IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 6 Ver. V (June. 2016), PP 40-47
www.iosrjournals.org

Comparison of Preemptive Versus Postoperative Caudal Epidural Bupivacaine with Morphine for Postoperative Analgesia in Children

Dr. K.S.Krithiga, M.D, D.A[1], Dr. Jayasankaranarayanan**,** M.D.[2],
[1,2]*Senior Assistant Professors, Department of anaesthesiology, Coimbatore medical college*

Abstract:
Aim of Study: *To compare the preemptive versus postoperative caudal epidural bupivacaine with morphine for postoperative analgesia in children.*
Materials and Methods: *100 ASA 1 & 2 children in the age group 2 to 12 years scheduled for sub-umbilical surgeries were enrolled in this prospective, double-blind, randomized, controlled study. All children were premedicated with syrup promethazine 1mg/kg, induced with thiopentone 2.5% iv 5 mg/kg, intubated with suxamethonium 2mg/kg .No opioids, benzodiazepines or other drugs affecting pain processing were used in traoperatively. Controlled ventilation with atracurium and maintenance with halothane and 66% nitrous oxide in 33% oxygen.Group 1 patients received a mixture of 0.66ml/kg bupivacaine 0.25% and morphine 0.02mg/kg after the induction of anaesthesia but 15 min before the surgical incision. Group 2 patients received the same drug mixture at the conclusion of surgery but before reversal of neuromuscular blockade. Post operatively the children were observed in the recovery room for 30 minutes using Aldrete score. Then children were shifted to postoperative ward and intensity of pain measured using the objective pain scale devised by HANNALLAH RS. The time to first analgesia [**TFA**] /duration of analgesia was determined from the performance of caudal block until the child had AN **OPS** of 5, when the rescue analgesic was given.(ops- objective pain score)*
Observation: *TFA in group 1 patients was significantly prolonged [11.39+-0.98 hrs] compared with group 2[9.22+-0.81 hrs]*
Conclusion: *The study demonstrates that preemptive caudal epidural bupivacaine and morphineadministration is superior to the same mixture given postoperatively for pain relief.*

- **Aims and Objectives**

- To evaluate the analgesic efficacy of single dose administration of bupivacaine and morphine mixture, given through caudal epidural route for postoperative analgesia in children undergoing sub-umbilical surgeries.
- To compare the duration of analgesia with preemptive versus postoperative caudal epidural bupivacaine and morphine.

- **<u>Sacral Canal and the Caudal Epidural Space</u>**

The sacral canal is a caudal extension of the spinal canal. The spinal canal contains the last spinal nerve roots, which forms the cauda equina and also the filum terminale that anchors spinal cord to coccyx and sacrococcygeal ligament. The dural sac projects upto S3 - S4 level at birth, reaching the adult level of S2 during second year of life.

The caudal epidural space in a neonate is filled with epidural fat, which has a gelatinous spongy appearance with distinct spaces between the fat globules and very few connective tissue fibers. This facilitates uniform and rapid spread of the local anaesthetic solutions. Between 6 to 7 years of age, the epidural fat gets denser and is surrounded by fibrous strands, thus reducing uniform spread of local anaesthetic solutions. The epidural space is richly vascularised and the veins are without valves; thus an inadvertent intravascular injection can lead to instantaneous systemic toxicity.

Caudal anaesthesia requires identification of the sacral hiatus. The sacrococcygeal ligament overlying the sacral hiatus lies between the sacral cornu. To facilitate locating the cornu, the posterior superior iliac spine should be located and by using the line between them as one side of an equilateral triangle, the location of sacral hiatus is approximated. After the sacral hiatus is identified the index and middle finger of the palpating hand are placed on the sacral cornu, and the caudal needle is inserted at an angle of approximately 45 degree to the skin in relation to

the coccyx. While advancing the needle, a decrease in resistance to needle insertion should be appreciated as the needle enters the caudal space. The needle is advanced until bone is contacted and then slightly withdrawn, and the needle is redirected rostrally at a 20 to 30 degree angle to the skin. During redirection of the needle and after a loss of resistance is encountered again, the needle is advanced approximately 2 to 3 mm into the caudal canal.

