A CLINICAL STUDY OF CLONIDINE 0.5µg/kg AND 1µg/kg AS AN ADJUVANT TO 0.25% BUPIVACAINE IN PAEDIATRIC CAUDAL BLOCK FOR CIRCUMCISION

Madhava Reddy¹, Ranjitha Gangadharaiah²

HOW TO CITE THIS ARTICLE:
Madhava Reddy, Ranjitha Gangadharaiah."A Clinical study of Clonidine 0.5µg/kg and 1µg/kg as an Adjuvant to 0.25% Bupivacaine in Pediatric Caudal Block for Circumcision". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 02, January 13; Page: 359-368, DOI:10.14260/jemds/2014/1834

ABSTRACT: BACKGROUND AND OBJECTIVES: Regional techniques are now increasingly being used in pediatric patients to provide post-operative analgesia. Caudal epidural block is one of the most common regional techniques used in pediatric anesthesia. AIMS AND OBJECTIVES: 1. To assess the safety and efficacy of 0.25% Bupivacaine with Clonidine in pediatric caudal block. 2. To compare the duration of analgesia with different dosages of Clonidine as an adjuvant. METHODS: This study was conducted in the department of Anesthesiology with co-operation from the department of Pediatric Surgery at KIMS hospital and research centre, Bengaluru from December 2008 to September 2010. Study design: Comparative Randomized study. Sampling method: Purposive sampling. Statistical analysis: Using Student’s t test and chi-square test. In this study caudal block was given in 60 children aged between 1-6 years, posted for circumcision who were divided into two groups. Group I consisting of 30 children who received 0.25% Bupivacaine 0.5ml/kg with Clonidine 0.5µg/kg as adjuvant and group II consisting of 30 children who received 0.25% Bupivacaine 0.5ml/kg with Clonidine 1µg/kg. All the children were premedicated with Inj. Atropine 0.01mg/kg and Inj. Midazolam 0.1mg/kg. Caudal block was performed in all children after induction with Propofol and maintained on spontaneous ventilation with Oxygen, Nitrous oxide and Halothane. Intraoperatively the hemodynamic changes were monitored by recording the heart rate, blood pressure and SPO₂ and the onset of action was noted. Postoperatively the duration of sedation was assessed using the sedation score, duration of analgesia using the observational pain scale, motor block using the modified Bromage scale and any complications that occurred were noted. RESULTS: Intraoperatively there was a minimal fall in the heart rate and no significant variation in the mean arterial pressure in both the groups. Postoperatively all the vital parameters were unaltered until the child experienced pain when there was an increase in heart rate. The duration of sedation was 134.00±18.02 mins in group I and 139.50±20.52 mins in group II. We did not observe any case of motor block in both the groups. The duration of analgesia was observed as 423.50±22.86 mins in group I and 456.00±38.52 mins in group II which was statistically significant (p<0.001). CONCLUSIONS: Caudal epidural block using Clonidine as an adjuvant to Bupivacaine prolongs the duration of analgesia. There is no significant difference in the onset of action between the two groups. Duration of sedation was observed to be similar in group I and group II. There was no case of motor blockade in both the groups. Though the difference in the duration of analgesia between the two groups is statistically significant (p<0.001), clinically the difference is about 30 mins only. Hence a lesser dose of Clonidine can be used in short surgical procedures like circumcision, so that any undesired side effects can be minimized further.
INTRODUCTION: “For all The Happiness Mankind can gain is not in Pleasure but in Rest from Pain” -JOHN DRYDEN

Pain is a protective mechanism designed to alert the body to potentially injurious stimuli. The inability to react and to answer questions as adults do has contributed to the false impression that children do not feel pain as much as adults do\(^1\). It is now well established that nociception occurs in neonates also. Basic excitatory connections develop early in fetal life and receptors are widely distributed\(^2\).

Post-operative pain relief in a child is a main concern to the Anesthesiologist as pain not only affects the patient but also increases anxiety in the parents which can be relieved by good postoperative analgesia.

