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Research Article

A Comparative Evaluation of Levobupivacaine Hydrochloride and Levobupivacaine Hydrochloride with Clonidine Hydrochloride for Caudal Epidural Anaesthesia in Paediatric Patients Undergoing Elective Infraumbilical Surgeries

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Abstract: The study was carried out on 60 paediatric patients of either sex with age group between 2-8 years belonging to ASA grade I & II scheduled for elective infra-umbilical surgeries. The patients were randomly divided into two groups according to the drug administered. Group L (n=30, control) – 1ml/kg of levobupivacaine hydrochloride 0.25% and 0.5 ml of normal saline injected through the caudal route. Group LC (n=50) - 1 ml/kg of levobupivacaine hydrochloride 0.25% with 1 µg/kg clonidine (made up to 0.5ml in normal saline) injected through the caudal route. After induction of anesthesia and caudal block, patients were observed during the intraoperative and postoperative period for duration of analgesia, duration of motor blockade, post- operative FLACC scores, and hemodynamic and respiratory parameters. Any side effects or complications were recorded, if present.In our study the mean (±SD) duration of analgesia was significantly prolonged in group LC (503.66±89.53) min compared to group L (237.66±49.59) min. The Mean (±SD) FLACC scores which were compared between two groups in the postoperative period showed higher values in Group L as compared to Group LC. The mean (±SD) FLACC score at the time of rescue analgesia was found to be higher in group L (4.16±0.69) compared to group LC (3.16±0.74) which was significantly lower. The mean duration of motor blockade was 106.83±27.80 min for Group L and 99.33±30.27 min for Group LC which were comparable statistically ($p>0.05$) and the mean(±SD) Modified Bromage scores in the postoperative period were found to be comparable in both groups($p>0.05$).The mean pre-induction heart rates were 122.06±11.93 in group L and 122.80 ±16.23 for Group LC. Compared to pre-induction values, significant fall in heart rates were observed in both groups after 15 min. Intergroup comparison of both groups showed a significant decrease in pulse rates ($p<0.05$) 30 min after induction in LC reaching pre induction levels after 4 hours. The mean pre-induction values of systolic blood pressures were 99.00±6.04 mm Hg in Group L and 101.80±5.72 mm Hg in Group LC. Significant fall in mean values were seen by 15 min of induction. Intergroup comparison showed a fall in mean values in the LC group 30 min post induction ($p< 0.05$) which soon reached near pre induction values by 60 minutes. The mean diastolic blood pressures in the pre induction period were 63.23±1.88 mm Hg in group L and 62.96±3.13mm Hg in Group LC. Significant fall in Mean±SD values were noted 30 minutes following block in both groups. Intergroup analysis showed a significant decrease in mean values of Group LC 30 minutes post induction which normalised by 1 hour post induction. As per our pre-induction criteria, no significant hypotension or bradycardia was observed in any patient. No significant change was observed in the respiratory rate and SpO_2 in both the groups. One subject in group LC had complaints of vomiting. 3 subjects (10%) in L group also had complaints of postoperative shivering while no shivering was noted in the LC group. No other complications were noted in both groups.
Keywords: Caudal epidural anaesthesia, Levobupivacaine, Clonidine, Paediatric patients.

INTRODUCTION

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”[1].

Pain perception in children is complex and often difficult to assess .Children suffer post-operative pain in the same way as adults; the main difference is that factors such as fear, anxiety, coping style and lack of social support can further exaggerate physical pain in children. However, in spite of its frequency, pain in infants, children, and adolescents is often

underestimated and under treated. It has also been shown that infants and children, who experience pain in early life, show long-term changes in terms of pain perception and related behaviours. The greatest advance in paediatric pain medicine is the recognition that untreated pain is a significant cause of morbidity and mortality after surgical trauma [2]. Several advances in developmental neurobiology and pharmacology, knowledge of new analgesics and newer applications of old analgesics in the last two decades have helped the paediatric anaesthesiologist in managing pain in children more efficiently. Regional anaesthesia provides excellent post-operative analgesia and attenuation of stress response in children. It is safer, easier to perform and cost effective, and should be used in all cases where possible [3].

