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A COMPARATIVE STUDY OF THE EFFECT OF CAUDAL VS INTRAVENOUS CLONIDINE ON POST OPERATIVE ANALGESIA PRODUCED BY CAUDAL LEVOBUPIVACAINE IN CHILDREN UNDER GOING SUBUMBLICAL SURGERIES.

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ABSTRACT

Aims & Objectives: To assess and compare duration of analgesia, hemodynamic changes, adverse effects of caudal v/s intravenous clonidine on postoperative analgesia produced by caudal levobupivacaine.

Methods: After approval from the ethical committee a randomized, double blind, controlled type study of 90 children of ASA I/II, aged between 2 to 8 years, posted for subumbilical surgeries under caudal block were taken and randomly allocated in three groups.

- Group A (L)(n=30) - received levobupivacaine 0.25% (0.75 ml/kg) and 5ml normal saline IV.
- Group B (LC_{cau}) (n=30)- received levobupivacaine 0.25% (0.75 ml/kg) and 2µg/kg clonidine caudally and 5ml normal saline IV.
- Group C (LC_{iv}) (n=30)- received levobupivacaine 0.25% (0.75ml/kg) caudally and 2µg/kg clonidine and normal saline making total volume of 5ml IV.

Results: There was no significant difference in the duration of surgery in all three groups (40±16.1 min in group L, 44±19.4min in group LC_{cau} and 45.5±19.4 min in group LC_{iv}). The CHIPPS scores for assessment of post operative pain were significantly higher in patients of group L as compared to group LC_{cau} and $LC_{iv.}$. The mean duration of post operative analgesia was (342.8±110.6min in group L, 461.4±125.6min in group LC_{iv} and 671.3±82.3min in group $LC_{cau.}$) ($P<0.01$) The mean sedation scores in all the three groups were comparable (P value between groups >0.5) and no motor block was observed in all the three groups. The mean rescue analgesia was highest in group L (1.4±0.6) significantly less rescue analgesics required in the group LC_{cau} as compared to group LC_{iv} (0.1±0.3 v/s 0.9±0.3)(p=<0.05).

Conclusion: Addition of clonidine (2µg/kg) as an adjuvant to caudal levobupivacaine has long lasting post operative analgesia and less no. of rescue analgesics requirement without additional side effects as compared to intravenous clonidine with caudal levobupivacaine.

KEYWORDS

caudal block, clonidine, levobupivacaine,

INTRODUCTION

Caudal anesthesia is very popular and commonly used regional anesthetic technique in pediatrics patients. [6]. Thepopularity of this procedure is due to clearly defined anatomical landmarks in children , safely , ease of technique and high success rate .Caudal anesthesia was first used in Paris in 1901 by Jean-Anthanase Sicard and Fernard Cathelin[2,3]. Caudal analgesia reduces the amount of inhaled and intravenous anesthetic requirement, attenuates the stress response to surgery, facilitates a rapid, smooth recovery and provides good post-operative analgesia[7].

In pediatric patients lateral decubitus position is efficacious because it permits easy access to airway when general anesthesia or heavy sedation has been administered prior to performing block.

S-levobupivacaine enantiomer of bupivacaine also has anesthetic activity, but with less cardiac and neural toxic effects than bupivacaine, while still possessing a similar duration of sensory blockade [12 -15]. So levobupivacaine has been shown to be safe and effective for epidural and spinal anesthesia. In order to decrease intra and post operative analgesic requirement after single shot of caudal epidural blockade , various additives such as morphine, fentanyl , tramadol , dexmedetomidine , clonidine with local anaesthetics have been investigated[16 -18]. The use of clonidine (α-2 adrenergic agonist) has become increasingly popular in paediatric anaesthsia when administered caudally with local anaesthetic agents. The α-2 receptors are located primarily on afferent terminal centrally and peripherally, but they are also found on the spinal cord and within several brain stem nuclei known to be involved in analgesia. Clonidine inhibits transmission of nociceptive stimuli in the dorsal horn of spinal cord. This augments local anaesthetic blockade and prolongs duration of analgesia.

