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A COMPARATIVE STUDY BETWEEN DEXMEDETOMIDINE AND CLONIDINE USED AS ADJUNCTS TO BUPIVACAINE FOR POST-OPERATIVE ANALGESIA BY CAUDAL BLOCK IN PAEDIATRIC PATIENTS

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ABSTRACT

Caudal anaesthesia/analgesia is simple to perform, reliable and safe. Various adjuvants are tried with local anaesthetic to prolong duration of post-operative analgesia in caudal block in paediatric patients with variable results. This prospective study was designed to assess and compare the efficacy of clonidine and dexmedetomidine used as an adjuvants to bupivacaine for caudal analgesia in paediatric patients. A 100 patients of ASA grade I or II ,age group of 6 months to 6 years undergoing infra-umblical surgeries were included in one of the following two groups. Group D received 1 µg/kg Dexmedetomidine while group C received 1 µg/kg Clonidine both with Bupivacaine plain 0.25% 1 ml/kg. Post-operative analgesia was assessed using CRIES scale. The mean duration of post-operative analgesia in group D was 14.16 ± 1.65 hours and in group C it was 11.24 ± 2.48. The prolongation of post-operative analgesia was significantly longer in group D compared to group C and the requirement of rescue analgesic doses in the first 24 post-operative hours was less in group D compared to group C. The incidence of adverse effects were statistically insignificant between the two groups.The addition of both dexmedetomidine and clonidine with bupivacaine administered caudally significantly increase the duration of post-operative analgesia.

Key words: Bupivacaine, caudal analgesia, clonidine, dexmedetomidine

INTRODUCTION

Pain is perhaps the most feared symptom of disease, which a man is always trying to alleviate and conquer since ages. It is defined by the international association for study of pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" [1]. Children are special in this regard as it is also very difficult to differentiate between restlessness or crying due to pain from that of hunger or fear. An effective pain therapy to block or modify the myriad physiologic responses to stress has become an essential component of modern pediatric anaesthesia and surgical practice [2].

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The clinical experience suggests that caudal anaesthesia/analgesia is simple to perform, reliable and safe [3]. The main disadvantage of caudal anaesthesia/analgesia is the short duration of action after a single shot injection[4]. The use of caudal catheters to administer repeated doses or infusions of local anaesthetics is not popular, partly because of concerns about infection. Prolongation of caudal analgesia using a 'single-shot' technique has been achieved by the addition of various adjuvants, such as epinephrine, opioids, ketamine, and α_2 agonists [5]. Other agents are occasionally used like corticosteroids, buprenorphine, neostigmine, tramadol, midazolam and biodegradable bupivacaine/polyester microspheres. Addition of adjuvants to local anaesthetic often obviates the placement of a caudal catheter to prolong post-operative pain relief, thus reducing morbidity and costs.[6]

Clonidine, is an α_2 adrenergic agonist, offers several benefits in children when added to local anaesthetics

either neuraxially[7,8,9] or peripherally[10]. It increases the duration of nerve blockade without eliciting hemodynamic disorders, decreases plasma peak concentration of the local anaesthetics, and produces a slight sedation for 1 to 3 hours post-operatively (which does not preclude hospital discharge). Clonidine provides a substantial anti-nociceptive effect by acting on the α_2 receptors in the dorsal horn of spinal cord and brain stem nuclei implicated in pain[11,12]

Dexmedetomidine has much higher affinity for α_2 adrenergic receptors than clonidine and negligible α_1 effect. It has an α_2/α_1 selectivity ratio of 1600:1, which is eight times more potent than clonidine (200:1)[13], major advantage is its higher selectivity compared with clonidine for α_{2A} receptors which is responsible for the hypnotic and analgesic effects. Dexmedetomidine possesses anxiolytic, sedative, sympatholytic and analgesic properties without respiratory depressant effect[14].The sympatholytic effect of dexmedetomidine decreases heart rate and mean arterial pressure by reducing noradrenaline release[15]. In addition, dexmedetomidine has the ability to reduce both the anaesthetic and opioid analgesic requirements during peri-operative period[16].

The study was conducted to compare the efficacy of clonidine & dexmedetomidine used as adjuvants to bupivacaine in caudal block to provide intra-operative anaesthesia as well as post -operative analgesia in paediatric patients.