Paediatric central neuraxial blocks have a history dating back a century. Bainbridge published a report on spinal anaesthesia in an infant of 3 months, in May 1900, for the repair of a strangulated hernia [4]. The first publication mentioning caudal blocks in children was written by Campbell in 1933 and the second one by Leigh and Belton in 1951. In 1954, Rouston et al of Canada described lumbar epidural anaesthesia for inguinal hernia repair in infants and children. In 1967, Fortuna from Brazil reported a series of 170 patients between the ages of 1–10 years who received caudal epidural anesthesia [5].

Caudal anaesthesia is the oldest, and at presents the most common epidural technique in children. Single dose injection in caudal anaesthesia is the most effective and most prevalent form of regional block in children [6]. This method is easy, reliable and safe especially in children weighing less than 10 kg.

Single dose injection of anaesthetics is suitable especially for infra-umbilical surgeries like abdominal, perineal and lower limb surgeries, where it can provide intra operative as well as post-operative analgesia. Bupivacaine is the most commonly used local anaesthetic for caudalanalgesia [7]. Levobupivacaine is generally as effective as bupivacaine for the management of post-operative pain.

The main disadvantage of caudal analgesia is the short duration of action after a single injection [8]. The use of caudal catheters to administer repeated doses or infusions of local anaesthetics is not popular, partly because of concerns about infection. Prolongation of Caudal analgesia using a' single shot' technique has been achieved by the addition of various adjuvant such as epinephrine, opioids, ketamine and α2agonists.Opioids carry the risk of post-operative respiratory depression and ketamine has the potential of neurotoxicity if inadvertently injected intrathecally. Clonidine is an imidazoline derivative with α_2 agonistic activity .After its administration into the subarachnoid or epidural space, 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.

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METHOD AND MATERIAL

The present study was carried out in the Department of Anaesthesiology, G. R. Medical College and J.A. Group of hospitals, Gwalior (M.P) after obtaining approval from the ethical committee. The present study was done on 60 paediatric patients of ASA grade I & II of either sex of age group 2-8 years scheduled for elective infra-umbilical surgeries.

Selection Criteria Patients of ASA grade I & II

- Age group 2-8 years of either sex.
- Elective infra-umbilical surgeries like herniotomies, anorectal procedures, urethral surgeries and lower limb surgeries.

Exclusion Criteria:

- Unwilling parent/guardian
- Any child less than 2years or more than 8 years with body weight >20 kg.
- Local skin infections.
- Any anatomical spinal/caudal deformity.
- Any systemic diseases like congenital heart disease, bleeding/clotting disorders, medical conditions.
- Known history of sensitivity to local anaesthetic of amide type or clonidine.
- Neurological defects in growth, as well as demyelinating disease of the CNS.

All the patients underwent a thorough pre-anaesthetic check-up preoperatively, and a written informed consent was taken from the parents/ guardians, explaining all risks and benefits.

Selected 60 patients were randomly divided into two groups depending upon the drug given. The following standard anaesthesia regimen was followed:

- All patients were visited on the pre-operative day and relevant demographic data collected. A thorough preoperative evaluation was done. Baseline vital parameters were noted. Relevant laboratory investigations were done in all patients. Informed consent was obtained from the appropriate person.
- Pre- operative fasting**:** Solid foods were restricted for 6 hours, breast milk for 4 hours and clear fluids for 2 hours prior to surgery.
- Uniform premedication of inj. Glycopyrrolate 0.01 mg/kg iv and Inj. Midazolam 0.05 mg/kg iv was given 15 minutes before induction of anaesthesia.
- Intradermal sensitivity test to levobupivacaine hydrochloride was performed.
- Once the child was brought to the operation theatre table, baseline standard monitoring like

PR, BP (systolic, diastolic & mean), RR, ECG & SPO2 were recorded before surgery.

- An intravenous line was placed in all children for administration of drugs and for fluid infusion of Lactated Ringer solution. Induction of anaesthesia was achieved with 50% N2O and 0.5-1% halothane in oxygen using Jackson Rees circuit.

One minute before placement in lateral decubitus position, an injection of ketamine (1 mg/kg weight) was given .The patient was placed in left lateral decubitus position, either by the paediatric surgeon or the anaesthesiologist, and mask ventilation continued.