• Complications of Caudal ANAESTHESIA

1. Intravascular or in Traosseous Injection
This may lead to grand mal seizure and cardio respiratory arrest.
2. Dural Puncture
Extreme care must be taken to avoid this as a total spinal block will occur if a dose for a caudal block is injected into the subarachnoid space.
3. Perforation of the Rectum
While simple needle puncture is not important, contamination of the needle is extremely dangerous if it is then inserted into the epidural space.
4. Sepsis
This should be very rare occurrence if strict aseptic procedures are followed.
5. Urinary Retention
This is not uncommon and temporary catheterization may be required.
6. Subcutaneous Injection
This should be obvious as the drug is injected.
7. Haematoma
8. Absent or Patchy Block

• Calculation of the Volume of Local Anaesthetic for Caudal Anaesthesia

Many formulae based on weight, age and number of spinal segments to be blocked and the parameter 'D' (Distance from C7 to sacral Hiatus) have been used to determine the dose of local anesthetic required.
TAKASAKI M et al suggested a calculation depending on the weight of the patient in kg.
V = 0.056 ml X Body weight (in kg) X number of spinal segments to be blocked.

MODIFIED ARMITAGE EN et al

Sacral	0.5 ml / kg
Thoracic (T_{10})	0.75 ml / Kg
Thoracic (T_6)	1 ml / Kg
Mid Thoracic (T_4)	1.25 ml / Kg

of 0.25% bupivacaine.

In our study the dose calculation is based on the recommendation of **Takasaki M, Dohi S, Kawabata Y, Takahashi T (30) (Anaesthesiology 1977; 47: 527 – 9)**. A specified volume of 0.66 ml/kg of 0.25% bupivacaine attains an analgesic level of T_{10}, which is the level required for sub-umbilical surgeries. Based on weight a volume of 0.06 ml/kg/seg attains the level of T_{10}.

• Material and Methods

The study population consisted of 100 ASA 1 & 2 children in the age group of 2 years to 12 years admitted to undergo sub-umbilical surgeries at our hospital. Exclusion criteria consisted of local infection in the caudal region, bleeding diathesis, aspirin ingestion on the previous week, preexisting neurological or spinal diseases and congenital anomaly of the lower back. The study was approved by the institutional ethics committee. A written consent was taken from the parents of all children recruited for the study.

All children were premedicated with syrup promethazine 1mg/kg, 120 minutes before the surgery, and were shifted to the operating room half an hour before surgery.Thereafter, baseline objective pain score (OPS) and cardiorespiratory parameters viz., pulse rate(PR), systolic blood pressure(SBP), and respiratory rate(RR) were recorded. Anaesthesia was induced after preoxygenation with intravenous 2.5% thiopentone 5 mg/kg. Orotracheal intubation was performed after administration of suxamethonium 2 mg/kg with an appropriate size uncuffed endotracheal tube. No opioids , additional benzodiazepines or other drugs affecting central pain processing were used intraoperatively. Controlled ventilation of the lungs was achieved with atracurium in intermittent doses. General anaesthesia was maintained with 0.5- 2% halothane and 66% nitrous oxide in 33% of oxygen. The

halothane dose was adjusted in order to keep the patient hemodynamically stable. During the entire operative procedure, monitoring of heart rate and oxygen saturation was continuously performed while blood pressure was recorded every 5 minutes. After conclusion of the surgery, residual neuromuscular paralysis was antagonized with the mixture of atropine (20micro gms/kg) and neostigmine (40 micro gms/kg).

