Original Research Paper

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EVALUATION OF CLONIDINE AS ADJUVANT WITH CAUDAL LEVOBUPIVAINE FOR POST-OPERATIVE ANALGESIA IN PAEDIATRIC AGE GROUP

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ABSTRACT

Background: A prospective, randomized, double-blind study was designed to evaluate the effects of caudal levobupivacaine vs. clonidine as adjuvant in children undergoing minor surgical procedures.

Methods: Sixty children of 2-8 years of age with ASA-I physical status posted for minor surgical procedures were divided in to two groups. Group L received 0.25% levobupivacaine @1 mg/kg caudally and group C received clonidine @1µg/kg along with levobupivacaine. The patient's vital data and post-operative analgesia, sedation status, motor blockade were assessed every hourly by individual scores for 24 hours. Any adverse events were also noted.

Results: The mean duration of analgesia in group C is significantly higher(16.53+4.26)than group L(4.17+1.53).the CHIPPS scores were lower in group C than group L which is statistically significant and 4 patients in group C did not require any rescue analgesia this is also statistically significant. There were no incidences of bradycardia, hypotension, in either of the groups during study observation.

Conclusions: Clonidine as adjuvant with caudal levobupivacaine is more efficient than levobupivacaine alone in terms of post-operative analgesia, in caudal route and it is without any adverse side effects.

KEYWORDS : Levobupivacaine; Clonidine; Caudal route; Minor surgical procedures; Post-operative Analgesia.

INTRODUCTION

Caudal analgesia provides excellent and predictable pain relief and is safe and easy to perform in children.1Levobupivacaine, a pure S-enantiomer of Bupivacaine. The rationale behind substituting bupivacaine with levobupivacaine is to reduce the incidence of unwanted motor blockade and its wider safety margin.[2]

Clonidine, an alpha-2 agonist, has been shown to have analgesic effect when administered epidurally. The alpha-2 receptors are located primarily on afferent terminals centrally and peripherally, but they are also found on the spinal cord and within several brainstem nuclei known to be involved in analgesia.

The objective of this study was to compare the adjuvant effect of clonidine with levobupivacaine 0.25% in caudal route in paediatric age group posted for elective minor surgical procedures by observing the post-operative analgesia, sedation and motor blockade as well as any postoperative side effects.

METHODOLOGY

In this prospective, randomized, double-blind study, the study protocol was approved by the Ethical Committee and informed consent was obtained for each patient from parent/legal guardian.

In this study 60 patients of ASA Grade I and ASA Grade II, of either sex aged between 2-8 years posted for elective minor surgical procedures were included. The children with congenital spine anomalies, congenital heart disease, any history of allergy to anaesthetic medication, History of CNS disorder, Mental retardation were excluded from study. All patients were evaluated for fitness.

In the pre-operative room, baseline heart rate, blood pressure and oxygen saturation of the subject were noted before the commencement of the trial.

The children were randomly divided by computer generated table into Group L or Group C of 30 patients each. Group L received 0.25% levobupivacaine @1 mg/kg ,Group C received 0.25% levobupivacaine @1 mg/kg and clonidine @1µg/kg .All drugs were prepared by an anaesthetist who is not involved in the study and each drug was administered by the observer was completely blind to the study and to the group allocation of the child.

All caudal analgesia was administered after intravenous induction of general anaesthesia, caudals were performed in the left lateral position under strict asepsis, using a 22 G needle. After a gentle aspiration, the drug should be injected over a period of 60-90 seconds.

The success of block of was assessed by haemodynamic response and vitals were recorded every 15 min during intra operative period and Post-operative period.

Children were evaluated for adequacy of post-operative analgesia, Sedation and motor block by CHIPPS Score, modified ramsay sedation score, modified bromage scale respectively. The scores were assessed every hourly for first 12 hours, and 2nd hourly up to 24 hours. Rescue analgesia will be given if CHIPPS score≥4 by i.v. paracetamol and time was noted.

Children were observed for any signs of respiratory depression, apnoea and oxygen desaturation, nausea, vomiting, hypotension, bradycardia, urinary retention.