Then, the sacrococcegeal area was cleaned with Povidone solution. Under strict aseptic conditions, sacral hiatus was identified by running the thumb up from coccyx towards the sacrum. After localisation, the sacral hiatus was punctured with a 24 G hypodermic needle whose bevel was facing anteriorly at an angle of 60-70^{o} until the sacrococcygeal ligament was pierced, when a distinct pop was felt.. Then, the needle was withdrawn some millimeters, inclined until putting it in horizontal and then advanced cephalad while aspirating. If there was no CSF or bloody return, an injection of 1 to 2 ml of air was given (Whoosh test) for confirmation. If there was no formation of a wheal in the subcutaneous tissue, the anaesthetic was injected slowly, after which the child was returned back to the supine position.
After the drug was injected the following parameters were recorded.

Baseline observations were recorded before caudal anaesthesia. Heart rate, electrocardiogram, systolic and diastolic blood pressure, respiratory rate and peripheral arterial haemoglobin oxygen saturation were monitored intra-operatively. Data monitoring performed continuously but for statistical analysis, data were recorded at preinduction, and intervals of 5 min till 30 min after which readings were recorded every 10 min till 1 hour. After 1 hour, readings were taken at 2, 4 and 8 hours.

After waiting for 15 min for full effect of caudal block to manifest, surgeon was allowed to start the procedure. Effectiveness of the block was assessed by haemodynamic stability and decreased requirement for inhalational anaesthetics. No other narcotics, analgesics or sedatives were used intra-operatively. After the commencement of surgery, halothane concentration was gradually decreased and then discontinued.

Block was considered adequate when there was no increase in respiratory rate, heart rate and systolic blood pressure by 30%, just after surgical incision compared to pre-operative values.

If there was an inadvertent increase in heart rate more than 30% of the pre-procedural heart rate at the time of surgical incision, or if there was a failure of caudal block as perceived by an increased modified Bromage score, or if the child required additional supplemental doses of ketamine for analgesia, the case was excluded from the study and supplemental analgesia in the form of further doses of ketamine was given.

At the end of surgery Nitrous oxide was discontinued and 100% oxygen through a face mask was administered for 3-5 minutes. Once the vitals were stable and the child was awake, the child was shifted in left lateral position to the post- operative recovery room. After arrival to the recovery room, the child was monitored for four hours with Sp O2, respiratory rate, NIBP and heart rate. After that the child was shifted to the ward. Any other complications were also noted.

Time from onset of Motor Blockade(taken from administration of caudal block) to Modified Bromage scale 1Each child's pain intensity was assessed at 1 hour, 2 hours, 4hours and 8 hours post operatively using the FLACC observational pain scale. Post-operative analgesia was assessed by using the paediatric observational FLACC pain scale

OBSERVATIONS

The present study was conducted in 60 patients of ASA I and II of either sex belonging to the age group 2-8 years scheduled for elective infra-umbilical surgeries.

Table 1: Distribution of Patients according to the drug administered

S NO	GROUPS	NUMBER OF PATIENTS (n)	DRUGS AND THEIR DOSES
1	**L**	**30**	0.25%Levobupivacaine hydrochloride (1ml/kg) + normal saline (0.5 ml) injected through caudal route.
2	**LC**	**30**	0.25%Levobupivacaine hydrochloride(1 ml/kg)+ Inj. Clonidine (1µg/kg) made up to 0.5 ml in Normal saline injected through caudal route

The table-2 shows that the Modified Bromage Score at time periods of shifting, 75 min, 90 min, 120 min and 180 min after induction were 1.90 ± 0.40, 1.90 ± 0.45, 1.53 ± 0.62 ,1.13 ± 0.50 and 0.06 ± 0.25 for group L and 1.80 ± 0.55,1.73 ± 0.44,1.46 ± 0.50,0.90 ± 0.60,0.13 ± 0.34 for group LC.

The table-2 shows that the mean duration of motor of blockade in both the groups was 106.86± 27.80 min for Group L and 99.33±30.27 min for Group LC.

The table-3 shows that the difference between Modified Bromage scores and the duration of motor block between the two groups at various time intervals is statistically insignificant.

The table-4 shows that there is significant decrease (P<0.05) in the FLACC of Group LC as compared to Group L at 240 min and 480 min after induction. The above table shows that patients of Group LC had significantly lower FLACC scores at the time of first analgesia request (p< 0.05).