After induction, children were randomly allocated in a double-blind fashion to receive caudally a mixture of 0.66ml/kg bupivacaine 0.25% and morphine 0.02mg/kg after the induction of anaesthesia but 15 min before surgical incision (group 1) or the same drug mixture at the conclusion of surgery but before the reversal of residual neuromuscular paralysis (group 2). To perform the caudal block the children were placed in the sims position with legs drawn upto the abdomen. The sacral hiatus was palpated by identifying the coccyx at the base of the spine. The sacral cornu lying laterally confirmed the location of the hiatus. Once identified, the area was thoroughly cleaned and draped. A 21 gauge hypodermic needle was inserted in the hiatus at right angles to the skin. Once the sacrococcygeal membrane was penetrated, the angle of the needle was changed and directed up the canal for further 0.5 cm. The injection was made after gentle aspiration to rule out any intrathecal or intravascular administration.

Postoperatively the children were transferred to the recovery room and observed continuously for 30 minutes. The recovery of all children was assessed using modified **Aldrete's score** (Table 3). Children were then shifted to the post operative ward where, monitoring of respiratory rate, oxygen saturation, pulse rate blood pressure and objective pain scale were continued at 0.5,2,4,8,12 and 24h after surgery. The intensity of pain was measured using the objective pain scale devised by HANNALLAH Rs (25). The time to first analgesia [TFA] /duration of analgesia was calculated from the performance of caudal block until the child had an OPS of 5, when the rescue analgesic was given. Occurrence of any significant side effects was also made a note of.

- **Modified Aldrete's Score**

OBSERVATION	CRITERIA	SCORING
Activity	• Able to move all 4 extremities voluntarily or on command	2
	• Able to move 2 extremities voluntarily or on command	1
	• Not able to move extremities voluntarily or on command	0
Respiration	• Able to deep breathe and cough freely	2
	• Dyspnoea or limited breathing	1
	• Apnoeic	0
Circulation Systolic BP	• ± 20 % of Pre-anaesthetic level	2
	• ± 20-50% of Pre-anaesthetic level	1
	• ± 50 % of Pre-anaesthetic level	0
Consciousness	• Fully awake	2
	• Arousable	1
	• Not responding	0

- **Interpretation**

This system is designed to assess the patient's transition from phase I recovery to phase II recovery, from discontinuation of anesthetics until return of protective reflexes and motor function.

Total Score is 10, Patient's score 8 is considered fit for transfer.

Limitation: This scoring system may not be adequate after ambulatory procedures requiring GA because it fails to consider common side effects in PACU i.e pain, nausea and vomiting.

- **Observation and Analysis**

Hundred patients posted for elective sub-umbilical surgeries who were admitted in the Department of Pediatric surgery, COIMBATORE MEDICAL COLLEGE HOSPITAL, of Physical status ASA I and II were taken up for the study.

They were randomly divided into two groups of 50 patients each. One group received bupicavaine and morphine mixture in the dose of bupivacaine 0.25%, 0.66 ml/kg and morphine in 0.02 mg/kg, 15 minutes before surgery and other group at the end of the surgery. All of them received standardized general anaesthesia for the surgeries as per the guidelines. The patients were assessed by the same observer in the postoperative period, who was blinded for the group assignment.

- **Age Distribution**

The age distribution in both groups ranged from 2-12 years as follows

Table1.

AGE GROUP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0 - 3 YRS	30	30.0	30.0	30.0
	4 - 6 YRS	48	48.0	48.0	78.0
	7 - 9 YRS	14	14.0	14.0	92.0
	10 - 12 YRS	8	8.0	8.0	100.0
	Total	100	100.0	100.0	

