



COMPARITIVE STUDY OF DEXMEDETOMIDINE AND CLONIDINE USED AS ADJUVANTS IN CAUDAL ANAESTHESIA FOR POST OPERATIVE ANALGESIA IN PAEDIATRIC PATIENTS

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ABSTRACT

Background: Inadequate treatment of post-operative pain adversely affects physiology, psychology and social interactions in children. Effective pain relief has a positive outcome on surgical stress response, post-operative recovery, early ambulation and psychological and emotional state of paediatric patients in early post-operative period. Dexmedetomidine, an α_2 receptor agonist, helps to prolong effective analgesia by acting on the pontine locus ceruleus. Clonidine another α_2 agonist provides a substantial antinociceptive effect by acting on the dorsal horn of spinal cord and brain stem nuclei implicated in pain. Both of these drugs serve as a promising adjunct in caudal block to provide post-operative analgesia.

AIM: The study was undertaken to compare dexmedetomidine and clonidine as an adjuvant along with Bupivacaine in caudal block with the following aims:

1. Primary objectives: 1) Post-operative analgesia, 2) Intra-operative and post-operative haemodynamic parameters, & 3) Intra-operative and post-operative sedation.
2. Secondary objectives: To evaluate adverse effects and complications, if any.

Material and Method: It was a randomized, prospective, double blinded, comparative hospital based study at Department of Anaesthesiology, Gandhi Medical College, Bhopal. 60 ASA Grade I-II patients, 6 months-6 years of either sex, scheduled for infra-umbilical surgeries were randomly allocated into two groups:

Group 1: received 1 microgram/kg clonidine and

Group 2: received 1 microgram/kg dexmedetomidine,

Added to 0.5% Bupivacaine plain (3mg/kg body wt.) and diluted with normal saline upto total body weight of child through caudal epidural.

- i) Postoperative analgesia by FLACC score,
- ii) Sedation by Ramsay Sedation Score,
- iii) Hemodynamic variables were recorded for 12 hours.

Results: Although there was not much significant difference between the haemodynamic parameters in both the groups, the duration of analgesia was significantly higher in the patients belonging to the Group 2. Likewise, the average numbers of rescue analgesic doses received by Group 1 patients were more compared to patients in Group 2.

Conclusion: From our study we conclude that Dexmedetomidine $1\mu\text{g}/\text{kg}$ is significantly superior to clonidine $1\mu\text{g}/\text{kg}$ in caudal block for causing sedation and in prolonging the duration of analgesia.

KEYWORDS : Caudal Analgesia, Dexmedetomidine, Clonidine, Post-operative pain. .

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 and 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 anesthesia and surgical practice [2].

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 anesthetics 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 anesthetic often obviates the placement of a caudal catheter to prolong post-operative pain relief, thus reducing morbidity and pain.

Clonidine, is an α_2 adrenergic agonist, offers several benefits in children when added to local anesthetics 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 anesthetics, and produces a slight sedation for 1 to 3 hours postoperatively (which does not preclude hospital discharge). Clonidine provides a substantial antinociceptive 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 [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 anesthetic 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 pediatric patients undergoing infra-umbilical surgeries.

Material and Methods

After obtaining approval from the Ethical committee, a written informed consent was obtained from all the parents of the children

who participated in this study. This study was conducted in 60 children of American Society of Anaesthesiologists(ASA) grade I and II, aged 6 months-6 years, undergoing elective infra-umbilical surgeries like herniotomy, orchidopexy, hypospadias repair etc. The patients with a history of evidence of infection at back, allergy to drugs, congenital malformations of back, pre-existing neurological or spinal diseases were excluded from this study.

All the patients underwent a pre-anaesthetic check-up a day prior to surgery, and all the routine and specific investigations were noted. The children were kept nil by mouth 6 hours prior to surgery. Before surgery a written and informed consent was taken from the parents. An intravenous line was secured, standard monitors like electrocardiogram, pulse oximeter and non-invasive blood pressure were applied and baseline hemodynamic parameters were recorded. All children were premedicated with injection glycopyrrolate 0.02mg/kg and ondansetron 0.1mg/kg. Injection ketamine 1mg/kg was given for analgesia & sedation.

Caudal block was performed with full aseptic precautions with the patient in left lateral position:

Group 1: received 1 microgram/kg clonidine and Group 2: received 1 microgram/kg dexmedetomidine,

Added to 0.5% Bupivacaine plain (3 mg/kg body wt.) and diluted with normal saline upto total body weight of child.

The site of injection was dressed and the patient was turned supine. Heart rate, BP, respiratory rate and oxygen saturation were recorded before caudal block and immediately after caudal block, and every 10 minute during surgery thereafter. Adequate analgesia was defined as haemodynamic stability as indicated by the absence of increase in systolic BP or HR of more than 20% compared with baseline value and from the intraoperative requirement of injection ketamine. All the patients were observed for 2 hours in recovery room before returning to the ward. HR, BP, RR were recorded continuously. Duration of postoperative sedation was assessed according to the Ramsay sedation score.