The table-5 shows the mean sedation scores of both groups at the time of shifting, at 75 min,90 min, at 120 min and at 240 min which were 3.13 ± 0.73,3.50 ± 0.50, 4.00 ± 0.00 ,4.00 ± 0.00 and 4.00 ± 0.00 for Group L and 2.63 ± 0.71, 3.06 ± 0.73, 3.43 ± 0.62, 3.83 ± 0.37 and 4.00 ± 0.00 for Group LC respectively.

The table-6 showing the mean (±SD) values of heart rate (beats/min) at different time intervals in both the groups.

The table-7 shows the (mean ±SD) diastolic blood pressure (mm Hg) at different time intervals in both the groups

The table-8 shows the (mean ±SD) of respiratory rate/ min at different time intervals in both the groups

Table-9 shows the comparison of side effects revealed 10 % of subjects in group L had post operative shivering and compared to group LC where 3.33% had nausea and vomiting.

Table 2: Comparison of Duration of Motor Blockade and Modified Bromage Score (Mean ± SD) in both the groups

Modified Bromage Scores	**Group L Mean ± SD**	**Group LC Mean ± SD**
AT THE TIME OF SHIFTING	1.90 ± 0.40	1.80 ± 0.55
75 min	1.93 ± 0.45	1.73 ± 0.45
90 min	1.53 ± 0.62	1.46 ± 0.50
120 min	1.13 ± 0.50	0.90 ± 0.60
180 min	0.06 ± 0.25	0.13 ± 0.34
Duration of Motor Blockade (min)	**106.83±27.80**	**99.33±30.27**

Table 3: Inter Group Statistical Comparison Mean (±SD) of Duration of Motor Block and Modified Bromage Scores between the two groups

Modified Bromage Scores	**Group L vs. LC**	
	t value	**P value**
AT THE TIME OF SHIFTING	0.803	0.426(#)
75 min	1.722	0.090(#)
90 min	0.452	0.653(#)
120 min	1.615	0.112(#)
180 min	0.851	0.398(#)
Duration of Motor Block (min)	**0.99**	**0.322(#)**

(#) - Not significant, ($) –Significant

Table 4: **Statistical Comparison of FLACC scores (Mean±SD) between two groups**

FLACC scores	**Group L vs LC**	
	t value	**P value**
60 min	1.42	0.160
120 min	0.162	0.872
240 min	5.50	0.000
480 min	5.35	0.000
FLACC at the time of first analgesia request	5.35	.000($)

Table 5: Comparison of Sedation Score (Mean ± SD) in both the groups

SEDATION SCORES	Group L Mean ± SD	Group LC Mean ± SD
AT THE TIME OF SHIFTING	3.13 ± 0.73	2.63 ± 0.71
75 min	3.50 ± 0.50	3.06 ± 0.73
90 min	4.00 ± 0.00	3.43 ± 0.62
120 min	4.00 ± 0.00	3.83 ± 0.37
240 min	4.00 ± 0.00	4.00 ± 0.00

Table 6: Comparison of Mean (±SD) heart rate (beats/min) in both the groups at different time intervals

Time (min)	Group L	Group LC
	Mean ±SD	Mean ±SD
Pre Induction	122.06±11.93	122.80 ±16.23
0	138.10 ± 15.96	132.93 ± 18.00
5	139.50 ±15.26	134.16 ±17.28
10	134.60 ±17.17	129.53 ± 16.91
15	125.66 ±14.78	125.60 ±15.68
20	123.20± 11.44	120.66 ±12.26
30	123.90 ± 9.99	118.13 ±11.45
40	122.50±9.27	116.13±12.74
60	121.66 ± 9.55	114.73 ±11.78
120	121.30 ± 10.03	115.93 ± 10.68
240	121.00 ±8.70	116.13± 9.52
480	120.33 ±8.50	114.33 ± 19.84

Table 7: Comparison of mean (± SD) diastolic blood pressure (mm Hg) at different time intervals in both the groups.