STATISTICAL ANALYSIS

Data were analysed using SPSS® version 16 (Statistical Packages for the Social Sciences, Chicago, IL, USA). Results were expressed as mean ± standard deviation (SD) or numbers (percentages).Quantitative data were compared using one-way analysis of variance (ANOVA) and unpaired t-test; qualitative data were analysed using a chi-square test. A p-value of < 0.05 was considered statistically significant.

STATISTICAL ANALYSIS

In present study, children in the two study groups were in the age group of 2-8 years with mean age of 5.03±2.28 in Group L and 5.30±2.35 in Group C, mean weight of 13.83±4.17 in Group L and 14.08±4.25 in Group C and with almost equal male and female population. The two groups were comparable with respect to age, weight (Table-4).There were no statistical differences in the demographic parameters (Graph-1).

Pre-operative vitals heart rate, MAP, SPO2 between group L and group C were comparable and there is no statistical difference (Table-4) (Graph-2).

Both the heart rate and mean arterial blood pressures were comparable and without statically significant values during the intra operative and post period of 24 hours. There is no incidence of bradycardia and hypotension was noted in both the groups (Table-5, 6).

EVALUATION SCALES

TABLE – 1 CHILDREN AND INFANTS POSTOPERATIVE PAIN SCALE

CHIPPS SCORE	
Crying	
None	0
Moaning	1
Screaming	2
Facial Expression	
Relaxed/ smiling	0
Wry mouth	1
Grimace (mouth and eyes)	2
Posture Of The Trunk:	
Neutral	0
Variable	1
Rear up	2
Posture Of The Legs:	
Neutral, released	0
Kicking about	1
Tightened legs	2
Motor Restlessness:	
None	0
Moderate	1
Restless	2

TABLE – 2 MODIFIED RAMSAY SEDATION SCALE

Modified Ramsay Sedation Scale	
Anxious, agitated, restless	1
Cooperative, oriented, tranquil	2
Responds to commands only	3
Brisk response to light glabellar tap or loud noise	4
Sluggish response to light glabellar tap or loud noise	5
No response	6

TABLE – 3 MODIFIED BROMAGE SCALE

Modified Bromage Scale	
Free movement of legs and feet	0
just able to flex knees with free movement of feet	1
unable to flex knees, but with free movement of feet	2
unable to move legs or feet	3

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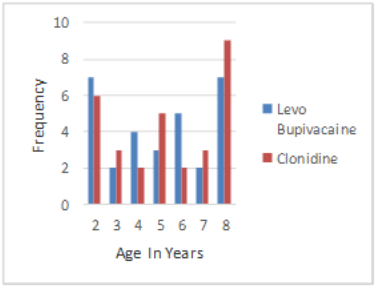
TABLE – 4 DEMOGRAPHIC DATA & PRE OPERATIVE VITALS

	Group L	Group C	P value	significance
Demographic Data				
Age (years)	5.03± 2.28	5.30± 2.35	0.653	Not significant
Weight (kg)	13.83± 4.17	14.08± 4.25	0.818	Not significant
Pre-Operative Vitals				
HR (Per Minute)	110.4± 23.27	108.36± 16.57	0.697	Not significant
MAP (mmHg)	79.10± 12.64	75.74± 8.52	0.232	Not significant
SPO2 (%)	99.83± 0.38	99.60± 0.62	0.088	Not significant

GRAPH– 1 AGE DISTRIBUTION



GRAPH– 2 PRE OPERATIVE VITALS

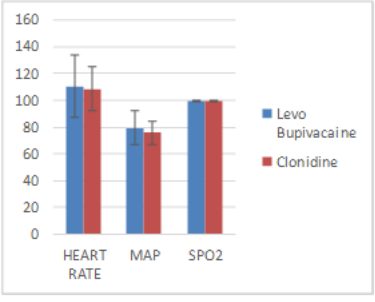


TABLE – 5 INTRA OPERATIVE VITALS

	Group L	Group C	P value	significance
Heart Rate				
5 Min	99.50±20.12	97.03±16.79	0.607	Not significant
10 Min	98.93±21.35	96.70±16.26	0.650	Not significant
20 Min	94.90±19.85	95.60±15.97	0.880	Not significant
30 Min	92.67±19.29	95.70±13.96	0.488	Not significant
40 Min	91.27±17.28	94.70±13.80	0.399	Not significant
50 Min	90.83±17.12	92.78±11.01	0.601	Not significant
60Min	92.21±15.06	90.45±10.91	0.616	Not significant
Mean Arterial Pressure				
5 Min	70.57±11.87	68.27±5.85	0.345	Not significant
10 Min	66.93±8.54	67.06±7.39	0.949	Not significant
20 Min	65.53±9.38	67.26±6.58	0.411	Not significant
30 Min	65.70±9.15	67.20±7.37	0.487	Not significant
40 Min	66.57±8.38	66.70±6.21	0.945	Not significant
50 Min	65.10±8.41	67.89±5.50	0.133	Not significant
60 Min	68.57±8.92	65.27±6.15	0.100	Not significant

TABLE – 6 POST OPERATIVE VITALS

	Group L	Group C	P value	significance
Heart Rate				
1 hr	95±10.46	93.31±13.45	0.567	Not significant
2 hr	96.9±8.58	94.96±12.55	0.487	Not significant
3 hr	97.10±7.89	94.83±11.96	0.389	Not significant
4 hr	97.72±7.50	103.76±35.51	0.365	Not significant
5 hr	95.66±7.71	95.13±11.11	0.830	Not significant
6 hr	95.58±6.92	95.54±12.02	0.987	Not significant
7 hr	99.57±5.32	96.30±11.93	0.175	Not significant
8 hr	98.24±6.24	96.0±12.06	0.376	Not significant
9 hr	94.78±4.68	97.13±13.15	0.360	Not significant
10 hr	98.01±5.27	98.87±12.89	0.736	Not significant
11 hr	97.25±6.57	97.96±12.32	0.781	Not significant
12 hr	96.42±8.12	98.09±12.59	0.543	Not significant
14 hr	95.54±7.29	98.92±14.19	0.250	Not significant
16 hr	96.58±6.48	93.85±13.82	0.331	Not significant
18 hr	98.47±5.37	95.71±16.67	0.391	Not significant
20 hr	97.54±6.14	98.40±5.36	0.565	Not significant
22 hr	95.63±4.58	93.21±5.76	0.071	Not significant

24 hr	94.59±6.34	94.28±4.67	0.830	Not significant
Mean Arterial Pressure				
1 hr	75.53±6.96	77.43±5.95	0.260	Not significant
2 hr	75.66±6.13	77.50±4.71	0.197	Not significant
3 hr	77.07±5.84	78.66±4.51	0.242	Not significant
4 hr	77.04±5.21	78.63±4.73	0.220	Not significant
5 hr	76.04±6.50	78.17±4.87	0.156	Not significant
6 hr	74.14±3.05	75.26±5.67	0.344	Not significant
7 hr	77.22±4.28	75.06±4.97	0.076	Not significant
8 hr	78.24±4.26	76.97±5.30	0.310	Not significant
9 hr	75.41±5.29	77.10±4.95	0.206	Not significant
10 hr	76.27±5.14	78.45±4.68	0.091	Not significant
11 hr	77.58±4.35	75.93±4.47	0.153	Not significant
12 hr	78.51±3.69	76.28±5.23	0.060	Not significant
14 hr	77.24±4.08	78.77±5.05	0.215	Not significant
16 hr	78.23±5.10	77.28±5.21	0.478	Not significant
18 hr	77.54±3.98	75.74±4.63	0.112	Not significant
20 hr	75.38±4.51	77.10±3.31	0.097	Not significant
22 hr	75.42±5.17	77.40±4.45	0.117	Not significant
24 hr	74.41±4.57	65.70±5.12	0.307	Not significant

In group L CHIPPS score of 4 was achieved @ 2nd hourly by three patients. The remaining patients were achieved CHIPPS score of 4 by 7 hours, but where as in group C the first patient achieved the CHIPPS score of 4 @12 hours and all patients did not achieve score 4 even after 24 hours(Table-7, 8), (Graph-3,4).

In group C 4 patients did not require any rescue analgesia. This is statistically significant and considerable.

TABLE – 7 CHIPPS SCORES OF GROUP L AT DIFFERENT TIME INTERVALS

Time	Score 0	Score 1	Score 2	Score 3	Score ≥4
1 hr	24	4	2	0	0
2 hr	5	19	3	0	3
3 hr	1	6	9	5	9
4 hr	0	2	4	6	18
5 hr	0	0	3	5	22
6 hr	0	0	1	2	27
7hr	0	0	1	0	29
8hr	0	0	0	0	30
9hr	0	0	0	0	30
10hr	0	0	0	0	30
11hr	0	0	0	0	30
12hr	0	0	0	0	30
14hr	0	0	0	0	30
16hr	0	0	0	0	30
18hr	0	0	0	0	30
20hr	0	0	0	0	30
22hr	0	0	0	0	30
24hr	0	0	0	0	30

GRAPH– 3 CHIPPS SCORE DISTRIBUTION IN GROUP L

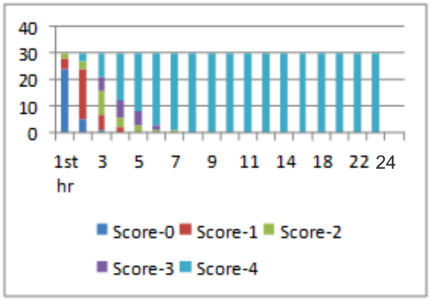
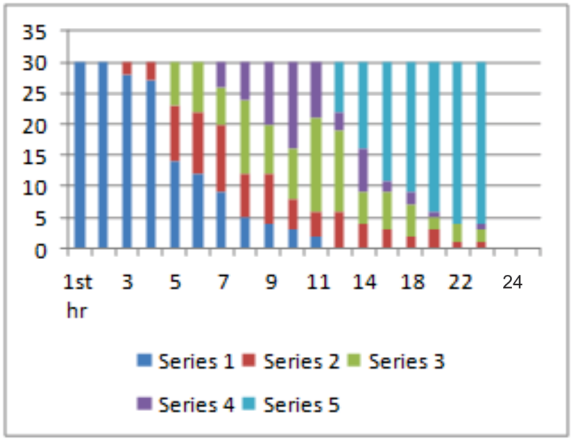


TABLE – 8 CHIPPS SCORES OF GROUP C AT DIFFERENT TIME INTERVALS

Time	Score 0	Score 1	Score 2	Score 3	Score ≥4
1 hr	30	0	0	0	0
2 hr	30	0	0	0	0
3 hr	28	2	0	0	0
4 hr	27	3	0	0	0
5 hr	14	9	7	0	0
6 hr	12	10	8	0	0
7hr	9	11	6	4	0
8hr	5	7	12	6	0
9hr	4	8	8	10	0
10hr	3	5	8	14	0
11hr	2	4	15	9	0
12hr	0	6	13	3	8
14hr	0	4	5	7	14
16hr	0	3	6	2	19
18hr	0	2	5	2	21
20hr	0	3	2	1	24
22hr	0	1	3	0	26
24hr	0	1	2	1	26

GRAPH– 4 CHIPPS SCORE DISTRIBUTION IN GROUP C



The duration of time required attaining CHIPPS score of 4 is considered as duration of analgesia and for every patient it was noted (Table-9).

TABLE – 9 DURATION OF ANALGESIA OF EACH PATIENT IN THE STUDY

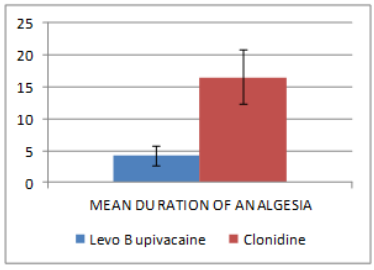
Duration Of Analgesia	Group L	Group C
1st pt	2	16
2nd pt	4	20
3nd pt	6	12
4th pt	5	14
5th pt	4	24
6th pt	7	12
7th pt	2	16
8th pt	4	14
9th pt	5	18
10th pt	4	12
11th pt	6	22
12th pt	2	14
13th pt	4	12
14th pt	5	16
15th pt	3	24
16th pt	4	12
17th pt	1	20
18th pt	3	24
19th pt	6	12
20th pt	5	22
21sh pt	3	12
22nd pt	6	20
23nd pt	4	14
24th pt	3	16
25th pt	7	12
26th pt	4	24
27th pt	3	16
28th pt	6	14
29th pt	4	18
30th pt	3	14

The Mean duration of analgesia in group L was 4.17±1.53hrs and in group C was 16.53±4.26hrs, the p value is >0.001 and it is statistically significant, (Table-10) (Graph-5).