Table2.
GROUP * AGE GROUP

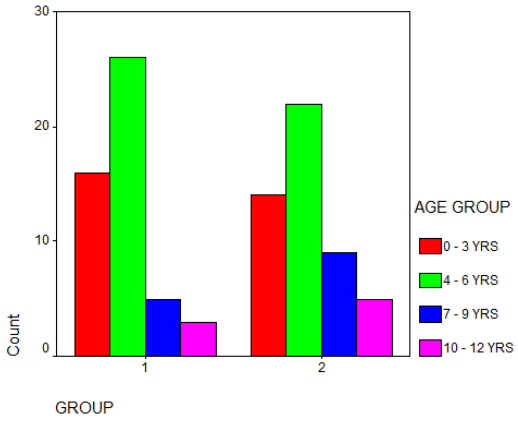
Crosstab

			AGE GROUP				
			0 - 3 YRS	4 - 6 YRS	7 - 9 YRS	10 - 12 YRS	Total
GROUP	1	Count	16	26	5	3	50
		% within GROUP	32.0%	52.0%	10.0%	6.0%	100.0%
	2	Count	14	22	9	5	50
		% within GROUP	28.0%	44.0%	18.0%	10.0%	100.0%
Total		Count	30	48	14	8	100
		% within GROUP	30.0%	48.0%	14.0%	8.0%	100.0%

When age group was classified, most of the children were less than 6 years of age.

- **Age Distribution**

In this bar diagram, the horizontal axis represents age in years and vertical axis represents the number of patients. The age distribution is not significant

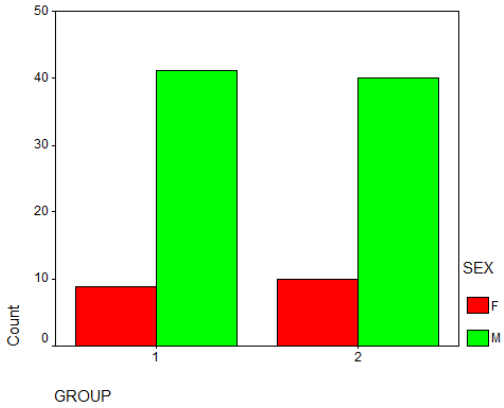


- **Sex Distribution**

Table3

Crosstab

			SEX		
			F	M	Total
GROUP	1	Count	9	41	50
		% within GROUP	18.0%	82.0%	100.0%
	2	Count	10	40	50
		% within GROUP	20.0%	80.0%	100.0%
Total		Count	19	81	100
		% within GROUP	19.0%	81.0%	100.0%



When the distribution of males and females among the two groups was analyzed 81 % of them were males and 19 % were females. Distribution was not significant. P>0.05

- **Duration of Analgesia**

Duration of analgesia in group I was 11.3940 ± 0.98 hours and in group II the duration of pain relief was 9.2260 ± 0.81hours. When ANOVA test (comparison of means) was used to analyse the duration of pain relief, the maximum duration was seen in group I (Preemptive group). The difference in means among the groups was statistically significant (P<0.005)

Table4.

Report

GROUP		DURATION	WEIGHT	AGE
1	Mean	11.3940	20.6200	4.8600
	N	50	50	50
	Std. Deviation	.9871	5.6166	2.3388
2	Mean	9.2260	18.2600	5.3200
	N	50	50	50
	Std. Deviation	.8189	5.4616	2.5590
Total	Mean	10.3100	19.4400	5.0900
	N	100	100	100
	Std. Deviation	1.4146	5.6378	2.4499

- **Discussion**

A number of clinical trials have been conducted to prove the efficacy of preemptive analgesia using different techniques and different types of drugs with conflicting results. Two mechanisms operate to produce the changes in sensitivity found in inflammatory pain.

Peripheral sensitization enables low intensity stimuli to produce pain by activating sensitised A and C nociceptors which normally have high thresholds and require intense stimuli to activate them. Central sensitization on the other hand represents an input in normal low threshold A sensory fibres producing pain as a result of changes in sensory processing in the spinal cord.

It implies that analgesia given before the painful stimulus prevents or reduces subsequent pain as described by *Mc Quay HJ* (4).