MATERIAL AND METHODS

In our study, a total of 100 patients of ASA grade I or II, between 6 months to 6 years of age, weighing around 8-20 kg, posted for infra-umbilical surgeries like lower abdominal, urogenital and certain orthopedic surgeries were selected and divided into two groups (each containing 50 patients). All the baseline parameters like the pulse rate (PR), blood pressure (BP) and peripheral oxygen saturation (SpO_2) were observed and recorded. All patients were given syrup midazolam 0.5 mg/kg with honey orally 30 minutes (min) prior to the induction and intravenous (IV) line secured, Inj. Glycopyrrolate 4 µg/kg IV given. The drug to be given for caudal anaesthesia was prepared by diluting 0.5% bupivacaine with distilled water to yield concentration of 0.25%. Now the volume of 1 ml/kg body weight of the 0.25% bupivacaine was taken to which the study drug, either Dexmedetomidine1 µg/kg in group D or Clonidine 1 µg/kg in group C was added. To keep child immobile, 8% sevoflurane in 100% oxygen was started & after the child ceased responding to painful stimuli it was turned to left lateral position for the administration of caudal block. The prepared drugs were administered into the caudal space via a 23 gauge hypodermic needle under all aseptic and antiseptic precautions and the patients were turned supine immediately after the injection, then the sevoflurane was turned off, oxygen continued for 5 minutes then turned off. After confirmation of onset of anaesthesia by absence of response to toe pinch, the surgeon was allowed to do painting and draping the surgical part. If patient moves at the time of surgical incision and increase in PR or MAP above 20% from baseline value was adjudging as failure of caudal anaesthesia and patients were immediately given general anaesthesia with endotracheal intubation and maintained with oxygen (50%) nitrous oxide (50%) and sevoflurane and all these type of patients were excluded from the study. IV fluids were administered according to body weight and the fasting status in the form of Isolyte-P solution.

After the surgical procedure completed the patients were shifted to recovery unit and monitored for about 2 hours and then shifted to ward. In recovery unit as well as in post-operative ward patients were monitored for PR, BP, SpO_2 and analgesic score by using CRIES scale[17]. Patients were monitored for 24 hours. Analgesic score of 0 signifies excellent analgesia whereas a score of 10 indicates ineffective analgesia. Patients were given rescue analgesia in the form of syrup paracetamol 15 mg/kg body weight (syrup -120 mg/5 ml, 250 mg/5ml) when pain score is 4 or more and time to first rescue analgesia were noted and this is considered as duration of post-operative analgesia. Patients monitored for complications like post-operative nausea and vomiting (PONV), urinary retention and respiratory depression.

CRIES SCALE

It is an analgesic score described in **(Table I)**
Score 0-excellent analgesia
Score 10-ineffetive analgesia

CRIES SCALE (Analgesic score)

TABLE I: Cries scale (Analgesic score)

	0	1	2
*C*rying	No	High Pitched	Inconsolable
*R*equires O_2 to keep SpO_2 > 95%	No	< 30% Of O_2	> 30% Of O_2
*I*ncreased in HR or MAP	No	< 20%	> 20%
*E*xpressions	None	Grimace	Grimace/Grunt
*S*leepless	No	Wakes at Frequent Intervals	Constantly Awake

Statistical analysis

The data were collected and comparison of variable between two groups were done by using unpaired student 't' test. P value of < 0.05 was considered to be statistically significant. Data analysis was carried out using MedCal software package.
(pvalue≥0.05).

OBSERVATION AND RESULTS

Demographic data

The demographic data between the two groups were comparable in terms of age, weight, and duration of surgery and distribution of surgical procedures which was statistically non-significant **(Table 2)**

Table 2: Demographic data

Demographic data					
Characteristics		**Group D**	**Group C**	**P value**	**Significance**
Total patients		50	50		
Age (years)		3.35±1.55	3.07±1.34	0.33	NS
Weight (kg)		13.68±2.65	13.84±2.43	0.77	NS
Sex	Male	44(88%)	45(90%)		
	Female	6(12%)	5(10%)		
Surgery duration(hrs)		53.1±11.42	50.1±12.71	0.21	NS
Surgical procedures					
SPCL		6	3		
High ligation		15	17		
Circumcision		14	13		
Orchidopexy		3	6		
Hernia repair		5	6		
Glans cyst excision		0	1		
PMSTR		7	4		

SPCL= Supra Pubic Cystolithotomy
PMSTR= posteromedial short tendon release

Vital parameters

Patients were haemodynamically stable in means of PR, MAP, SpO_2, throughout the intra-operative **(Figure 1)** as well as post-operative period **(Figure 2)** and the difference is not significant**.**

Post-operative analgesia

The total duration of post-operative analgesia as well as rescue analgesia required in 24 hours in both the groups were statistically significant (Table 3).