TABLE – 10 MEAN DURATION OF ANALGESIA

	Group L	Group C	P value	significance
Mean Duration Of Analgesia				
Hrs	4.17+1.53	16.53+4.26	<0.001	significant

GRAPH– 5 MEAN DURATION OF ANALGESIA



In group L all patients required rescue analgesia but in group C, four patients did not require any rescue analgesia, this is statistically significant with p value<0.001.

TABLE – 11 NUMBER OF PATIENTS DID NOT REQUIRE RESCUE ANALGESIA IN TWO GROUPS

	Group L	Group C	P value	significance
No of pts did not require rescue analgesia				
	0	4	<0.001	significant

The sedation scores were equal and without any statistically significance

DISCUSSION

Caudal epidural blockade is simple and a frequently used technique, providing very effective analgesia intra-operatively as well as postoperatively in paediatric patients.

Levobupivacaine in comparison to bupivacaine has a wider margin of safety, less motor blockade, less cardiovascular / neurological toxicity and similar duration of analgesia. [4,5,6]

In paediatric age group post-operative analgesia is most important, because Postoperative analgesia provides not only pain relief but also inhibits trauma induced nociceptive impulses thus blunting autonomic reflexes[7]. It allows the patients to breath and move freely to enhance early restoration of function.

The analgesic activity of alpha 2 agonist clonidine is mediated by both supra-spinal and spinal mechanisms. It is assumed that central alpha 2 adrenoceptors in the locus ceruleus (a supa-spinal site) and in the dorsal horn of the spinal cord are involved in this activity[8].

The α2-adrenoreceptor agonists, administered caudally, have been observed to prolong the motor and sensory block effects of local anesthetics. However, the precise mechanism of action has not been completely clarified. Certain pharmacodynamics and pharmacokinetic mechanisms have been suggested for clonidine-induced prolongation of caudal/epidural analgesia, although the precise one is not yet clarified. It has been suggested that epidural clonidine exerts an analgesic action through its direct suppression of nociceptive neurons in the spinal cord[9,10,11].

As per observations noted in this study in group L the mean duration of analgesia is 4.17+1.53

Hrs. and in group C the mean duration of analgesia is 16.53+4.26 hrs,it is statistically significant with p value <0.001, thus caudal clonidine prolongs the analgesia effects of caudal levobupivacaine.

CHIPPS scores were always lower in group C than group L at any time during the 24 hours of study period duration and in group c the 4 patients did not attain CHIPPS score of 4 ,this means they did not require any rescue analgesia in the post-operative period but in group L all patients needed rescue analgesia at an early time than the group C and it is statistically significant with p value<0.001 , this can be attribute to clonidine as adjuvant with caudal levo bupivacaine which decreases the requirement of other analgesic drugs in terms of frequency and dosage that are used for immediate post-operative analgesia.

From a similar study conducted by Akin et al[12] who concluded that this effect might be due to the spinal mode of action of caudal clonidine rather than its systemic absorption.

Sedation is a desired effect in most children, thus reducing the requirement of sedatives and anxiolytics in the postoperative period. Epidural clonidine has been associated with sedation reflecting systemic absorption and action on higher centers. However, in our study, the mean sedation scores in both the groups were comparable and statistically not significant. The lower dosage of clonidine @1 µg/kg might explain the lack of significant sedation in our s t u d y groups.

According to a previous report, a decrease in the HR and blood pressure was observed when 5µg/kg clonidine was added to the caudal block.[13]

In our study, we observed that the haemodynamic parameters were stable during intra operative and post-operative period and were comparable and statistically insignificant with p values >0.001 .this can be explained as we are using lower dose of clonidine @1 µg/kg. There is no incidence of side effects like pruritis and nausea and vomiting. No episodes of respiratory depression or urinary retention were noted.

Thus in our study caudal clonidine of 1µg/kg as adjuvant with caudal levo bupivacaine was found to be better in terms adequacy of post-operative analgesia. There were no major side effects were observed.

CONCLUSION

Caudal clonidine as adjuvant with caudal levobupivacaine was associated with lower CHIPPS scores and better post-operative analgesia without any adverse side effects.

Thus it can be concluded that clonidine can be used as adjuvant in caudal anaesthesia in paediatric age group undergoing minor surgical procedures under general anaesthesia.

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