Time (min)	Group L	Group LC
Pre Induction	63.23±1.88	62.96±3.13
0	65.13±1.79	65.06±2.95
5	64.83±2.35	64.33±3.55
10	65.26±1.70	64.40±3.03
15	65.46±2.82	63.87±3.92
20	63.53±2.55	62.26±3.77
30	62.60±4.71	59.13±6.50
40	62.53±4.24	59.73±5.84
60	63.26±4.01	60.46±5.24
120	63.07±3.00	61.27±4.01
240	61.60±2.64	60.50±3.75
480	62.87±3.30	61.13±4.09

Table 8: Comparison of mean (± SD) respiratory rate (/min) at different time intervals in both the groups.

Time (min)	Group L	Group LC
Pre Induction	21.66±2.35	21.44±2.47
0	21.80±2.36	22.26±2.79
5	22.80±2.09	22.53±2.72
10	22.60±2.73	23.46±3.69
15	23.07±3.11	21.93±3.01
20	22.06±2.91	21.06±2.86
30	21.00±2.71	19.93±1.92
40	19.53±1.54	20.20±1.76
60	20.53±2.02	20.20±1.76
120	20.40±1.84	21.40±2.47
240	20.067±1.11	20.80±2.20
480	20.46±2.33	21.40±2.47

Table 9: Comparison of side effects and complications in both the groups

Complications	Group L		Group LC	
	No.	%	No.	%
Nausea and vomiting	0	0	1	3.33
Hypotension	0	0	0	0
Bradycardia	0	0	0	0
Shivering	3	10	0	0
Dyspnoea	0	0	0	0
Respiratory depression	0	0	0	0

DISCUSSION

The past few decades have witnessed many advances in the understanding and management of pain in children. Many studies, however indicate that pain in children is underestimated by health care professionals, and, therefore, children receive sub-therapeutic doses of analgesics [1]. The issue of under medication appears to be particularly problematic in the post-operative setting [2].

Racemic bupivacaine is gradually being replaced by ropivacaine or levobupivacaine. This change is driven by the reduced potential for systemic toxicity and the lower risk of unwanted motor blockade. There is now sufficient paediatric data to recommend either of the new agents [3-5, 6-9, 11-12] for single injection caudal blockade, ropivacaine and levobupivacaine provide similar postoperative analgesia compared to racemic bupivacaine with slightly less early postoperative motor blockade, [13] and with no discernible differences between ropivacaine and levobupivacaine[13].

Out of the various adjuvants being used for caudal block nowadays, alpha 2 agonists like clonidine have become very popular. Clonidine, which was introduced into paediatric practice in 1973 for the treatment of migrane, has expanded in clinical role to be used as a sedative, premedicant and analgesic [14]. It is nowadays the favoured adjuvant for single shot caudal blocks because of relatively lower adverse effects.

The present study was conducted with the primary aims to evaluate and compare the duration of analgesia and motor blockade of levobupivacaine hydrochloride and levobupivacaine hydrochloride with clonidine .The aims also included the comparison of duration of postoperative sedation and to observe any untoward complications, if present.

In this study, caudal epidural block using levobupivacaine hydrochloride alone and levobupivacaine hydrochloride and clonidine hydrochloride was administered to 60 subjects belonging to the age group of 2-8 years of ASA grade I who were scheduled for elective infra-umbilical surgeries after dividing them into groups of 30 each.

Group L (Control) (n=30) 0.25% levobupivacaine 1 ml/kg + 0.5 ml NS injected through the caudal route
Group LC- (n=30) - 0.25% levobupivacaine 1 ml/kg + 1 µg/kg clonidine administered through the caudal route.

Observations, tabulations and statistical calculations were done by applying student t- test by using SPSS version 17. Very few studies have been done combining caudal levobupivacaine hydrochloride and clonidine hydrochloride. Most of the literature scans done reveal various studies in which clonidine hydrochloride has been added to bupivacaine and ropivacaine. Even though bupivacaine is a drug which has been traditionally used for caudal block since its advent, several studies [15, 16] state that levobupivacaine, which is the enantiomer of the pure racemic bupivacaine S (-) is less toxic, provides similar analgesic effect as bupivacaine, has a wider safety margin and causes less motor block Out of the various studies in which levobupivacaine has been used, concentrations range from 0.125% to 0.25% with drug volumes even up to 1.25 ml / kg. We wanted a concentration and dose of drug which would provide adequate motor block as well as analgesia as pre-emptive caudal block was to be given and adequate intra operative conditions were needed.