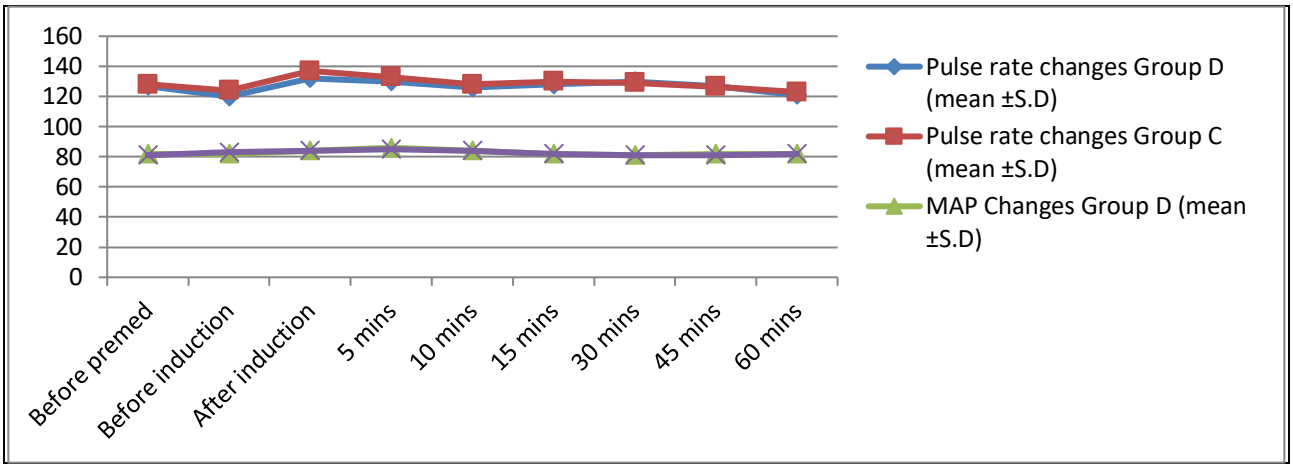

Figure 1: Intra operative Pulse rate and MAP changes

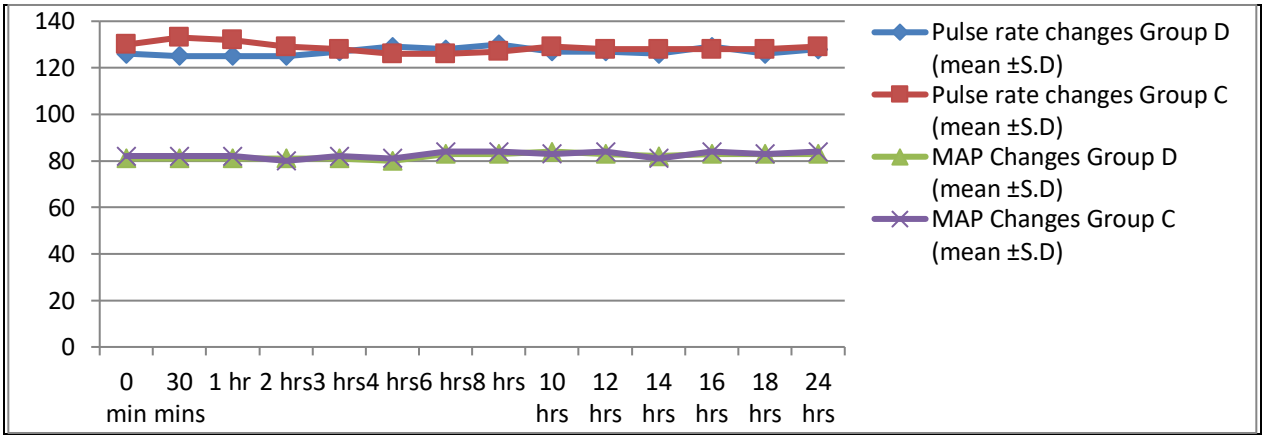

Figure 2: Post operative Pulse rate and MAP changes

Table 3: Duration of post-operative analgesia and post-operative analgesic requirement