Hence, the present study was conducted with primary aim to compare the effects of caudal v/s intravenous clonidine on post operative analgesia with caudal levobupivacaine for sub umbilical surgeries in pediatric patients.

METHODS

After obtaining written informed consent from parents and local Ethics Committee approval , 90 children aged between 2-8 years, ASA grade I/II, undergoing elective subumbilical surgeries were included in this randomized, double blinded, observational study. Patients with negative consent from parents / guardians, coagulation disorders, vertebral deformity, neuropathy, local infection at the site of injection and any other chronic illness were excluded from the study.

After standard fasting time, the children were taken into operation room, and IV cannula was inserted. Midazolam 0.01-0.1mg/kg given IV. Anesthesia induced with sevoflurane 8% in oxygen 100% by face mask followed by placement of laryngeal mask airway. Anesthesia was maintained with sevoflurane 2-3% in oxygen and nitrous oxide (50:50). An intravenous infusion of isolyte-P, 10ml/kg/hr was commenced. Heart rate, non invasive blood pressure, SpO_2 and end tidal CO_2 were monitored.

Children were randomized using a chit in box technique to one of the three treatment groups before caudal block was performed. The study drug was prepared by an investigator unaware of the group assignment. The caudal block was performed with the child positioned in the left lateral position by the anaesthetist using an aseptic technique and a 22 gauge needle. After negative aspiration of blood or cerebrospinal fluid. Levobupivacaine (0.25%, 0.75% ml/ kg) was injected caudally together with or without clonidine (2µg / kg) .Simultaneously, the content of the second syringe, containing 5 ml of 0.9% saline with or without clonidine (2 µg /kg), was administered intravenously.

The group assignments were as follows:

Group A (L) (n=30): Levobupivacaine 0.25% (0.75ml/kg) and 5 ml normal saline IV

Group B ($LC_{(CAU)}$) (n=30): Levobupivacaine 0.25% (0.75 ml/kg) and clonidine (2µg/kg) caudally and 5 ml. normal saline IV

Group C ($LC_{(I.V.)}$) (n=30): Levobupivacaine 0.25%(0.75 ml/kg) caudally and clonidine (2µg/kg) and normal saline making total volume of 5 ml IV

In all groups surgery was initiated after 10 min. has elapsed so that

caudal block became effective. An intraoperative successful blockade is defined as a hemodynamic (H.R. or NIBP) response <20% compared with baseline in response to surgical incision. Post operative pain was assessed by children and infants post operative pain scale (CHIPPS) hourly for 12 hours and time for first dose of rescue analgesic was recorded, sedation score and modified Bromage scale score for motor block was noted. Any side effects (headache, hypotension, bradycardia, respiratory depression, PONV, pruritis, postural hypotension) were noted.

The differences between mean values of both groups were analyzed using students test. For the known parametric data Kruskal Wallis test was used. The level of significance and α error were kept 95% and 5% respectively, for all statistical analysis p value <0.05 were considered as significant(s) and p value >0.05 as statistically non significant (ns).

RESULTS

All three groups were comparable with respect to age, sex ratio, weight, ASA physical status and duration of surgery. There was no statistical difference in baseline hemodynamic parameters. A gradual decline in mean BP was seen in all the three groups. However, the decline was <20%, hence statistically non significant (Table 1,2). The CHIPPS score for assessment of post operative pain were highest in plain levobupivacaine group as compared to levobupivacaine + iv clonidine group and least in levobupivacaine + caudal clonidine group for 1-12hours post operatively. Statistically analysis of CHIPPS for pain shows significant difference with (p<0.05) (table 4).

The mean duration of post operative analgesia was 342.8±110.6 min in group L and 461.4±125.6 min in group LC_{iv}, while it was 671.3±82.3 min in group LC_{cau}. The difference was highly significant (p value<0.01).

The mean rescue analgesic requirement was highest in group L (1.4±0.6). Significantly less rescue analgesics required in group LC_{cau} as compared to group LC_{iv}(0.1±0.3 v/s 0.9±0.3) p value <0.05(Table 5).

No significant statistical difference was seen in the trend of oxygen saturation among the groups (p >0.05).