Literature reviews proved that a concentration of 0.25% 1 ml/kg levobupivacaine provided best combination of qualities In this study, clonidine was used in a dose of 1µg/kg. Even though Clonidine has been used in doses ranging from 1-5 µg/kg, we chose a dose of 1 µg/kg in our study as other studies like Klimscha *et al.;* [17] have shown that increasing the dose from 1 µg/kg to 2 µg/kg did not enhance the analgesic effect of clonidine but increased the incidence of side effects like respiratory depression, bradycardia and hypotension while increasing the dose [18].

Demographic profile

The 60 subjects belonging to 2-8 years age group (24-96 months), the mean age (in months) of Group L was 58.46 ± 24.08 and that of Group LC was 60.60±23.33. These mean ages were found to have no significant difference (p> 0.05). The mean weights of both groups were 14.06±2.61 kg for Group L and 14.46 ± 2.81 kg for group LC. After applying appropriate

statistical tests, it was found that these values had no significant difference and were comparable. (p> 0.05).

Out of the 30 patients in each study group, majority of patients of group L (27) and group LC (26) were noted to be males. As opposed to this, only 3 and 4 patients in Groups L and LC respectively, were noted to be females. This result may be due to the fact that most of the surgeries which occurred in these groups namely circumcision, hydrocele repair, inguinal hernia repair and urethroplasty are more common in the male population.

Duration of Analgesia

One of the primary aims of this study was to find out the effect of adding clonidine 1µg/kg to levobupivacaine on the duration of analgesia. Data in the Mean ± SD of the durations of analgesia in both groups when calculated were 237.66± 49.59 min for Group L and 503.66±89.53 min for Group LC respectively. The statistical analysis of this result with the help of student t test revealed that there was a significant difference in the durations of analgesia of both groups with Group LC having a significant increase in the duration of analgesia as compared to Group L (p< 0.05).

The addition of adjuvant clonidine in a dose of 1 µg/kg seems to provide a longer duration of analgesia as compared to the control group. Our results are in accordance with Akin A *et al.;* [19] who compared the effect of clonidine on levobupivacaine administered by caudal route and concluded that clonidine given by the caudal route prolonged the duration of analgesia .However, the concentration of drugs used in this study was different in that they used a concentration of 0.25% 1ml/kg levobupivacaine and 2µg/kg of clonidine.

Parameswari A [20] postulated that addition of clonidine 1 µg/kg to 1 ml/kg 0.25% bupivacaine significantly increased the duration of analgesia from 288.7±259.1 min to 593.4±423.3 min which is similar to our findings.

Upadhyay *et al.;* [21] concluded that the addition of clonidine to bupivacaine significantly increased the duration of analgesia (p<0.05) from 5.59±0.633 hours in control group α 2 adrenoceptor agonists like clonidine, have been known to prolong the effects of local anaesthetics. This has been explained by three possible mechanisms. First, clonidine blocks Aδ and C fibres manifesting as an increase in Potassium conductance in isolated neurons thus intensifying local anaesthetic conduction block. Secondly, clonidine may cause local vasoconstriction, thus decreasing local anaesthetic spread and removal around neural structures by action on post synaptic α2 receptors. Thirdly, clonidine combined with spinal local anaesthetics or used in peripheral blocks intensifies and prolongs analgesia [22].

Duration of Motor Block

The mean duration of motor block in Group L was 106.83 ±27.80 min and that in Group LC was 99.33 ± 30.27 min. Statistical comparison of the mean duration of motor blockade between both groups showed that the difference in duration of motor blockade between two groups was statistically insignificant (p > 0.05).

Our results are in accordance with Cook *et al.*; [23] who compared the effects of adrenaline, clonidine and ketamine on the duration of analgesia, motor block and post-operative pain and concluded that there was no difference in the duration of motor blocks in adrenaline, clonidine(2 µg/kg) , ketamine when added to bupivacaine 0.25%.

Koul A *et al.;* [24] who evaluated the effects of adding clonidine to bupivacaine 0.25% 0.75 ml/kg and concluded that there was no difference in motor blockade duration in both groups.