Scale	Description
1	Anxious and agitated or restless, or both
2	Cooperative, oriented, and tranquil
3	Response to commands only
4	Brisk response to light glabellar tap or loud auditory stimulus
5	Sluggish response to light glabellar tap or loud auditory stimulus
6	No response to light glabellar tap or loud auditory stimulus

Duration of analgesia (time from caudal block to the first dose of rescue analgesic) was recorded according to FLACC score. The time of first rescue analgesia received, the total numbers of doses received in 12 h were noted in both the groups postoperatively.

Category	Scoring	0	1	2
Face	No particular expression or smile	Occasional grimace or frown withdrawn, disinterested	Frequent-constant quiver chin, clenched jaw	
Legs	Normal position, relaxed	Uneasy, restless, tense	Kicking or legs drawn up	
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back & forth, tense	Arched, rigid or jerking	
Cry	No cry (awake or asleep) occasional complaint	Moans or whimpers; sobs; frequent complaint	Crying steadily, screams, screams	
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to, distractible	Difficult to console or comfort	

All the observations were recorded and the results were analysed. Statistically data was presented as a Mean ± Standard deviation. A value of P <0.05 was considered as a statistically significant

difference with unpaired student's t-test.

Statistical Analysis

Sample size estimation was done using sample size and power analysis by software G*power (version 3.1.9.2) to detect a mean IOP difference of approximately 15% between the two study groups with alpha error 0.05 and beta error 0.10 (power of study=0.90) based on previous similar studies^{1,2}. This revealed the minimum required sample size to be 13 for each study group.

All observations were tabulated and analysed using independent student't' test and chi-square test in Statistical Package for Social Sciences (SPSS) software version 22. Statistically significant difference in findings was considered when p-value was <0.05.

Results

This study was a randomized, prospective, double blinded hospital based study of comparison of clonidine and dexmedetomidine used as adjuvant with plain bupivacaine for caudal analgesia in children posted for infra-umbilical surgeries. This study was conducted on 60 children of ASA Grade I and II, aged 6 month-6 years, either sex, and was randomly allocated into two groups, 30 patients in each group.

1) The mean age, weight and sex distribution in all groups were nearly same without any significant differences.

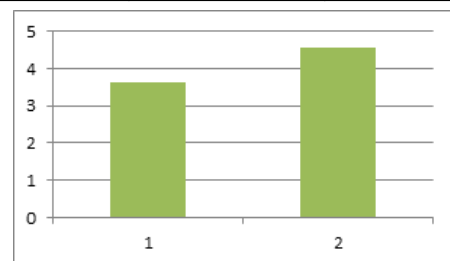
Variables	Group 1	Group 2	p value
Age in years: Mean ±SD	3.70±1.39	3.83± 1.37	0.7096
Weight(in kg) Mean± SD	11.23± 1.45	11.70 ±1.62	0.2455
Sex ratio Male: Female	19:11	21:9	-

2) There was no significant difference between the groups with respect to the intraoperative and postoperative systolic BP and pulse rate.

	Group 1	Group 2	p value
Preoperative vitals(Mean± SD)	112.70± 8.37	113.80± 6.77	0.6503
Pulse	102.40± 4.52	103.90± 4.88	0.3196
BP			
Intraoperative vitals(Mean ± SD)	106.30 ±8.78	107.30± 6.75	0.6887
Pulse	98.20 ±6.39	97.50± 4.25	0.6855
BP			
Postoperative vitals(Mean ± SD)	110.50± 7.73	110.20 ±5.91	0.89105
Pulse	101.20 ±5.41	101.90 ±3.40	0.6268
BP			

3) There was a significant difference between the intraoperative and postoperative sedation scores in both groups. The sedation scores were more in group 2 as compared to group 1 (p-value<0.0001).

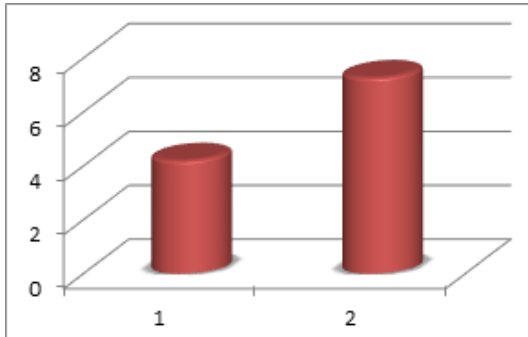
Sedation scores	Group 1	Group 2
Mean ± SD	3.65± 0.49	4.55± 0.60



Comparison of sedation scores between two groups.

4) As per the following table and graph, the duration of analgesia was significantly higher in group 2 as compared to group 1 (p value<0.0001).

	Group 1	Group 2
Duration of analgesia(Mean±SD)	4.200± 0.299	7.275± 0.573



Comparison duration of analgesia between two groups.

5) The number of rescue analgesics required by the patients belonging to group 1 was higher than patients of group 2. Moreover, the time of requirement of first rescue analgesic was less in patients of group 1 as compared to group 2 (p<0.0001).