Caudal epidural block is one of the most common regional techniques used in pediatric anaesthesia\(^3\). Recently it has gained popularity especially for short surgical procedures below the umbilicus, as it is a simple, safe and reliable technique\(^4\). The main disadvantage of this single shot caudal block is its shorter duration of action even with the use of long acting local anesthetic agents such as Bupivacaine\(^3\). To avoid epidural catheter placement and yet prolong the duration and improve the quality of intra-operative and post-operative analgesia of local anesthetics, various drugs like Opioids 5, 6, 7, Epinephrine, Midazolam\(^8\), Ketamine\(^9\), Neostigmine\(^10\), Clonidine\(^11, 12, 3\), etc. have been used as adjuvants with various advantages, disadvantages and adverse effects.

Clonidine, an alpha 2 adrenergic agonist produces analgesia by its central action\(^13, 14\). It is a more potent analgesic with minimal acceptable side effects when used epidurally\(^15\). Clonidine is used as an adjuvant with local anesthetics like Lignocaine, Bupivacaine and Ropivacaine in caudal block to improve the intra-operative and post-operative analgesia and to reduce the dose of local anesthetic, in turn to decrease the toxicity of local anaesthetics\(^16\).Clonidine is known to produce analgesia of variable intensity and duration, which is dose dependent. Many authors used Clonidine as an adjuvant to local anesthetic with different dosages ranging from 1μg/kg to 3μg/kg. A few used 0.5μg/kg as an adjuvant in pediatric caudal block.

For short surgical procedures like circumcision where post-operative analgesia is the main concern and motor blockade is not required, lower concentration and volume of Bupivacaine and lower doses of Clonidine can be used so that the adverse effects of these drugs can be reduced further.

This study is used to assess the efficacy, safety and duration of analgesia of a low volume of Bupivacaine with a low dose of Clonidine as an adjuvant for caudal block; hence we are comparing 0.5μg/kg with 1μg/kg of Clonidine as an adjuvant to 0.25% Bupivacaine at a volume of 0.5ml/kg in children undergoing circumcision.

AIMS AND OBJECTIVES:
1. To assess the safety and efficacy of 0.25% Bupivacaine with Clonidine in pediatric caudal block.
2. To compare the duration of analgesia with different dosages of Clonidine as an adjuvant.

MATERIALS AND METHODS: This study was conducted in the department of Anesthesiology with co-operation from the department of Pediatric Surgery at KIMS hospital and research centre, Bengaluru from December 2008 to September 2010.
Study design: Comparative Randomized study. Randomization was done as follows: odd numbers were taken as group I and even numbers as group II.

Sampling method: Purposive sampling

Statistical analysis: Using Student’s t test and chi-square test.

60 children aged 1 to 6 years of ASA physical status-I posted for circumcision were taken up for the study after obtaining consent from their parents.

Inclusion Criteria:
1) Children between 1 to 6 years
2) Posted for circumcision with informed written consent from their parents
3) ASA physical status-I

Exclusion Criteria:
1) Parental unwillingness
2) Body weight > 25 kgs
3) Children with preexisting neurological or spinal disease, cardiovascular, respiratory, renal, hepatic or any other systemic disease
4) Bleeding diathesis
5) Infection at the site of block
6) Abnormalities of the sacrum
7) Allergic to local anesthetics
8) Aspirin ingestion in the preceding week
9) Chronic use of any anti-inflammatory drugs

GROUP I received 0.25% Bupivacaine 0.5ml/kg + 0.5 µg/kg Clonidine, whereas GROUP II received 0.25% Bupivacaine 0.5ml/kg + 1 µg/kg Clonidine

On admission a thorough preoperative evaluation of the patient was done. Then a written informed consent was taken from the parents after explaining the procedure, advantages and its consequences in their own language.

