] that can provide analgesia for variety of infraumbilical and supraumbilical surgical procedures. It and reduces both the requirement of inhaled and intravenous anaesthetics, attenuates stress response to surgery, facilitates smooth recovery and good postoperative analgesia. The main disadvantage is short duration of action [2]which can be prolonged by using adjuncts like epinephrine, opoids, ketamine, a2 agonist[3] etc.

Ropivacaine is a long acting amide anaesthetic used for caudal anaesthesia .It provide pain relief with less motor blockage but has a improved safety profile over bupivacaine with a reduced CNS and cardiotoxic effects ,thus make it more suitable agents for caudal epidural analgesia.

Dexmedetomidine is commonly used a2 agonist as an adjunct in caudal anaesthesia to decrease the need of additional analgesic without significant hemodynamic and respiratory effect. Its a2/a1 selectivity is 1600:1, which is 8times more potent than clonidine[4].

The objective of this study was to compare the effects of dexmedetomidine combined with ropivacaine and and ropivacaine alone for postoperative analgesia and also determine the other effects; i.e. mean sedation score ,mean emergence time and hemodynamic parameters in children undergoing lower abdominal surgeries.

METHODS :

After obtaining approval of the institutional review board

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and informed written consent from the parents, this randomised, prospective, double blind study was conducted on sixty paediatric patients of ASA grade I-II status, of both the sexes between age groups of 1 - 6 years , scheduled for lower abdominal surgeries of expected to last less than 2 hrs. (hypospadias, anorectal surgeries, herniotomy, epispadiasis) under general anaesthesia combined with caudal analgesia.

Patients with known allergy to the drugs, suspected coagulopathy, infection at the site of caudal block, history of developmental delay, neurological diseases, skeletal deformities were excluded from this study. The children were randomly allocated into two groups based on computer generated random number table.

Group R (n=30) Received 0.25% ropivacane 0.5ml/kg .

Group RD (n=30) Received 0.25% ropivacaine 0.5ml/kg with dexmedetomidine 1µg/kg .The maximum volume of drug was kept 15 ml for both the groups. The person who gave the caudal block and the observer in the PACU were blinded to the group. The drugs for caudal administration was prepared immediately before injection by the nurse who was not involved the study. During the preoperative visit, patients were assessed and the procedure was explained to the parents. Patients were fasted for 4 hours and premedicated with oral midazolam 0.5 mg/kg 30 minutes prior to the induction of anaesthesia. After recording baseline vital parameters ,i.v line was secured and fluid therapy was standardized during and after the surgery.During surgery children received N/4 saline(diluted in Dextrose 5%) 6 ml /kg/ hr. All patients received glycopyrolate 0.05 mg/kg and Inj. fentanyl 1µ/kg i.v followed by Induction with thiopentone (5-7mg/kg) and atracuronium besylate 0.5 mg/kg i/v was used to facilitate endotracheal intubation. Anaesthesia was maintained with N_2O (50%) and O_2 (50%) and with inhalational sevoflurane (2%) with a maintenance dose of atracurium besylate (0.15 mg/kg) on controlled ventilation. After the intubation, patient was placed in the lateral decubitus position with knees pulled up toward the chest for the caudal block. After sterile preparation and drape, block was given with 20-gauge needle inserted at an angle of 70° to the skin over the Sacral hiatus and a single dose drug was injected according to group. No other narcotics, analgesics or sedatives were used intraoperatively. Standard monitoring was used during surgery. Heart rate (HR), mean arterial pressure (MAP) and oxygen saturation (SpO_2) were recorded before surgery and every 5 min till *20* and then every 15 minutes till the end of surgeries .At the end of surgery, the residual neuromuscular blocking was reversed using a mixture of atropine (0.02 mg/kg) and neostigmine (0.05 mg/kg). After extubation patients were transferred to PACU for observation and were monitored for vital sign (HR ,NIBP,SPO2)

Using the pediatric observational **FLACC pain score**[8] **(table 1)**, each patient's pain intensity was assessed at arrival in PACU and then every 4 hours for 24 hours in the postoperative period.

The **total duration of analgesia** (from the time of caudal injection to the time at which FLACC score was 4 or more) was also recorded. Rescue analgesia with Paracetamol (15mg/kg) was given intravenously to the patient when FLACC score was 4 or more. The total duration of analgesia (time to first request of analgesia) and total consumption of analgesia(paracetamol)in the first 24 hours were recorded.