	Group 1	Group 2
Number of rescue analgesics(Mean±SD)	2.25± 0.64	1.25± 0.44
Time in hours of requirement of first rescue analgesic(Mean±SD)	2.95± 0.359	6.450± 0.095

6) There were no significant adverse effects noted in either group.

Discussion

Caudal epidural analgesia is one of the most popular and commonly performed regional blocks in paediatric anaesthesia. It is a reliable and safe technique that can be used with general anaesthesia for intra and post-operative anaesthesia in patients undergoing abdominal and lower limb surgeries.

The main disadvantage of caudal block is the short duration of action. Dexmedetomidine {alpha 2 receptor agonist}, when used as an adjunct to caudal blocks, prolongs the duration of analgesia effectively. It causes sedation, thus allaying the anxiety and irritation intra-operatively. This study was undertaken to compare the effects of clonidine(1µg/kg) and dexmedetomidine(1µg/kg) added to 0.5% Bupivacaine plain(3 mg/kg) and diluted with normal saline upto total body weight of the child injected through caudal epidural block.

Dexmedetomidine is a highly selective alpha2 receptor agonist, the analgesic action of intrathecal or epidural dexmedetomidine results from the direct stimulation of pre and post synaptic alpha 2 receptors in the dorsal grey matter of spinal cord thereby inhibiting the release of nociceptive neurotransmitters. It has 8 fold increased affinity for alpha 2 receptors as compared to clonidine. It is more selective for alpha 2a receptors that are responsible for sedative and analgesic actions. The side effects of neuraxial dexmedetomidine include hypotension and bradycardia.

El-Hennawy et al [17] 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.

Lee et al AP [18] administered clonidine in a dose of 2µg/kg along with local anesthetic agent in children undergoing orthopedic 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.ne increases the duration of caudal anaesthesia.

In our study we therefore used clonidine (1mcg/kg) and dexmedetomidine (1mcg/kg) as adjuvant to bupivacaine for caudal anaesthesia in paediatric patients undergoing infra-umbilical surgeries to evaluate duration of post-operative analgesia and concluded that dexmedetomidine provides better post-operative analgesia with minimum hemodynamic alterations.

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 12 hours in dexmedetomidine group was less as compared to clonidine group

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REFERENCES

- Lloyd-Thomas AR. Pain management in paediatric patients. *BJA*. 1990; 64:85-104
- De Beer DA, Caudal additives in children. *BJA*. 2003; 90:487-98
- Hager H, Marhofer P, Sitzwohl C, Adler L, Kettner S, Semsroth M. caudal clonidine prolongs analgesia from caudal S(+)-ketamine in children. *Anesth Analg*. 2002;94:1169-72
- Lloyd-Thomas AR. Pain management in paediatric patients. *Br J Anaesth*. 1990;64:85-104. [PubMed]
- De Beer DA, Thomas ML> caudal additives in children- Solutions or problems? *Br J Anaesth*. 2003;90:487-98. [PubMed]
- Lee JJ, Rubin AP. Comparison of a bupivacaine-clonidine mixture with plain bupivacaine for caudal analgesia in children. *Br J Anaesth*. 1994;72:258-62. [PubMed]
- Fares KM, Othman AH, ALieldin NH> Efficacy and safety of dexmedetomidine added to caudal bupivacaine in paediatric major abdominal cancer surgery. *Pain physician*. 2014;17:393-400.
- Upadhyay KK, Prabhakar TB, Handa R, Haridas B. Study of the efficacy and safety of clonidine as and adjuvant to bupivacaine for caudal analgesia in children. *Indian J Anaesth*. 2005;49:199-201.
- Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: A behavioural scale for scoring postoperative pain in children. *Pediatr Nurs*. 1997;23:293-7. [PubMed]
- Parameswari A, Dhev AM, Vakamudi M. efficacy of clonidine as an adjuvant to bupivacaine for caudal analgesia in children undergoing sub-umbilical surgery. *Indian J Anesth*. 2010;54:458-63. [PubMed].
- Kehlet HS. Surgical stress: the role of pain and analgesia. *Br J Anaesth* 1989; 63:185-95.
- Wayslack TJ, Abbot CV. Reduction of postoperative morbidity following patient controlled morphine analgesia. *Can J Anesth* 1990; 37:726-.
- Coursin DB, Maccioli GA. Dexmedetomidine. *Curr Opin Crit Care* 2001; 7: 221–6
- Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic and analgesic properties of small dose Dex infusions. *Anesth Analg* 2000; 90:699-705
- Guler G, Akin Z, Tosun E, Eskitascoglu O, Mizrak A, Boyaci A. Single dose dexmedetomidine attenuates airway and circulatory reflexes during extubation. *Acta Anaesthesiol Scand* 2005; 49: 1088-.
- Gmbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. *Can J Anesth* 2006; 53.
- A.M. El-Hennawy, A.M. Abd-Elwahab, A.M. Abd-Elmaksoud. H.S. El-Ozairy, S.R. Boulis. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. *Br J Anaesth* 2009; 103:268-274.
- Lee JJ, Rubin AP. Comparison of a bupivacaine–clonidine mixture with plain bupivacaine for caudal analgesia in children. *Br J Anaesth* 1994; 72: