# Neostigmine as an adjunct to Bupivacaine, for caudal block in burned children, undergoing skin grafting of the lower extremities

Dr. Pramod Gupta, Dr Amy Grace MD

*Department of Anaesthesiology and Critical Care Safdarjang Hospital &Vardhman Mahavir Medical College New Delhi, India guptapdnb@yahoo.co.in*

# ABSTRACT

In this study we compared the duration and intensity of **caudal block**ade when two different concentrations of bupivacaine were used, along with a fixed dose of neostigmine. Fifty burned pediatric patients undergoing skin grafting of the lower extremeties were prospectively randomized to receive caudal analgesia with either 0.125% or 0.25% bupivacaine, along with neostigmine @ 6mcg/kg [total volume of the drug was 0.5ml/kg]. Both the groups also received intravenous ondansetron as pre-medication. The two groups were then assessed for duration and efficacy of post-operative analgesia and any postoperative complications. Both the groups received good pain relief. ($p<0.05$) The duration of pain relief was however noted to be higher in the 0.25% group, Group B.25N with $p=0.000$ and Group B.125N with $p<0.05$ although the degree of pain relief was more or less the same. Rescue analgesia was once in Group B.25N as compared to thrice in Group B.125N in 24hrs. Patients were also found to be more haemodynamically stable postoperatively in the 0.25% group [Group B.25N with $p<0.003,0.005,0.004,0.003$ at 4hrs,8hrs,12hrs,24hrs post-operatively than Group B.125N although intra-operatively no difference was noted ($p>0.05$). The two groups were also comparable in terms of sedation scoring [0/4 in both groups, with $p>0.05$], and no complications was noted with any patients of either group.

Implications: Neostigmine as an additive to caudal bupivacaine, prolongs the duration of the block without any adverse effect. Patients receiving 0.25% bupivacaine were hemodynamically more stable and more active post-operatively and premedication with an ondansetron prevents the occurrence of

post-operative emesis.

**KEYWORDS:**

Caudal block - Bupivacaine with neostigmine - Post-operative analgesia

# INTRODUCTION

Approximately 90% of burns in children, are caused by household accidents or child abuse. Flame burns with full thickness are more common in age group > 5 yrs. Skin grafting is almost always necessary for burned patients. Skin grafts can be obtained from many different parts of the body, the lower limbs being the most common site. Pain is highly unpleasant sensory and emotional experience, especially in children. Therefore, postoperative pain management plays a vital role in deciding the outcome of surgery, and can be considered as a pre-requisite for improved post-operative outcome.

Caudal analgesia with a local anaesthetic, with or without additives is one of the most popular regional blocks in children. This technique is usually performed after an inhaled or IV induction and is a useful adjunct during general anesthesia and for providing postoperative analgesia after genital, lower abdominal, and lower limb operations (1).

Caudal additives that are commonly are - Morphine, Fentanyl, Midazolam, Ketamine, Tramadol, Neostigmine, Butorphenol and Clonidine.

This prospective double blind randomized study compared the effect and duration of two different concentrations of bupivacaine (0.25% & 0.125%), with

neostigmine (6 microgmg/kg) as an adjuvant, on post-operative analgesia in burned pediatric patients undergoing skin grafting of the lower extremeties.

The study also aims to assess the effect of ondansetron (0.1 mg/kg) as an antiemetic when was given as a premedication and to look for any complications and compares the incidence between the two groups.

## MATERIAL AND METHOD

This prospective double blind randomized study was conducted on burned pediatric patients undergoing skin grafting of the lower extremeties, after approval from the Local Ethics committee and parental consent was obtained in each case. 50 burned children (5-15yrs), of either sex, ASA grade 1, wt. of 10-40 kg and ht. of 110-150 cm were included. Patients were randomly divided into two groups of 25 patients each. Group B.125N patients received 0.5ml/kg of total volume.i.e. Bupivacaine 0.125% With Neostigmine (6 microgm/kg), and Group B.25N patients received 0.5ml/kg of to volume i.e. Bupivacaine 0.25% with Neostigmine (6microgm/kg). Patients who had a history of adverse reaction to Local anesthetics, with any spinal deformity, neurological diseases, hyperthermia, coagulopathy/ bleeding diathesis and patients whose parents /guardians did not give consent, were excluded from the study.

All the patients underwent a thorough pre-anesthetic check-up preoperatively, and a written informed consent was taken from the parents/ guardians, explaining all risks and benefits. After the initial pre-procedure instructions , the patients were

taken up to the Operating Room. On O.T. Table Baseline monitoring like PR, BP (systolic, Diastolic & mean), RR, ETCO2, ECG & SPO2 were recorded.

After securing IV access, premedication with I/V ondansetron ( 0.1 mg/kg) was given ½ an hour before operation.

Induction was done with I/V fentanyl (1.5 microgm/kg), I/V propofol (1-2 mg/kg) & I/V vecuronium (0.1 mg/kg).The trachea was intubated with appropriate sized tube & lungs were ventilated. Maintenance of anesthesia was done with O2 (33%) / N2O (67%) with Isoflurane (0.6 %) and Anasthesia was maintained on O2/N2O with Isoflurane and supplementary doses of I/V Vecuronium bromide.

Under all aseptic precautions available, caudal block was performed with 23 gaze .needle with short bevel , using loss of resistance technique with saline for space identification. The allocated dose of drug of one of the groups was injected. The duration of analgesia was taken as from time of drug injection to time of 1st dose of the rescue analgesia. The degree of analgesia was analysed by objective assessment of vitals including - pulse rate, blood pressure (systolic/diastolic/mean) $SpO_2$, $EtCO_2$ & ECG at every 10 min interval preoperatively. N-M block was reversed with neostigmine and glycopyrolate and trachea was extubated.

Post operatively, the patients were shifted to Recovery Room for further assessment.

The degree of pain relief was analysed at intervals of 4/8/12/24 hrs, objectively by monitoring pulse rate and blood pressure and subjectively by using – Eastern

Ontario pain scale with the following variables: Blood pressure, Crying, Movement/Agitation, Verbal evaluation of pain scoring. Each variable was given a score of 2 .The maximum pain score taken was 8, and the minimum taken was 0. Rescue analgesia used was Tab. Diclofenac 1 mg/kg at score of 2/8 or on demand. Sedation was also assessed by sedation scoring based on Eye Opening. Sedation score taken was scale of 4 i.e. (0-spontaneous Eye Opening, 1- Eye Opening on speech, 2- Eye Opening on physical stimuli 3-Unarousable.)

PHYSICAL ACTIVITY SCORE taken was, GR.- 0 no independent leg lifting GR.- 1 independent leg lifting with pain GR. 2 ILL without pain all grade taken at 1 hour.

Any complications were looked for and noted, with special emphasis on – Respiratory depression, hypotension, nausea / vomiting, pruritis and urinary retention.

The following data were prospectively collected by a blinded observer and compared : age (yr), weight (kg), height (cms), along with intra-operative and post-operative vitals monitoring, sedation score, duration and degree of post-operative analgesia, and any post-operative complications, and the need for rescue analgesia in the post-operative period.

The data were summarized on a standard proforma by mean ± SD, median, and interquartile range. The data were compared by using Student's *t*-test. The nominal data were compared by $x^2$ tests. A *P* value of <0.05 was considered statistically significant. On the basis of the power analysis with the $x^2$ test and power = 0.80, a

sample size of 25 per group was selected. The two-sample Student's *t*-test based on equal group size ($n$ = 25; Table 1) will detect differences of size 0.85 SD and was used to see difference of duration of analgesia, vitals changes, pain scoring, sedation scoring between the two groups.

**Table 1**

A Comparison of Patient's Age, Sex, Weight, Duration of post-operative analgesia, Number of times of rescue analgesia requirement, Sedation score

| GROUP | B.125N | B.25N | |
|---|---|---|---|
| NO.of patients | 25 | 25 | |
| Age, yrs (mean ± SD) [a] | 10.20_+1.78 | 8.7+_2.55 | 0.67 |
| Sex [Male]<br>[Female] | 20 (80%)<br>5(20%) | 17(66.7%)<br>8(33%) | 0.68 |
| Weight (kg) (mean ± SD) [a] | 21.67+_2.88 | 18.22+_3.59 | 0.167 |
| Duration of post-operative analgesia (hrs) | 13.27+_2.34 | 17.13+_1.12 | 0.00 |
| Number of times of rescue analgesia requirement in 24 hrs [c] | 3 | 1 | |
| Sedation score [d] | 0/4 | 0/4 | |
| | | | |

n=number of patients

[a] The values are expressed as Mean ± S.D

[b] Student's t test

[c] Rescue analgesia used – Tab. Diclofenac 1 mg/kg

[d]Sedation was assessed by sedation scoring based on Eye Opening. Sedation score taken was scale of 4 i.e. (0-spontaneous Eye Opening, 1- Eye Opening on speech, 2- Eye Opening on physical stimuli 3-Unarousable.)

# RESULTS

A total of 50 patients were studied; 25 in each Group . There were no significant differences ($P > 0.05$) between the two groups with regard to demography. Sedation score, physical activity and complications ($p>0.05$).(Table 1,2). The mean baseline values of pulse rate, systolic blood pressure, diastolic blood pressure & $SpO_2$ were comparable in both the groups during the intra-operative period. ($p>0.05$)The systolic blood pressure, mean arterial pressure at 10 minute and 20 minutes during the post caudal period was higher in group B.125N A as compared to basal values. [$p <.05$] but the pulse rate values were not significant. Similarly, the post caudal pulse rate and blood pressure in group B.25N was not significant. [$p> 0.05$]. However, pulse rate in group B.25N patients was lower and more stable in comparison to group B.125N patients at 4hr, 8hr, 12hr & 24hr postoperatively (with p values of 0.0 03, 0.005, 0.004, 0.003 respectively).The mean arterial pressure values at 12hrs and 24hrs postoperatively was significantly higher in group B.25N patients. ($p<0.05$) . (more active) [Fig. 1, 2,] The mean duration of analgesia in group B patients [17.13 $\pm$ 1.12hrs] ($p=.001$) was significantly higher than that of group B.125N patients [13.25 $\pm$ 2.34hrs] .Pulse

rate at 12hrs was also significantly higher in Group B.125N patients. ($p<0.05$). The Pain score in both the groups were </= 2. Rescue analgesia requirement was once in group B.25N patients as compared to thrice in group B.125N patients in 24 hours. [Fig. 3]

Failed caudal was one that was excluded from the study. All the patients had sedation score of 0/4. All the patients had physical activity score of 2 within 1hr. None of the patient had respiratory depression, hypotension, nausea, vomiting, pruritis or urinary retention postoperatively.

**Table 2: Complications**

| **VARIBLES** | **Gr. A** | **Gr. B** |
|---|---|---|
| Respiratory Depression | None | None |
| Hypotension | None | None |
| Nausea Vomiting | None | None |
| Pruritus | None | None |
| Urinary Retention | None | None |

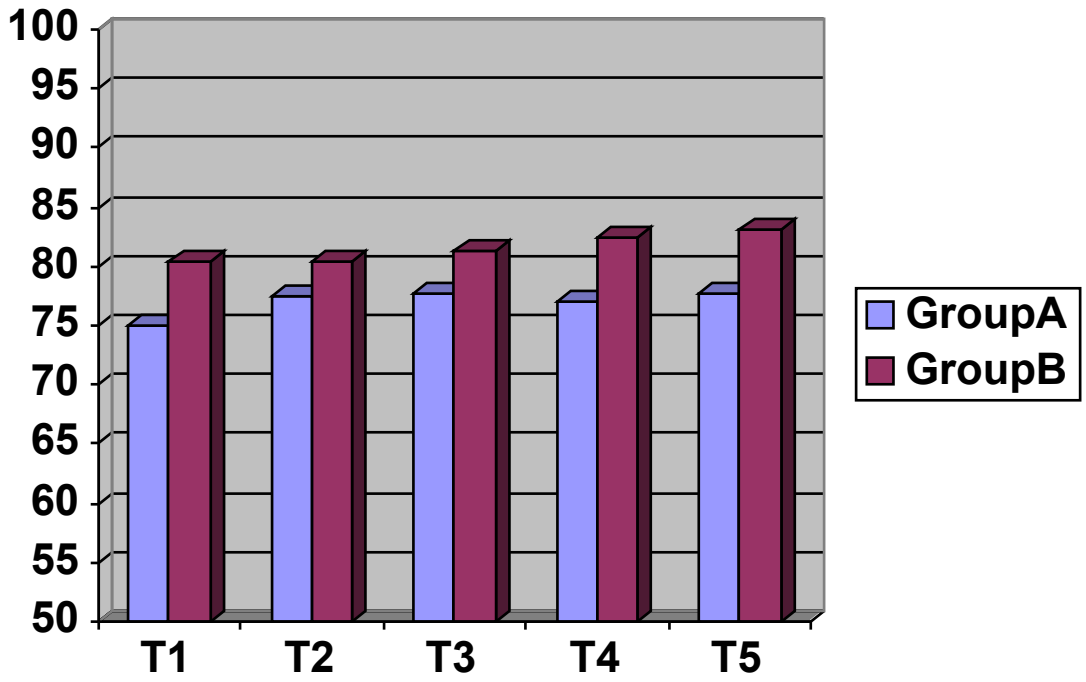


**Fig 1. Post- operative changes in M.A.P.**

M.A.P. is Mean arterial pressure.

Group A is the 0.125% group, and Group B is the 0.25% group.

The Y-Axis indicates the M.A.P in mmHg . The X-Axis indicates the time in hours. T1 is the basal M.A.P. reading at 0 hours.T2, T3, T4 , T5 are the M.A.P. readings taken at 4hrs,8hrs, 12hrs, 24hrs post-operatively.

The mean baseline values blood pressure were comparable in both the groups during the intra-operative period. ($p>0.05$)The mean arterial pressure at 10 minute and 20 minutes during the post caudal period was higher in group A as compared to basal values. [$p <.05$The mean arterial pressure values at 12hrs and 24hrs

postoperatively was significantly higher in group b patients. ($p<0.05$). (more active)

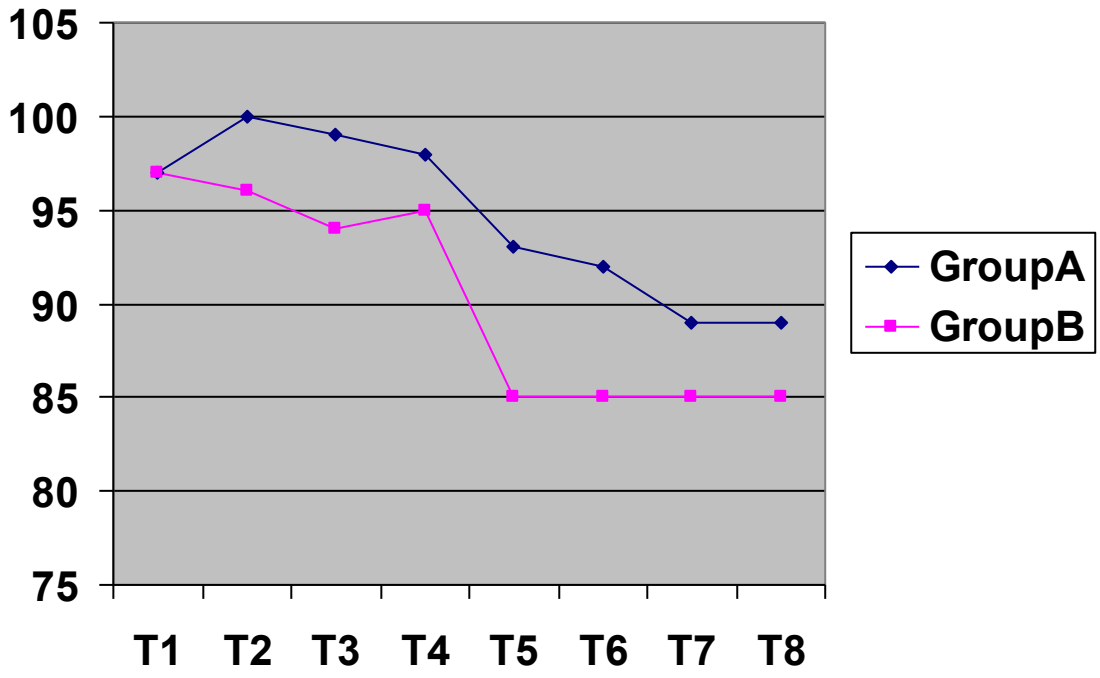


**Fig. 2 Intergroup changes in heart rate during the intra operative and post-operative period.**

The Y-Axis indicates the heart rate per minute and the X-Axis indicates the time.T1 is the basal reading at 0 hours.T1, T2, T3 shows the intra operative time in minutes i.e.,at 10,20,30minutes respectively.T4, T5, T6, T7, T8 shows the post-operative time in hours i.e., at 4hrs,8hrs, 12hrs, and 24 hrs respectively.

The mean baseline values of heart rate and the post caudal heart rate were comparable in both the groups during the intra-operative period. ($p>0.05$).

However, pulse rate in group B patients was lower and more stable in comparison to group A patients at 4hr, 8hr, 12hr & 24hr postoperatively (with p values of 0.0 03, 0.005, 0.004, 0.003 respectively)

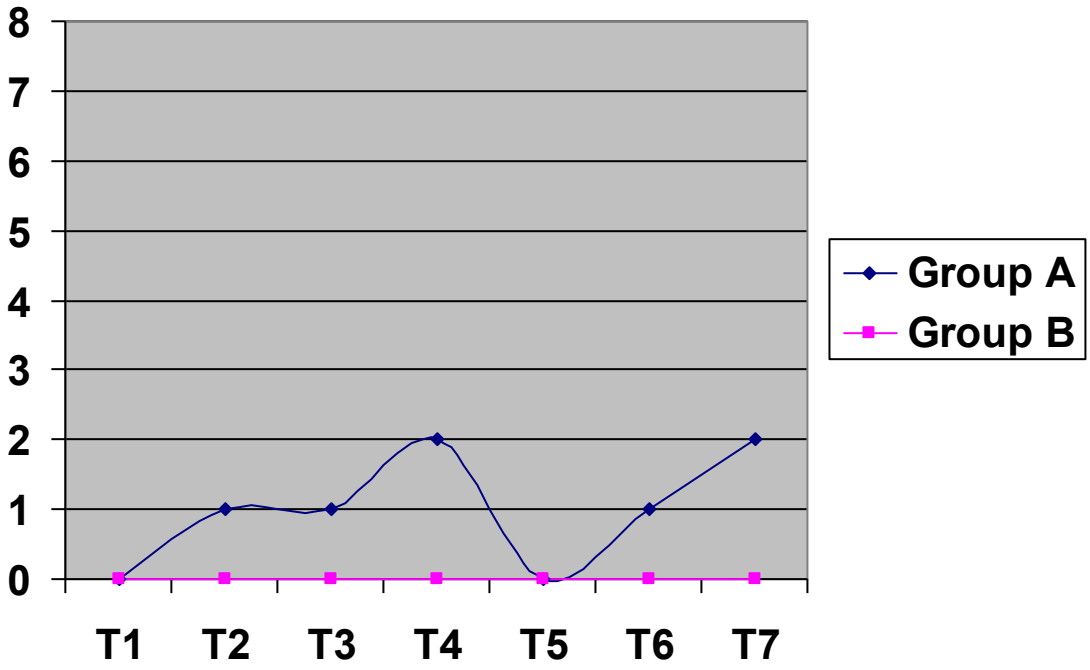


**Fig. 3 Pain scores of the two groups in the post-operative period**.

The Pain scale used in this study is the Eastern Ontario pain scale which included the following variables: Blood pressure, Crying, Movement/Agitation, Verbal evaluation of pain scoring. Each variable was given a score of 2.The maximum pain score is 8, and the minimum is 0. Rescue analgesia was given at a score of 2/8 or on demand.

The Y-Axis indicates the pain score and the X-Axis indicates the post-operative

time in hours, where T1, T2, T3, T4, T5, T, T7 are 0,4,8,12,1,20,24 hrs respectively. Although the degree of pain relief in both the groups was good($p<0.05$ in both groups), Group A required rescue analgesia thrice as compared to once in Group B.

## DISCUSSION

Caudal analgesia with a local anaesthetic, with or without additives is one of the most popular regional blocks in children. As an adjunct with general anesthesia, it provides excellent intraoperative and postoperative analgesia in children undergoing lower limb procedures [(1)].The volume, dose, and concentration of the injected drug determines the quality and level of caudal block**ade**. According to Armitage [(2)]. Bupivacaine 0.25% in volumes of 0.5, 1, and 1.25 mL/kg will provide analgesia to sacral, lower thoracic, and midthoracic dermatomes, respectively.

The results obtained in this study showed that both concentrations of injection Bupivacaine, i.e., 0.125% and 0.25%, with neostigmine as an adjuvant, compared favourably with regards to analgesia. In general, the pain experienced by our patients receiving 0.125% bupivacaine with neostigmine was greater than those receiving 0.25% bupivacaine with neostigmine , as reflected by the Pain score and the pulse rate changes, but this was not clinically significant.