Morphine as an adjunct to bupivacaine was used for caudal epidural to explore the following advantages of the combination (i) the afferent input to the central nervous system is prolonged and extensive during and after surgery. Central sensitization may therefore be generated not only during surgery but also in the postoperative period because of persistent inflammation and hyperalgesia at the wound site. Short duration epidural or spinal local anaesthesia do not seem to be an effective way of preventing postoperative pain, even though they are effective way for intraoperative analgesia, as these treatments need to be supplemented either by preincisional regional infiltration or by opioids (2). Consequently, continuous infusion becomes an essential part of the regime if drugs having shorter

duration of action are employed (20) or the nociceptive block should preferably be performed with drugs having prolonged analgesic action (18) (ii) Ideal analgesic technique should be targeted at 3 sites: the periphery, sensory inflow in nerves and the cells in the central nervous system (2). Since anti inflammatory action of the local anaesthetics has been proposed (12), they may reduce inflammation at the wound site and afferent transmission of nociceptive signals to the CNS. Also, extradural administration of local anaesthetic blocks the afferent transmission in peripheral nerves, while opioids suppress the excitability of dorsal horn neurons . (iii) Addition of morphine would prevent the breakthrough pain and subsequent neuronal sensitization with ongoing inflammation and hyperalgesia at the wound site after disappearance of regional anaesthesia in the late postoperative period (iv). The combination of 2 drugs may improve pain relief through synergism and also reduce side effects.

Caudal route was chosen for our study as it is one of the safest and simplest technique in paediatric surgery which is also very reliable as per the experience of *Armando Fortuna* (27) who demonstrated a success rate of 94.8% whereas 96%success report was reported by *Dalens et al* (35).

The local infiltrations and nerve blocks although may have been performed in a standardized and thorough way, may some time result in incomplete block. This will reduce only some of the surgical stimuli, thus not protecting the dorsal horn from painful stimuli. This might have resulted in the failure of such studies to demonstrate preemptive analgesia (12, 13). Epidural space in children has spongy, gelatinous lobules and distinct spaces as opposed to the densely packed fat lobules and fibrous strands that characterize the mature epidural space (26). This difference favours rapid longitudinal spreads of drugs within the juvenile epidural space and make caudally administered local anaesthetics and opioids highly effective in treating postoperative pain in children. The use of epidural techniques also offer the advantage of allowing single shot injection of local anaesthetics and opioids offering effective prolonged postoperative analgesia as compared to nerve blocks and local infiltrations (29).

Pain intensity was assessed using objective pain scale (OPS). The OPS score has previously been shown to be a sensitive and reliable tool in evaluating postoperative pain in children (25). Significantly lower OPS scores in group I has demonstrated the clinical advantage of administering a single dose mixture of bupivacaine and morphine through caudal epidural route preemptively.

In another study *Holthusen M et al* (17) failed to demonstrate any advantage of preoperative compared with postoperative caudal block with 1% lidocaine on postoperative pain in children after circumcision. This might have been as a result of using 1% lidocaine where ongoing inflammation and hyperalgesia at the wound site may evoke neuronal sensitization after disappearance of regional anaesthesia in the postoperative period (2). Addition of an opioid might therefore prevent central sensitization that may otherwise develop. Opioids ability to modify the hyperexcitability of spinal cord neurons has been demonstrated in various other studies (18).

Duration of analgesia was significantly more in group I patients receiving preemptive mixture of bupivacaine and morphine (11.39 0.98 hours) as compared to group II. (9.22 0.81 hours) which is advantageous during the first 24 hours after surgery. *Krane J et al* (31) have reported the use of caudal morphine in children for postoperative analgesia with doses varying from 0.03 – 0.1 mg/kg. The greater doses provided longer lasting analgesia than bupivacaine but side effects like nausea, vomiting, urinary retention and pruritis were common. In another study by *Mayhew J F et al* to determine the effectiveness of morphine 0.03 – 0.04 mg/kg found that the minimum duration of pain relief was 6 hrs and maximum of 24 hours with 23% having nausea and vomiting, 3% having voiding problems and 7% pruritis. This justifies the rationale of using low dose of morphine (0.02 mg/kg) in our patient population. In our study, inspite of using a smaller dose of morphine, the duration of analgesia was longer which could be due to synergistic effect of bupivacaine and morphine.

The incidence of nausea and vomiting was similar in both the groups.