Laha A *et al.;* [25] who observed no difference in duration of motor blocks between clonidine added to ropivacaine and plain ropivacaine groups.

FLACC scores

FLACC scores were measured for a period of 8 hours in the post -operative period . Comparison of the mean duration of FLACC scores at 60 min, 120 min, 240 min and 480 min after induction to be 0.66±0.66, 1.53±0.93, 3.53±1.22, 4.46±0.937 for group L and 0.93±0.78,1.56±0.62,2.20±0.48 and 2.96±0.85 for Group LC patients. Statistical analysis of the same showed a significant decrease in the FLACC scores of Clonidine group at 240 min and 480 min after induction.(p<0.05) as compared to the control group.

The mean FLACC score at the time of first analgesia request was found to be 4.16 ±0.69 in the control group as opposed to 3.16 ±0.74 in the group with clonidine. Statistical analysis using t test revealed a significant decrease in the mean FLACC scores at the time of first analgesia request in the LC group.

Singh J *et al.;* [26] concluded that patients in the group with clonidine had significantly lower FLACC pain scores as compared to other groups studied(fentanyl, ketamine and normal saline) which is similar to our result.

El Hennawy *et al.;* [27] compared the effects of caudal clonidine and caudal dexmedetomidine when combined with caudal bupivacaine and concluded that 4 hours after discharge from the ICU, the FLACC pain scores were significantly more in the control group than either clonidine or dexmedetomidine groups which is similar to our result. However the duration of

analgesia observed in the group with clonidine in this study(12 hours) is more than the analgesia duration we obtained(9 hours). We chose the FLACC scale to evaluate pain post-operatively as it is easy to use, is validated and gives us an objective evaluation.

Sedation Scores

The mean sedation scores of both groups at the time of shifting, at 75 min, 90 min, at 120 min and at 240 min were 3.13 ± 0.73, 3.50 ± 0.50, 4.00 ± 0.00 ,4.00 ± 0.00 and 4.00 ± 0.00 for Group L and 2.63 ± 0.71, 3.06 ± 0.73, 3.43 ± 0.62, 3.83 ± 0.37 and 4.00 ± 0.00 for Group LC respectively. By 4 hours, no sedation was observed in patients of both groups.

Statistical comparison of both groups revealed a statistically significant difference in the sedation scores of both groups at the time of shifting, 75 min, 90 min and 120 min after induction. Group LC had significantly lower sedation scores as compared to Group L indicating higher sedation in the clonidine group.

Lak M *et al.;* [28] concluded that the patients in clonidine group were more sedated compared to the control group in the post-operative period which is similar to our study result.

Meghani Y *et al.;* [29] compared caudal bupivacaine and bupivacaine plus clonidine for post-operative analgesia and concluded that the period of sedation was significantly longer in the children who received clonidine.

Upadhyay *et al.;* [30] concluded that there was a significant difference in the sedation scores of the patients with an increase in sedation of patients in clonidine group.

However, in our study, at no time during the study period were the patients deeply sedated. All patients had a sedation score more than 1 in the post-operative period. the post .

Sedation after epidural clonidine results from activation of α2- adrenoceptors in the locus coeruleus, an important modulator of vigilance. This suppresses the spontaneous firing rate of the nucleus, thereby resulting in increased activity of inhibitory interneurons such as GABA-ergic pathways to produce CNS depression [31].

Hemodynamic parameters

The mean pre-operative heart rate before induction was 122.06±11.93 in group L and 122.80 ±16.23 for Group LC. As initially, injection ketamine was given to the subjects for sedation so that caudal block could be administered, there was a significant increase in the pulse rate till 15 minutes after induction when the effect of ketamine decreased and caudal block became effective ($p<0.05$). This was followed by a significant fall in heart rates as compared to the preoperative values. Inter group comparison of LC with the control group L revealed that there was a significant decrease in pulse rates ($p<0.05$) 30 minutes after induction which gradually normalised in the post-operative period by 4-6 hours. However, at no time was the pulse rate less than the cut-off that we had specified in our methods and hence bradycardia was not considered to be significant.