Basal vital parameters like heart rate, blood pressure and Oxygen saturation were recorded after connecting the child with Philips V24E monitor. A good intravenous line was established and Isolyte P was connected. Inj. Atropine 0.01mg/kg IV and Inj. Midazolam 0.1mg/kg IV was given as premedication. Patients were induced with Propofol 2mg/kg IV and maintained on spontaneous ventilation with Oxygen, Nitrous Oxide and Halothane by using the Jackson Rees circuit. Sevoflurane causes emergence delirium as a side effect hence we used Halothane as the inhalational agent.

The child was put in the left lateral position and under aseptic precautions the sacral hiatus was identified. Caudal epidural space was identified by using the loss of resistance technique and the drug was deposited after confirming negative aspiration for blood and CSF.

FIGURE 1: performing the block
Intraoperatively the onset of action and duration of surgery were noted. The onset of action is defined as the time in minutes between local anesthetic injection and the absence of gross movements or absence of significant increase in heart rate on application of the mechanical stimulus. Heart rate, blood pressure and $\text{SPO}_2$ were recorded before and after induction and every 5 mins thereafter till the surgery was over. Any rescue doses of Propofol needed was noted.

Post-operatively the vital parameters were recorded every 15 mins and also the duration of sedation, duration of analgesia, any complications like bradycardia, hypotension, xerostomia, retention of urine, respiratory depression, nausea, vomiting etc. were noted in each group.

Sedation was assessed using the Sedation score where the duration of sedation is defined as the time from the onset of analgesia to spontaneous eye opening (sedation score <1).

| CRITERION                                         | SCORE |
|--------------------------------------------------|-------|
| Eyes open spontaneously                          | 0     |
| Eyes open in response to speech                  | 1     |
| Eyes open in response to physical stimulation    | 2     |

Modified Bromage Scale

| CRITERION                                    | SCORE |
|----------------------------------------------|-------|
| No motor block, child moves limbs freely     | 0     |
| Inability to raise legs                      | 1     |
| Inability to flex knees                      | 2     |
| No movement possible in legs                 | 3     |

DURATION OF ANALGESIA: In 1994 Samir et al. evaluated the duration of analgesia using the FACES (based on facial expression) scale. In 1994 Lee et al. assessed the quality of analgesia using a pain scoring system modified from Hannallah and colleagues which is based on five criteria: arterial pressure, crying, movement, agitation and localization of pain. Bock et al. in 2002 assessed the duration of analgesia using the pain/discomfort scale which includes blood pressure, crying, movement, agitation, posture and complaints of pain.

In our study we have used the observational pain scale to study the duration of analgesia. The duration of analgesia is defined as the time of onset of analgesia after caudal deposition of the drug to the time of appreciation of pain by the child post operatively. If the child complained of pain or if the pain score is $\geq 3$ the child received Paracetamol suppository 15mg/kg as a rescue analgesic.
RESULTS: The total number of children studied were 60.30 children in group I and 30 children in group II.

ONSET OF ACTION: The onset of action in the study was as early as 5mins and as late as 8mins. The mean onset of action in group I was 6.47±0.68mins and in group II was 6.43±0.63mins as represented in Table 1.

| Onset of action in mins | Group I       | Group II      | P value |
|-------------------------|---------------|---------------|---------|
| Mean                    | 6.47±0.68     | 6.43±0.63     | 0.844   |

Table 1: Mean Onset of action

Heart rate variations: The mean basal heart rate in group I was 131.5±10.42/min and in group II was 132.53±11.28/min as shown in Table 2. At the end of 30 mins the mean heart rate in group I was 106.13±7.39/min and in group II was 104.47±7.16/min.

| HR (bpm) | Group I       | Group II      | P value |
|----------|---------------|---------------|---------|
| 0 min    | 131.5±10.42   | 132.53±11.28  | 0.714   |
| 5 min    | 125.90±9.98   | 126.50±10.04  | 0.817   |
| 10 min   | 120.77±9.52   | 121.63±9.24   | 0.722   |
| 15 min   | 116.37±9.06   | 116.67±9.44   | 0.901   |
| 20 min   | 112.50±8.52   | 111.60±8.74   | 0.688   |
| 25 min   | 108.80±8.31   | 107.80±8.05   | 0.638   |
| 30 min   | 106.13±7.39   | 104.47±7.16   | 0.379   |