Clinical pain which arises as a consequence of either inflammation due to tissue injury or neuronal injury is pathological. It is divided into inflammatory (pain due to tissue damage) and neuropathic pain (damage to nervous system). Both inflammatory and neuropathic pain are characterized by changes in sensitivity as per Raja S et al (3).

A single preemptive treatment may be insufficient to completely eliminate postoperative pain hypersensitivity because it could be induced by the second phase of nociceptor input. Therefore, the most optimal treatment is to eliminate the effect of both the first and second phases of afferent input as described by *Woolf and Chong* (2)

Torebjork E et al (6) in his study has shown that after tissue injury, the input which are innocuous may also begin to pain. Comparable alterations were found to occur in humans following surgical trauma resulting in prolongation of postoperative pain as shown by *Dubner R* (5).*Woolf CJ* (7) concluded three important predictions related to the treatment of pain on the basis of recent information on the pathogenesis of clinical pain. One among them is that the adequate management of such pain will require techniques that are aimed at the changes that can occur in the central nervous system, instead of only interrupting the flow of sensory signals.

Seltzer Z (8) studied the role of injury discharge in the induction of neuropahtic pain behaviour in rats. The results of the experimental study revealed that acute pain behaviour may be eliminated or reduced if the afferent barrage of noxious stimuli is prevented from acting on the central nervous system by pre injury neural block with local anaesthetics. *Coderre TJ*(9) performed a study to see the tonic pain response of subcutaneous formalin injection on central nervous system plasticity in rats. It was observed that the acute pain behaviour can be eliminated or reduced by pre injury neural block with local anaesthetics.

Dierking et al (13) studied the effect of pre versus postoperative inguinal field block on postoperative pain after herniorraphy. Inguinal field block with lignocaine was given either 15 minutes before operation or immediately after operation (after closure of the surgical wound). There was no significant difference in time to first request for morphine or total morphine consumption and the duration of pain relief. *Dhal V et al* (14) conducted a double blind study on 50 children aged 2 to 10 years scheduled for hernioplasty. They found that the preincisional group needed significantly less halothane during the procedure and had a tendency towards faster awakening, after the end of anaesthesia with a lower pain score 30 minutes after the surgery.

Mark Tverskoy et al (15) hypothesised that neural blockade, by preventing nociceptive impulses from entering the central nervous system during and immediately after surgery suppresses the formation of the sustained hyperexcitable state in the central nervous system that is responsible for the postoperative pain.

Gunter et al (16) conducted a study in 24 boys who were randomized to receive caudal epidural anaesthesia with 0.33 ml/kg of 0.25% bupivacaine either before (group A) or after (group B) mathiew repair of distal hypospadias. They found that the halothane requirements were reduced in group A.

Holthusen H et al (17) did not demonstrate any significant difference between the two groups in postoperative analgesic requirements and the time for first analgesia (TFA). The reason attributed to the inconclusive result was (i) the stimulus could have been too small and too short to evoke central sensitisation, (ii) effective analgesia in either group and (iii) ongoing inflammation and hyperalgesia at the wound site which could have evoked neuronal senstisation after disappearance of regional analgesia. *Krane J et al* (31) compared the efficacy, duration and the side effects of preservative fee morphine injected into the caudal space in children with caudal bupivacaine and with intravenous morphine for relief of postoperative pain. They found that the duration of analgesia was significantly greater with caudal morphine than caudal bupivacaine and both were greater than intravenous morphine.

Wolf AR et al (32) investigated the value of combining morphine with bupivacaine for caudal analgesia. They found that none of the fifteen patients receiving the bupivacaine morphine mixture required postoperative opioids whereas eight of the fifteen patients receiving bupivacaine alone needed additional opioids.