The mean pre-induction values of systolic blood pressures were 99.00±6.04 in Group L and 101.80±5.72 in Group LC. There was a significant rise in systolic blood pressure in the first 15 minutes in both the groups followed by a significant fall in blood pressures which became similar to the pre-induction values in the post-operative period. Comparison between both groups revealed a significant fall in mean systolic blood pressure in the LC group 30 min following induction which soon normalised by 60 minutes.

The mean diastolic blood pressures in the pre induction period were 63.23±1.88 mm Hg in group L and 62.96±3.13mm Hg in Group LC. Similar to the systolic blood pressures, on intragroup comparison the diastolic blood pressures of the subjects in both groups showed a significant rise till 10 min post induction followed by a significant fall compared to pre - operative values which slowly normalised post operatively. Intergroup analysis between both these groups showed a significant fall in diastolic blood pressure in Group LC 30 minutes post induction which normalised by 1 hour.

Like the variations in heart rate, the blood pressure variations are due to induction with the drug ketamine which lead to an initial rise in blood pressure in both groups. As the fall in blood pressure was within normal limits as per our initial criteria for hypotension, it was not considered significant. At no time during the study period did any patient have significant hypotension or bradycardia which needed intervention. Our study results are in accordance with results of Manickam A *et al.*; [32] who compared the efficacy of clonidine as an adjuvant to ropivacaine in caudal block and stated that the mean heart rates and blood pressures were less in the clonidine group as compared to plain ropivacaine but none of the children required intervention as the parameters were not below the defined criteria..

Klimscha *et al.;* [33**]** who found that there were significant decrease in MAP from baseline values of 2 compared groups of bupivacaine with clonidine 1µg/kg and2µg/kg 5-20 minutes after injection, returning to normal within first hour. However, no difference was observed on comparing both groups. They observed no hemodynamic changes that required

drug treatment in the intraoperative or 6 hour postoperative period.

The mean respiratory rate/min in both groups before induction was 21.66±2.35 in Group L and 21.44±2.47 and in Group LC. Statistical analysis showed no variations in respiratory rates with baseline as well as between groups. Analysis of oxygen saturation values also showed no significant change. Our findings are similar to most of the studies on caudal anaesthesia. At no time during this study was there a decrease in respiratory rate or a fall in oxygen saturation requiring oxygen supplementation as demonstrated by Upadhyay *et al.;* [34]

Side effects and Complications

It was observed that while one subject in the clonidine group had nausea and vomiting. Though clonidine has been noted to decrease post- operative nausea vomiting as demonstrated by Vetter T *et al.;* [35] our study did not have such results.

One advantage of clonidine adjuvant which was noted was that 3 subjects in Group L had post-operative shivering while no subject in the clonidine group had shivering. These findings are similar to findings of Bergendahl H *et al . ;* **[**36] Who compared the effects of midazolam and clonidine administered rectally for premedication in 100 children undergoing adenotonsillectomy and concluded that clonidine group subjects had no shivering compared to 5 subjects in midazolam group.

Clonidine, probably acting through α2b receptors, synchronously decreases the cold response threshold while slightly increasing the sweating threshold suggesting that it acts on the central thermoregulatory system rather than preventing shivering peripherally [37].

A significant benefit of the use of clonidine for caudal anaesthesia is that it facilitates a local anaesthetic sparing effect, which inevitably reduces the risk of local anaesthetic toxicity. No other adverse effects or complications were noted with the use of clonidine.

One limitation noted during our study was that we monitored the patients post operatively only for a period of 8 hours to look for postoperative analgesia. The monitoring period should have been extended to the first 24 hours postoperatively and the number of doses of rescue analgesic used should also have been compared to a better idea of the quality of analgesia offered by adjuvant clonidine.

CONCLUSION AND SUMMARY

The following conclusions are drawn from the present study: Administration of clonidine hydrochloride (1µg/kg) with levobupivacaine hydrochloride 0.25% 1 ml/kg causes an increase in the duration of analgesia. Clonidine hydrochloride (1µg/kg) as an adjuvant to levobupivacaine hydrochloride provides superior quality of analgesia (decreased FLACC scores).No difference was noted in the duration or recovery from motor blockade was noted. Use of adjuvant clonidine seems to cause more sedation postoperatively as evidenced by lower sedation scores. No significant hemodynamic or respiratory instability occurred in both groups. No untoward effects or complications were observed.

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