Table 2: Comparison of heart rate in two groups of patients
Mean arterial pressure variations: Table 3 shows the intra operative mean arterial pressure in group I and group II. The basal mean arterial pressure in group I was 70.18±3.12mmHg and in group II was 70.28±2.91mmHg. After 30mins it was 69.80±2.95mmHg and 69.22±2.94mmHg respectively.

| MAP (mm Hg) | Group I       | Group II      | P value |
|-------------|---------------|---------------|---------|
| 0 min       | 70.18±3.12    | 70.28±2.91    | 0.898   |
| 5 min       | 69.53±3.42    | 69.28±3.50    | 0.776   |
| 10 min      | 69.12±3.40    | 68.04±3.54    | 0.233   |
| 15 min      | 68.61±3.07    | 68.00±3.41    | 0.469   |
| 20 min      | 69.49±2.7     | 68.96±3.85    | 0.537   |
| 25 min      | 69.76±2.61    | 68.68±3.20    | 0.159   |
| 30 min      | 69.80±2.95    | 69.22±2.94    | 0.450   |

Table 3: Comparison of mean arterial pressure in two groups of patients

Postoperative hemodynamic variations: There was not much variation in the hemodynamics postoperatively in both the groups. There was a minimal change in blood pressure in both the groups.

DURATION OF SEDATION: The mean duration of sedation in group I and group II was 134±18.02mins and 139.50±20.52mins respectively as shown in Table 4.

| Sedation     | Group I       | Group II      | p value |
|--------------|---------------|---------------|---------|
| Duration in mins | 134.00±18.02  | 139.50±20.52  | 0.275   |

Table 4: Duration of sedation

DURATION OF ANALGESIA: Table 5 represents the duration of analgesia in both the groups. In our study in group I, the shortest duration of analgesia was 375mins, the longest was 480mins and the mean duration of analgesia being 423.50±22.86 mins, whereas in group II the shortest duration of analgesia was 390mins, longest was 540mins and the mean being 456.00±38.52mins. These values are statistically significant (p<0.001).

| Duration of analgesia | Group I       | Group II      | p value |
|-----------------------|---------------|---------------|---------|
| Mean duration in mins  | 423.50±22.86  | 456.00±38.52  | <0.001  |

Table 5: Duration of analgesia

COMPLICATIONS: Among the 60 children studied, one case (3.3%) in group II had retention of urine for >12hrs and one case (3.3%) in group I had postoperative hematoma at the surgical site as complications.
DISCUSSION: Pain 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”. Due to the wrong notion that children neither suffer or feel pain, nor respond to or remember the painful experiences to the same degree as adults do, they have been undertreated for pain21.

Caudal analgesia is the most popular and commonly used regional block in pediatric surgery19. Bupivacaine has been the local anesthetic of choice due to its longer duration of action. In 1989 Bernard et al22 compared the efficacy of different local anesthetics and concluded that Bupivacaine provides a long duration of analgesia.

Different study groups have used different volumes of 0.25% Bupivacaine. Lee et al19 in 1994 used Bupivacaine 1ml/kg, Klimscha et al23 in 1998 used 0.75ml/kg and Pankaj et al5 in 1998 used 0.66ml/kg. In our study the volume of 0.25% Bupivacaine used was 0.5ml/kg which has been recommended by Armitage EN in 1979 to cover the sacral dermatomes and there is no evidence that a larger volume of the same concentration of local anesthetic increases the duration of caudal blockade3,24.

Postoperative analgesia can be prolonged by intermittent or continuous infusion of analgesics through caudal catheters or by the use of adjuvants. The use of caudal catheters is limited due to a high rate of infection and higher incidence of technical problems. Jorg et al25 in 2004 demonstrated bacterial colonization in those with caudal catheters. Hence a better choice for prolonging the duration of analgesia is the use of adjuvants for short surgical procedures like circumcision.