Sedation score was assessed by using **Ramsay's sedation scale** as follows:

1. Anxious and agitated or restless, or both
2. Co-operative, oriented, and calm
3. Responsive to commands only
4. Exhibiting brisk response to light glabellar tap or loud auditory stimulus
5. Exhibiting a sluggish response to light glabellar tap or loud auditory stimulus

6. Unresponsive

Complications such as postoperative nausea and vomiting (PONV), respiratory depression, hypotension and bradycardia were also noted. Respiratory depression was defined as a decrease in SpO2 of of less than 95% requiring supplementary oxygen. Hypotension was defined as systolic arterial pressure less than 70 plus twice the age in years and associated with altered peripheral perfusion. Bradycardia was defined as HR below 80 beats/min upto age 1 year and 60 beats/min for ages above 1 year. Failure of the caudal block was defined as any increase in heart rate or mean arterial pressure more than 20% of the pre-incision values. In our study we encountered 6 failed caudal blocks that were eliminated from the study. Primary end point of the study was to evaluate 30% decrease in analgesic consumption between the two groups at estimated time intervals postoperatively. Sample size is calculated on the basis of previous research and articles. Sample size was calculated by the formula $N = 2*(SD)^2*(Z\alpha/2 + Z\beta)^2/D^2$. In the study there were 2 groups of 30 patients each and the median time observed in R and RD group were 5.5hrs and 14.5hrs each so the effect time is 9hrs (D = 9).Standard deviation was calculated to be 4.2hrs.so by keeping the values in the formula we get a sample size of 30.

The quantitative data like hemodynamic variables, time for first analgesia etc. were analysed using independent student t test. Nominal data was analysed using chi square or fischer exact test and ordinal data was analysed with Mann Whitney test. *P* value of <0.05 was taken to be significant and *P* value of <0.001 was considered highly significant. Results were calculated using SPSS 20.0 (SPSS Inc., Chicago, IL, USA).

RESULTS:

From April 2011 to august 2014,a total of 60 patients who fulfilled the criteria were randomized for this study. Six patients were removed due to inadequate caudal block leaving 54 patients in each group. There were no significant differences among groups in demographic data and were comparable **(Table 2).** The mean duration of surgeries were also similar in both groups **(Table 2).** The mean duration of postoperative analgesia(time of first rescue analgesia) was significantly prolonged in group RD as compared to group R that is 4.53±1.46 hrs and 8.53±1.17 hrs in group R and group RD respectively (P <0.05) **(Table 3).** The mean requirement of paracetamol (rescue analgesia) was more in Group R patients (464±1.45mg) than in Group RD patients with a mean of 217±65.05 mg(p-value.0001) **(Table 3)**. Group R children had significantly higher FLACC score than with the Group RD children. Difference was significant upto 12 hours in both the groups **(Graph 1).** In Group R, most of the patients have FLACC score of 4 between 3 to 6 hours compared with Group RD patients having FLACC score of 4 between 7 to 10 hours of postoperative period. Mean sedation score was highly significant($p \leq 0.001$) at 4 and 8 hrs in group RD, meaning that children of group RD had significant sedation as com-

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pared to R group and children of RD group were asleep but easily arousable. From the twelve hour up to 24 hours both groups have more or less same sedation score **(Graph 2)** Perioperative haemodynamic changes(MAP and HR) between the groups were comparable and insignificant and required no treatment.

DISCUSSION

Managing the pain in paediatric population following surgery is challenging. The analgesic should be effective safe and devoid of side effect. Over the recent year, there has been growing interest in caudal block with promising results on efficacy as it reduces the need of supplemental analgesia and thereby decreasing the side effects. Results of our observations showed that addition of dexmedetomidine as an adjuvant to ropivacaine prologs the duration of postoperative analgesia, reduced the postoperative rescue analgesic consumption and prolonged the time of first analgesic request with stable haemodynamic parameters when compared with caudally administered ropivacaine alone in the first 24 hours of the postoperative period, which are in concordance with the other published reports.

Ropivacaine has a wide margin of safety and can be used safely for regional analgesia in paediatric population**(5-8).** Dexmedetomidine has fulfilled the quest for noble sedation agent for intensive care. Due to sympatholytic, sedative, analgesic, anxiolytic properties ,its use has been extended to various clinical situations as well as regional anaesthesia as a useful adjunct. Like clonidine, it prolongs the effect of local anaesthetic, without increasing incidence of side effect due to activation of α_1-receptors[8,9]It is a highly selective α2 adrenoceptor agonist.In conjunction with general anesthesia it lowers intraoperative anesthetic requirements and prolongs the postoperative analgesia[10,15] . It can be can be used effectively and safely in children due to its wide margin of safety, with appropriate monitoring and interventions to manage cardiovascular sequeale.Studies in the children also indicated that neuraxial administration of dexmedetomidine at no more than 2µg/kg and a concentration of no more than 2µg/ml does not cause neurotoxicity **.**

Although the mechanism of analgesia of α2-agonists has not been cleared, it is mainly mediated by α_{2c} and α_{2a} receptors present on the neurons of superficial dorsal horn in lamina II,there it inhibits the release of pro-nociceptive transmitters namely substance P and glutamate and causes hyperpolarization of spinal interneurons. Nakagawa et al[16] (1999) suggested the α_2-adrenergic mechanisms are involved in the modulation of nociception at the level of spinal noradrenergic systems. The activation of inwardly rectifying G1-protein-gated potassium channels causes membrane hyperpolarization which decreases the firing rate of excitable cells in the central nervous system (CNS). This is considered to be a significant mechanism of inhibitory neuronal action of α_2-adrenoceptor agonists. Another prominent physiologic mechanism is the reduction of calcium conductance into the cell, thus inhibiting neurotransmitter release. Thus these two different mechanisms causes analgesia by which the nerve is prevented from firing and propagation of its signal to its neighbour. In our study duration of postoperative analgesia (Time of first rescue analgesia) has a significantly higher difference with a mean of 8.53 hours in Group RD compared with 4.53 hours in Group R. There was a significant reduction in the FLACC score in group RD at 4 8, 12 hours postoperatively in comparison with group R.Even The mean requirement of paracetamol (rescue analgesia) was more in Group R patients with the mean of 464±1.456 mg than in Group RD patients with a mean of 217±65.054 mg.Other studies also showed significant prolongation of analgesia by adding dexmedetomidine to local anaesthetic. Our results regarding postoperative pain relief are in agreement with Anand et al[17] (2011) ,he found that by using demedetomidine 2µg/kg with ropivacaine(0.25%) 1ml/kg , the duration of postoperative analgesia recorded a median of 14.5 hours (13.90–15.09) in Group RD compared with 5.5 hours (4.97–6.03) in Group R, with a *P*-value of <0.001.Consistent with our study their FLACC score were higher with Group R patients compared with Group RD patients. Neogi et al[18] (2010) also compared clonidine 1µg/kg and dexmedetomidine 1µg/kg with ropivacaine 0.25% for caudal block in paediatric population and concluded that the duration of analgesia was prolonged for both drugs when compared with ropivacaine alone with good hemodynamic stability.

In the current study the duration of sedation was prolonged and there were significantly higher sedation scores in group RD in comparison with group R but the patients of group RD were asleep but easily arousable with verbal or physical stimuli than group R group .Its unique sedative properties is caused by hyperpolarization of excitable cells in the locus coeruleus[19]. It produces a unique form of sedation,in which patients become responsive as well as calm and cooperative when aroused Other studies also showed that administration of an α2-agonist via an intrathecal or epidural route provides an analgesic effect in postoperative pain without severe sedation**.** Confusion, a common problem for other sedatives, has not been with dexmedetomidine as it does not depend primarily on activation of the γ-aminobutyric acid system[20]**.**

The preoperative and intra operative haemodynamic variables like heart rate, mean arterial pressure, $Sp0_2$ between both groups were comparable and were not significant and therapeutic interventions were not required. No episodes of clinically significant postoperative complications such as Post Operative Nausea and Vomiting, respiratory depression, urinary retention, purities, hypotension and bradycardia were observed which are in concordance with the reports published by several other authors. Although bradycardia and hypotension are considered to be the most prominent adverse effects of α2-adrenoreceptor agonists,these side effects appear to be less pronounced in children than in adults which are in similar with the reports published by several other authors[21,22]**.** The antihypertensive effect of dexmedetomidine results from stimulation of α2 inhibitory neurones in the medullary vasomotor center (nucleus reticularis lateralis) of the brainstem, which leads to a reduction in norepinephrine release and sympathetic nerve outflow from the CNS to the peripheral tissues. Epidurally administered dexmedetomidine also decreases the electrical activity of preganglionic sympathetic nerves. Bradycardia is caused by an increase in vagal tone resulting from central stimulation of parasympathetic outflow, as well as a reduced sympathetic drive. Studies of Anand[17] et.al (2011) have also revealed better safety and analgesic profile of dexmedetomidine compared to other adjuvants.