	Group D	Group C	P value	Significance
Post-operative analgesia in hours (mean ± SD)	14.16 ± 1.65 (10-16)	11.24 ± 2.48 (8-18)	< 0.0001	S
Number of analgesic dose required in 24 hours (mean ± SD)	01.08 ± 6.27	01.90 ± 0.67	< 0.0001	S

Discussion

The study designed to compare the duration of post-operative analgesia between the dexmedetomidine 1 µg/kg in group D and clonidine 1 µg/kg in group C with 0.25% bupivacaine plain 1 ml/kg (2.5 mg/kg) in caudal anaesthesia as well as post-operative analgesia in paediatric patients undergoing infra-umblical surgeries. We found that the mean duration of post-operative analgesia in dexmedetomidine group was longer than the clonidine groupoperative period, requirement of rescue analgesic doses in the form of syrup paracetamol 15 mg/kg in 24 hours in dexmedetomidine group was less as compared to clonidine group. Our results are similar to those reported in the previous studies.

Arunapara meshwari *et al* [18] found that the clonidine in a dose of 1 µg/kg added to 0.25% bupivacaine for caudal analgesia, during sub-umbilical surgeries, prolongs the duration of analgesia of bupivacaine (10 hours) with less requirement of rescue analgesics without any side effects.

El-Hennawy *et al* [19] Single caudal dose of bupivacaine 0.25% (1 ml/ kg) combined with either dexmedetomidine 2 µg/ kg in normal saline 1 ml in group BD, clonidine 2 µg/ kg in normal saline 1 ml in group BC, or corresponding volume of normal saline in group B. They have found that the time of adequate caudal analgesia (FLACC scale score, 4) without the need for morphine is significantly higher in the groups receiving the bupivacaine-dexmedetomidine mixture [median (95% CI):16 (14–18) h] or bupivacaine–clonidine mixture [median (95% CI): 12 (3–21) h] than the group receiving plain bupivacaine [median (95% CI): 5 (4–6) h]. They concluded that addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia in children undergoing lower abdominal surgeries with no significant advantage of dexmedetomidine over clonidine and without an increase in incidence of side effects.

Neogi *et al* [17] study was designed to assess and compare the efficacy of clonidine 1 µg/kg (group C) and dexmedetomidine 1 µg/kg (group D) used as adjuvants to ropivacaine 0.25% 1 ml/kg and plain ropivacaine 0.25% 1 ml/kg (group R) for caudal analgesia in paediatric patients. They conclude that duration of post-operative analgesia was significantly prolonged in Group C (13.17±0.68 hours) and Group D (15.26±0.86 hours) in comparison to Group R (6.32±0.46 hours) ($p < 0.05$) without any alteration in haemodynamic and any side effects.

Lee *et al* AP [20] administered clonidine in a dose of 2µg/kg along with local anaesthetic agent in children undergoing orthopaedic surgery. They observed higher incidence of bradycardia and hypotension associated with 2µg/kg dose of clonidine. Klimscha *et al* [21] also reported that analgesic efficacy does not seem to be enhanced by increasing the dose of clonidine from 1µg/kg to 2µg kg.

In our study we used clonidine 1 µg/kg added to 0.25% bupivacaine in group C. It increases the duration of post-operative analgesia without any hemodynamic alterations.

In recent study done by Akilandeswarimanickam *et al* [22] on efficacy of clonidine 1 µg/kg with 0.1% ropivacaine and plain 0.1%, 0.2% ropivacaine for caudal analgesia in children. They found that the addition of clonidine 1 µg/kg to 0.1% ropivacaine provided increased duration (590.25 ± 83.93 minutes) and better quality of pain relief with no motor blockade and sedation compared to plain 0.1% ropivacaine (243.7 ± 99.29 minutes) and 0.2% ropivacaine (388.5 ± 82,35 minutes).The above previous studies supported our results, adding dexmedetomidine or clonidine to bupivacaine in caudal block provides adequate intra-operative anaesthesia as well as increases the duration of post-operative analgesia. The magnitude of haemodynamic changes between the two groups was similar. The episodes of clinically significant post-operative respiratory depression, hypotension, or bradycardia were not identified.

CONCLUSION

We found that the mean duration of post-operative analgesia in dexmedetomidine group was longer than the clonidine group. In post-operative period , requirement of rescue analgesic doses in the form of syrup paracetamol 15 mg/kg in 24 hours in dexmedetomidine group was less as compared to clonidine group.

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