A large number of additives to local anaesthetics have been used to extend the duration of caudal blockade in children.

In 1988 Elliot et al26 observed respiratory depression with the use of caudal Morphine 1.5mg. Whereas Pankaj et al5 in 1998 concluded that the duration of analgesia was prolonged with Morphine as an adjuvant and they observed no cases of respiratory depression.

Cook et al27 in 1995 studied the efficacy of Adrenaline, Ketamine and Clonidine as an adjuvant to Bupivacaine and proved Ketamine and Clonidine were better adjuvants than Adrenaline and they did not observe any complications with Ketamine. Whereas in 2005 Kumar et al28 observed hallucinations in those given caudal Ketamine and also concluded that Neostigmine and Midazolam are better adjuvants than Ketamine when they studied caudal block using Neostigmine, Midazolam and Ketamine. Midazolam has been observed to cause prolonged sedation8.

Addition of the alpha 2 adrenergic agonist Clonidine has been found to be capable of enhancing the quality and duration of caudally administered local anaesthetics in children. In 2009 Archna et al15 concluded that Clonidine prolonged the duration of caudal analgesia when added to Bupivacaine.

In our study we have used Clonidine 0.5µg/kg in group I and Clonidine 1µg/kg in group II as an adjuvant to 0.25% Bupivacaine 0.5ml/kg.

Constant et al11 in 1998 observed the duration of analgesia as 265 mins in those who received Clonidine 1.5µg/kg and 287mins in those who received caudal Clonidine 0.75µg/kg with Fentanyl0.5µg/kg as adjuvants to 0.25% Bupivacaine 1ml/kg. As per the study, the minimal increase in the duration of analgesia may be related to the difficulties in predicting and assessing pain in the postoperative period in young children.
In our study the mean duration of caudal analgesia in group I was 423.5mins and in group II it was 456mins.

Yildiz et al.\textsuperscript{12} in 2006 showed the mean duration of analgesia as 105mins with plain Bupivacaine 0.125% 1ml/kg, 240mins with Clonidine 1µg/kg, 350mins with Clonidine 1.5µg/kg and 650mins with Clonidine 2µg/kg as an adjuvant. In this study the duration of analgesia was doubled by increasing the dose of Clonidine from 1µg/kg to 2µg/kg. Whereas in our study we observed that the duration of analgesia increased by about 30mins when the dose of Clonidine was increased from 0.5µg/kg to 1µg/kg.

An exaggerated increase in the duration of analgesia has been noted by some observers. Samir et al.\textsuperscript{18} in 1994 observed the mean duration of analgesia as 987mins with Clonidine 1µg/kg as adjuvant to 0.25% Bupivacaine 1ml/kg and 460mins in those with plain Bupivacaine 0.25% 1ml/kg. These patients were premedicated with 0.3mg/kg of oral Diazepam, induced with Thiopentone and maintained with Halothane which may be the cause for increase in the duration of analgesia.

In contrast to the above studies, a few reported no increase in the duration of analgesia.

In 2000 De mey\textsuperscript{29} concluded that the addition of Clonidine to caudal Bupivacaine does not offer any additional benefit over Bupivacaine alone. In contrast to this, in our study we observed a difference in the duration of analgesia between those given Clonidine 0.5µg/kg and 1µg/kg as adjuvant.

Differences in the dose of Clonidine and the local anesthetic agents used, concomitant use of premedication, drugs used for rescue analgesia, different methods used to assess pain and statistical analysis may all account for the variability in the duration of analgesia.

Caudal epidural block using Clonidine as an adjuvant to Bupivacaine prolongs the duration of analgesia. There is no significant difference in the onset of action between the two groups. Duration of sedation was observed to be similar in group I and group II. There was no case of motor blockade in both the groups.

Though the difference in the duration of analgesia between the two groups is statistically significant (p<0.001), clinically the difference is about 30mins only. Hence the combination of a lesser dose of Clonidine with Bupivacaine can be safely and effectively used in short surgical procedures like circumcision.