In our study, we used neostigmine as adjuvant, as neostigmine is an anticholinesterase drug, which has been used for postoperative analgesia in caudal

block. It inhibits the breakdown of Acetylcholine and induces analgesia by increasing cyclic guanidine monophosphate by generating nitric oxide.

Numerous studies with different doses of caudal neostigmine has been reported but as an additive to bupivacaine but to Bupivacaine 0.125% and 0.25% has not been reported.

In a study of patients, Batra YK et al found that different doses of neostigmine for postoperative analgesia in children results in no significant alteration in vital signs. [3] The duration of caudal block was also probably increased by using neostigmine as adjuvant to bupivacaine as revealed by Mahajan R et al. They concluded that neostigmine potentiates the effect of caudal bupivacaine, but neostigmine alone in doses from 2- 10 mg / kg is not effective. [4] Even though Memis D et al tried low doses of neostigmine @ 1 mg / kg with bupivacaine for caudal block and found no significant advantage over bupivacaine alone.[5]

Neostigmine is also known to cause a high incidence of post operative emetic symptoms. Mahajan R et al found that caudal neostigmine in dose of 2mg / kg to 10 mg / kg causes high incidence of post operative nausea and vomiting from 15-30%.[6] In our study, None of our patients has any postoperative emetic symptoms, which points to the effectiveness of intravenous ondansetron for preventing post operative nausea and vomiting, when given as a premedication.

Neostigmine as adjuvant to caudal block has also been compared with other drugs such as ketamine and midazolam. Kumar P et al compared Midazolam, Ketamine and neostigmine coadministered with bupivacaine found all the groups, increases

the duration of caudal block.[7]

Johstan P et al studied ketamine with 0.25% Bupivacaine and 0.125% bupivacaine for caudal block and found them significantly comparable.[8]

Neostigmine (6mcg / kg) as an adjuvant to caudal bupivacaine (0.125% & 0.25%) prolongs the duration of block without any adverse effects. The patients receiving 0.25% bupivacaine, were more stable hemodynamically, and were more active and pain free postoperatively than patients receiving 0.125% bupivacaine. No extra fentanyl was required intraoperatively after the effect of caudal block was established in both the groups. The duration of the block was also significantly higher in group B.25N patients. It was found that intravenous ondansetron as premedication avoids the incidence of post operative nausea and vomiting. Parents of the patients and surgeons were fully satisfied with the study, and the children were happy and active as he / she did not receive any postoperative injections. Hence we can safely recommend the use of neostigmine as adjuvant to different concentrations of bupivacaine in caudal blocks in obiviating post operative pain in children undergoing skin grafting of lower extremeties, and also the use of intra-venous ondansetron as pre-medication to emesis

## REFERENCES

1. Rice LJ. Regional anesthesia and analgesia. In: Motoyama E, Davis P, eds. Smith's anesthesia for infants and children. 6th ed. St. Louis: Mosby, 1996.
2. Armitage EN. Caudal block in children. Anaesthesia 1979; 34: 396.
3. Batra YK, Arya VK et al. Dose response study of caudal neostigmine for postoperative analgesia in paediatric patients undergoing genito urinary surgery. Paediatric Anaesthesia .2003 Jul; 13 (6): 515-21.
4. Mahajan R, Grover VK et al. caudal neostigmine with bupivacaine produces a dose independent analgesia effect in children. Can J Anaesth. 2004 Aug; 51 (7): 702-706
5. Memes D, Turan A et al. Caudal neostigmine for postoperative analgesia in paediatric surgery. Paediatric anaesthesia 2003 May; 13 (4): 324-8.
6. Mahajan R, DAH de Beer et al. Caudal neostigmine in children Br. J. Anaesth. 2003 Nov; 91 (5): 761-762.
7. Kumar P, Rudra A, Pan Ali et al. Caudal additives in pediatrics: a comparison among midazolam, Ketamine and neostigmine coadministered with bupivacaine. Anaesth. Analg 2005 Jul; 101 (1): 69-73.
8. Johstan P, Findler D, Aldridge LM et al. The effect of Ketamine on 0.25% & 0.125% bupivacaine for caudal epidural block in children. Paediatric Anaesthesia 1999; 4 (1): 31-4.