Based on the study it can be concluded that caudal dexmedetomidine 1µg/kg along with the ropivacaine for paediatric abdominal surgeries achieved significant postoperative pain relief of 8 hours with better quality of sleep,haemodynamic stability and prolonged duration of arousable sedation. Thus eliminating the need of postoperative opiods.No episodes of clinically significant post-

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operative complications were observed.Hence dexmedetomidine as an adjuvant to ropivacaine is effective in paediatric lower abdominal surgeries. Despite the fact, we encountered no procedure related complications during the course of our study, we feel use of ultrasound in performing caudal block could have made the procedure more safe. However due to lack of resources we were unable to use ultrasound routinely.

TABLE 1. FLACC Score

Parameters	Findings	Points
Face	No particular expression or smile	0
	Occassional grimace or frown: withdrawn, disinterested	1
	Frequent to constant quivering chin, clenched jaw	2
Legs	Normal position or relaxed	0
	Uneasy, restless legs	1
	Kicking or legs drawn up	2
Activity	Lying quietly, normal position or moves easily	0
	Squirming , shifting back and forth, tense	1
	Arched, rigid or jerking	2
Cry	No cry (awake or asleep)	0
	Moans or whimpers, occasional complaints	1
	Crying steadily, sobs or screams, frequent complaints	2
Consolability	Relaxed, content	0
	Reassured by occasional touching hugging, distractable.	1
	Difficult to console or comfort	2

Table 2. Comparison of demographic and other data between two groups.

	GROUPS R	GROUPS RD	P value
Age (in yrs) (mean± S.D)	3.13 ± 1.613	2.67 ± 1.422	.239
Sex	Male = 19 Female= 11	Male =18 Female=12	.153
Weight (in kg) (mean± S.D)	15.47 ± 4.732	14.47 ± 4.337	.397
Height (in mt) (mean± S.D)	95.50 ± 14.036	89.93 ± 11.558	.691
Duration of surgery in mins) (mean± S.D)	69.17 ± 37.39	66.00 ± 10.54	.657

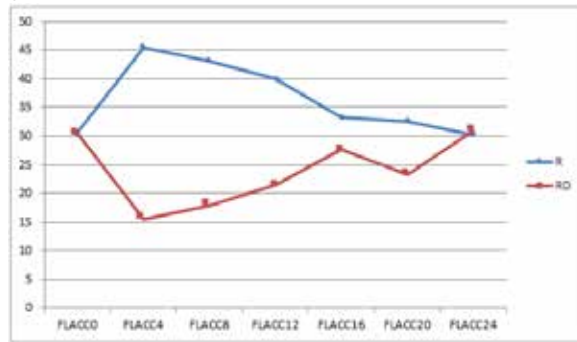
(*) indicates significance

Table 3. Total duration of analgesia and paracetamol consumption in the first 24 hours of the postoperative period.

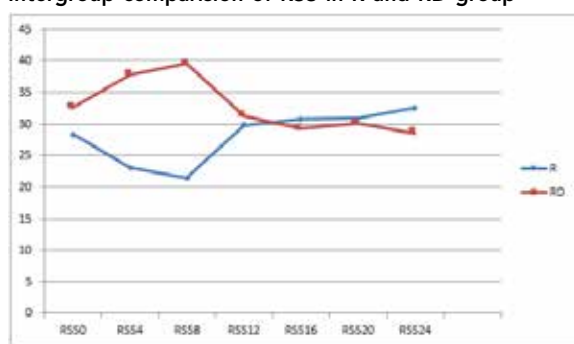
	GROUPS R	GROUPS RD	P value
Duration of analgesia (in hrs) (mean± S.D)	4.53 ± 1.46	8.53 ± 1.17	.0001
Total dose of Paracetamol(mg)	464.00± 141.97	217.00± 65.05	0.0001

(*) indicates significance

Intergroup comparision of FLACC score in R and RD group



Intergroup comparision of RSS in R and RD group



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