**ACKNOWLEDGEMENT:** I express my humble gratitude and thanks to Dr Chaya, Professor and Head of the department and Dr Narendra Babu, Professor of anesthesiology at KIMS, Bangalore for their constant guidance and support.

I thank Dr KP Suresh, Scientist (biostatistics), National Institute of Animal Nutrition and Physiology, for his invaluable help in the statistical analysis in this study.

It is my duty to express my gratitude to the children and their parents, for their participation and cooperation in this study, without whom the study could not have been conducted.

**REFERENCES:**

1. Eeva Liisa Maunuksela, Klaus T Olkkola.”Pediatric Pain Management” International Anaesthesiology Clinics 1991; 29(1):37-56.

2. Suellen M Walker.”Acute Pain Management in Pediatric Patients” International Anaesthesiology Clinics 1997; 35(2):105-130.
3. T G Hansen et al, S W Henneberg, S Walther Larsen, J Lund, M Hansen. “Caudal Bupivacaine supplemented with caudal or intravenous Clonidine in children undergoing hypospadias repair: a double blind study” British Journal of Anaesthesia 2004; 92:223-227.

4. J C Sanders. “Paediatric regional anaesthesia, a survey of practice in the United Kingdom” British Journal of Anaesthesia 2002; 89:707-710.

5. Pankaj Kundra, K Deepalakshmi, M Ravishankar. “Preemptive Caudal Bupivacaine and Morphine for Postoperative Analgesia in Children” Anaesthesia Analgesia 1998; 87:52-56.

6. A Hom Choudhuri, P Dharmani, N Kumarl, A Prakash. “Comparison of caudal epidural Bupivacaine with Bupivacaine plus Tramadol and Bupivacaine plus Ketamine for postoperative analgesia in children” Anaesthesia and Intensive Care 2008; 36(2):174-179.

7. Meena Doda, Sambrita Mukherjee. “Postoperative Analgesia in Children- Comparative Study between Caudal Bupivacaine and Bupivacaine plus Tramadol” Indian Journal of Anaesthesia 2009; 53(4):463-466.

8. Mohamed Naguib, Mohamed El Gammal, Yasser S Elhattab, Mohamed Seraj. “Midazolam for caudal analgesia in children: comparison with caudal Bupivacaine” Canadian Journal of Anaesthesia 1995; 42(9):758-764.

9. M Naguib, A M Y Sharif, M Seraj, M El Gammal, A A Dawlatly. “Ketamine for Caudal analgesia in children: comparison with caudal Bupivacaine” British Journal of Anaesthesia 1991; 67:559-564.

10. Mohamed Abdulatif, Mohga El Sanabary. “Caudal Neostigmine, Bupivacaine and their combination for postoperative pain management after Hypospadias surgery in children” Anaesthesia Analgesia 2002; 95:1215-1218.

11. I Constant, O Gall, L Gouyet, M Chauvin, I Murat. “Addition of Clonidine or Fentanyl to local anaesthetics prolongs the duration of surgical analgesia after single shot caudal block in children” British Journal of Anaesthesia 1998; 80:294-298.

12. T S Yildiz, F Korkmaz, M Solak, K Toker. “Clonidine addition prolongs the duration of caudal analgesia” Acta Anaesthesiologica Scandinavica 2006; 50:501-504.

13. Joel G Hardman. “Pharmacological basis of therapeutics” Goodman and Gilman, 10th edition, 2001, 233-234.

14. Yukio Hayashi. “Drugs affecting adrenoceptors:alpha 2 agonists” The pharmacological basis of Anesthesiology- Kharasch 1994; Chapter 27:607-623.

15. Archna Koul, Deepanjali Pant, Jayshree Sood. “Caudal Clonidine in day-care Paediatric surgery” Indian Journal of Anaesthesia 2009; 53(4):450-454.