- **Summary**

This study was designed to evaluate the efficacy of preemptive caudal epidural bupivacaine and morphine mixture for postoperative analgesia in children undergoing sub-umbilical surgeries. Hundred ASA physical status I & II children were randomly allocated to one of the two groups. Group I (Preemptive Group) received 0.66ml/kg of 0.25% bupivacaine with morphine 0.02 mg/kg preemptively after induction of anaesthesia but 15 minutes before surgery. Group II (Postincisional group) received the same drug mixture at the conclusion of surgery. Pain was assessed using objective pain scale (OPS). Time for first post operative analgesic (TFA) was noted for the groups. TFA in group I (11.39 0.98 hours) was significantly prolonged compared with group II (9.22 0.81 hours) $P < 0.05$). The incidence of nausea and vomiting also did not differ significantly between the two groups. The study demonstrates that preemptive caudal epidural bupivacaine and morphine administration is superior to the same mixture given postoperatively for pain relief.

- **Conclusion**

- Single dose administration of bupivacaine and morphine mixture through caudal epidural route provides effective postoperative analgesia in children undergoing sub-umbilical surgeries.
- Significantly better pain relief is achieved when the combination is given preemptively as compared to its administration after surgery.
- Duration of analgesia is significantly prolonged with preemptive administration of bupivacaine and morphine mixture.

Bibliography

[1]. **Bonica JJ.** Definitions and taxonomy of pain. In Bonica JJ, Editor. Management of Pain. Philadelphia : Lea and Febiger 1990.
[2]. **Woolf CJ, Mun Sen Chong.** Preemptive analgesia : Treating postoperative pain by preventing the establishment of central sensitizations. Anaesthesia Analgesia 1993 : 77 : 362-276.
[3]. **Raja SN, Meyer RA, Campbell JN.** Peripheral mechanism of somatic pain. Anesthesiology 1993 :77 : 362 – 376.
[4]. **MC Quary HJ.** Preemptive Analgesia (Editorial). British Journal of Anaesthesia 1992 : 69 : 1 – 3.
[5]. **Dubner R.** Neuronal plasticity and pain following peripheral tissue inflammation or nerve injury. In Bond M.R Woolf C.J. eds. Proceeding of the 6th world congress on pain Amsterdam : Elsevier, 1991 : 263 – 276.
[6]. **Torebjork E, Lundberg GL, LA Motte R.** Neural mechanisms for capsaicin induced hyperalgesia. Pain D.S. 1990 : (suppl. 5) : S114.
[7]. **Woolf C.J.** Recent advances in the pathophysiology of acute pain. British Journal of Anaesthesia 1989 : 63 : 139 – 146.
[8]. **Seltzer Z, Beilin BZ, Ginzburg R.** The role of injury discharge in the induction of neuropathic pain behaviour in rats. Pain 1991 : 46 : 327 – 36.
[9]. **Coderre TJ.** Central nervous system plasticity in the tonic pain response to subcutaneous formalin injection. Brain Research 1990 : 535 : 155 – 158.
[10]. **Woolf CJ, Wall PD.** Morphine sensitive and morphine insensitive actions of 'C' fibre input on the rat spinal cord. Neuroscience (letter) 1986 : 64 : 221 – 225.
[11]. **Dickensen AH, Sullivan AF.** Subcutaneous formalin induced activity of dorsal horn neurons in the rat : differential response to an intrathecal opiate administered pre or post formalin. Pain 1987 : 30 : 349 – 360.
[12]. **Dahl JB, Kehlet H.** Non steroidal anti-inflammatory drugs. Rational for use in severe postoperative pain. British Journal of Anaesthesia 1991 : 66 : 703 – 712.
[13]. **Dierking GW, Dahl JB, Kanstrup J, Dahl A, Kehlet H.** Effect of pre versus postoperative inguinal field block on postoperative pain after inguinal herniorraphy. British Journal of Anaesthesia 1992 : 68 : 344 – 48.
[14]. **Dahl V, Raedar JC, Erno DE, Kovdal A.** Preemptive effect of preincisional versus postincisional infiltration of local anaesthesia on children undergoing hernioplasty. Acta Anesthesiologica Scandinavica 1996 : 40 : 847 – 851.
[15]. **Mark Tverskoy M, Cozocov C, Ayache M et al.** Postoperative pain after inguinal herniorraphy with different types of anaesthesia. Anaesthesia Analgesia 1990 : 70 : 29 – 35.
[16]. **Gunter JB, John EF, Manley CB.** Caudal epidural anaesthesia reduces blood loss during hypospadias repair. Journal of Urology 1990 : 144 : 517 – 519.
[17]. **Holthusen H, Eichwede F, Stevens M, Willnow U, Lipfert P.** Comparison of preoperative with postoperative caudal block on postoperative pain in children. British Journal of Anaesthesia 1994 : 73 : 440 – 442.
[18]. **Kundra PK, Gurnani A, Bhattacharya A.** Preemptive epidural morphine for postoperative pain relief lumbar laminectomy anaesthesia Analgesia 1997 : 85 : 135 – 138.
[19]. **Huhn Choe Young-Soon Choi, Yun Hee Kim et al.** Epidural morphine plus ketamine for upper abdominal surgery. Improved analgesia from preincisional versus postincisional administration. Anaesthesia Analgesia 1997 : 84: 560 – 3.
[20]. **Dahl JB, Hansen BL, Hjorto NC, Erichsen CJ, Moiniche S, Kehlet H.** Influence of timing on the effect of continuous extradural analgesia with bupivacaine and morphine after major abdominal surgery. British Journal of Anaesthesia 1992 : 69 : 4 – 8.
[21]. **Eugene S Fu, Raephal M, Scarf JE.** Preemptive ketamine decreases postoperative narcotic requirements in patients undergoing abdominal surgery. Anaesthesia Analgesia 199: 84: 1086 – 90.
[22]. **Manuksela EC, Olkkala KT, Korpela R.** Measurement of pain in children with self reporting and behavioural assessment. . Clinical Pharmacology and therapeutics 1987: 42: 137 – 140.
[23]. **Daiva Bieri, Robert A. Reeve, Chamption GD, Louise Addicoat, John B. Ziegler.** Faces pain scale for self assessment of the severity of pain experienced by children. Pain 1990: 41: 139 – 150.
[24]. **Mc Grath PJ, Johnson G, Goodman JT, Schillinger J, Dunn J, Chepmen J, Cheops.** A behavioural scale for rating postoperative pain in children. Advances in Pain Research and Therapy. Vol 9, New York Raven, 1985: 395 – 402.
[25]. **Hannallah RS.** Postoperative analgesia in the pediatric patient. Canadian Journal of Anaesthesia 1992: 39: 649 – 654.
[26]. **Bernard Dalens.** Regional anaesthesia in children. Anaesthesia Analgesia 1989: 68: 654 – 72.
[27]. **Fortuna A.** Caudal anaesthesia – A simple safe technique in pediatric surgery. British Journal of Anaesthesia 1967: 39: 165 – 170.
[28]. **Hannallah RS, Broadman LM, Belman AB.** Comparison of caudal and ilioingunal / iliohypogastric nerve blocks for control of post-orchidopexy pain in pediatric ambulatory surgery. Anesthesiology 1987: 66: 832 – 34.
[29]. **Woolf AR, Valley RO, Feer OW.** Optimum concentration of bupivacaine for caudal analgesia. Anesthesiology 1988: 69: 102 – 106.
[30]. **Takasaki M, Dohi S, Kawabata Y, Takahashi T.** Dosage of lignocaine for caudal anaesthesia in infants and children. Anesthesiology 1977: 47: 527 – 9.
[31]. **Krane J, Jacobson EL, Lyons AM, Parrot C, Tyler CD.** Caudal morphine for post operative analgesia in children. Anaesthesia Analgesia 1987: 647 – 53.
[32]. **Woolf AR, Hughes D, Wade A, Mather SJ, Prys Roberts C.** Postoperative analgesia after pediatric orchidopexy : A evaluation of a bupivacaine morphine mixture. British Journal of Anaesthesia 1990: 64: 1430 – 35.
[33]. **Armitage EN.** Regional anaesthesia in pediatrics. Clinical Anesthesiology 1985: 3: 553 – 68.