16. Lt Col Upadhhyay, Brig Prabhakar T, Lt Col Handa R, Beena Haridas. “Study of the efficacy and safety of Clonidine as an adjunct to Bupivacaine for caudal analgesia in children” Indian Journal of Anaesthesia 2005; 49(3):199-201.

17. Charles J Cote. “Pediatric Anaesthesia” Miller’s Anesthesia, sixth edition 2005:2367-2407.

18. Samir Jamali, Sylvaine Monin, Christian Begon, Anne Marie Dubousset, Claude Ecoffey. “Clonidine in Pediatric Caudal Anaesthesia” Anaesthesia Analgesia 1994; 78:663-666.

19. J J Lee, A P Rubin. “Comparison of a Bupivacaine-Clonidine mixture with plain Bupivacaine for caudal analgesia in children” British Journal of Anaesthesia 1994; 72:258-262.
20. M Bock, P Kunz, R Schreckenberger, B M Graf, E Martin, J Motsch. “Comparison of caudal and intravenous Clonidine in the prevention of agitation after Sevoflurane in children” British Journal of Anaesthesia 2002; 88(6):790-796.
21. Mausumi Neogi, Dhurjoti Prosad Bhattacharjee, Satrajit Dawn, Nilay Chatterjee. “A Comparative Study Between Clonidine and Dexmedetomidine used as adjuncts to Ropivacaine for Caudal Analgesia in Paediatric Patients” Journal of Anaesthesia and Clinical Pharmacology 2010; 26(2):149-153.
22. Bernard Dalens, Abdou Hasnaoui. “Caudal anesthesia in Pediatric surgery” Anesthesia Analgesia 1989; 68:83-89.
23. W Klimscha, A Chiari, A Michalek Sauberer, E Wildling, A Lerche, C Lorber, et al. “The Efficacy and Safety of a Clonidine/Bupivacaine Combination in Caudal Blockade for Pediatric Hernia Repair” Anesthesia Analgesia 1998; 86:54-61.
24. Nigel R Coad, Willian R Hain. “Caudal anaesthesia for postoperative pain relief in children: A comparative trial of different regimens using plain Bupivacaine” Annuals of the Royal College of Surgeons of England 1989; 71:245-248.
25. Jorg Bubeck, Karin Boos, Helmut Krause, Karl Christian Thies. “Subcutaneous Tunneling of Caudal Catheters Reduces the Rate of Bacterial Colonisation to That of Lumbar Epidural Catheters” Anaesthesia Analgesia 2004; 99:689-693.
26. Elliot J Krane. “Delayed Respiratory Depression in a Child after Caudal Epidural Morphine” Anesthesia Analgesia 1988; 67:79-82.
27. B Cook, D J Grubb, L A Aldridge, E Doyle. “Comparison of the effects of Adrenaline, Clonidine and Ketamine on the duration of caudal analgesia produced by Bupivacaine in children” British Journal of Anaesthesia 1995; 75:698-701.
28. P Kumar, A Rudra, A K Pan, A Acharya. “Caudal Additives in Pediatrics: A Comparison Among Midazolam, Ketamine and Neostigmine Coadministered with Bupivacaine” Anesthesia Analgesia 2005; 101:69-73.
29. J C De Mey, J Strobbe, J Poelaert, P Hoebeke, E Mortier. “The influence of Sufentanil and / or Clonidine on the duration of analgesia after a caudal block for hypospadias repair surgery in children” European Journal of Anaesthesiology 2000; 17:379-382.

AUTHORS:
1. Madhava Reddy
2. Ranjitha Gangadharaiah

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Anaesthesiology, KIMS, Bangalore, RGUHS University.
2. Senior Resident, Department of Anaesthesiology, ESIC Medical College and PGIMSR, Bangalore, RGUHS University.

DATE OF SUBMISSION: 26/11/2013.
DATE OF PEER REVIEW: 27/11/2013.
DATE OF ACCEPTANCE: 27/12/2013.
DATE OF PUBLISHING: 09/01/2014.