No motor block was observed in any of the patients in the study (p>0.05).

The sedation score in all the three groups were comparable and no sedation was observed with the use of caudal / IV clonidine 2µg/kg. No statistical significant difference observed among the groups with regards to the mean sedation scores. (Table 3). Heart rate, systolic BP, diastolic BP, mean arterial pressure, oxygen saturation were comparable between groups and did not change significantly in intraoperative or post operative period. No adverse effects were encountered in either group of patients.

TABLE 1 (TREND OF HEART RATE)

	Group A(L)	Group B(Lccau)	Group C(LcIV)	p-Value b/w Gps			p-Value A v/s C			p-Value B v/s C		p-Value A v/c B	
	Mean	SD	p-Value	Mean	SD	p-Value	Mean	SD	p-Value				
Baseline	129.2	18.0		134.4	19.0		131.2	14.4		.507	0.6367	0.4704	0.2844
4min	127.2	17.6	0.3613	130.4	19.3	0.0991	128.7	14.3	0.1223	.771	0.7285	0.6995	0.5043
6min	126.8	16.4	0.3181	130.9	19.0	0.2305	127.7	15.7	0.0985	.631	0.8352	0.4836	0.3824
10min	125.9	17.5	0.1579	127.8	17.6	0.0329	126.0	14.7	0.0270	.882	0.9746	0.6691	0.6709
15min	124.0	17.9	0.0467	122.9	16.7	0.0010	124.6	15.7	0.0104	.921	0.8847	0.6798	0.8063
20min	116.2	17.3	0.0000	119.8	16.2	0.0001	121.1	16.4	0.0008	.505	0.2680	0.7585	0.4134
30min	112.9	16.6	0.0000	115.4	16.1	0.0000	117.1	16.7	0.0000	.607		0.6900	0.5503
45min	112.8	17.0		115.6	15.8		117.3	16.5		.571		0.6789	0.5207
60min	113.2	16.4		115.6	15.9		117.2	16.6		.630		0.6982	0.5669
75min	113.2	16.4		115.4	16.1		117.1	16.7		.654		0.6900	0.6018
At the end	113.3	16.3	0.0000	115.6	15.8	0.0000	117.3	16.5	0.0000	.634		0.6798	0.5872

TABLE 2 (TREND OF MAP)

	Group A(L)			Group B(Lccau)			Group C(LcIV)			p-Value b/w Gps	p-Value A v/s C	p-Value B v/s C	p-Value A v/c B
	Mean	SD	p-Value	Mean	SD	p-Value	Mean	SD	p-Value				
Baseline	79.9	11.3		76.1	13.4		79.5	13.8	0.0052	.462	0.8892	0.3438	0.2400
4min	69.9	8.3	0.0002	68.7	7.7	0.0037	72.1	13.7	0.0018	.423	0.4509	0.2359	0.5583
6min	72.3	8.1	0.0002	68.9	6.5	0.0036	71.0	14.1	0.0023	.422	0.6633	0.4594	0.0776
10min	67.8	8.2	0.0000	67.5	5.6	0.0009	70.8	13.8	0.0001	.372	0.3149	0.2441	0.8981
15min	67.3	7.3	0.0000	66.6	6.2	0.0003	69.4	12.7	0.0001	.485	0.4386	0.2944	0.7084
20min	66.9	6.3	0.0000	65.2	6.9	0.0001	69.2	13.1	0.0000	.264	0.4066	0.1528	0.3197
30min	65.9	6.1	0.0000	64.3	7.0	0.0001	68.6	13.2		.206	0.3173	0.1248	0.3564
45min	66.0	6.0		64.7	6.9		68.5	12.8		.257	0.3232	0.1575	0.4605
60min	63.2	6.4		63.7	8.0		67.9	12.5		.108	0.750	0.1262	0.8087
75min	63.0	5.8		64.0	5.4		67.9	11.8		.052	0.0454	0.1042	0.4850
At the end	65.8	6.1	0.0000	64.5	7.0	0.0001	67.5	13.0	0.0000	.448	0.5166	0.2679	0.4451

TABLE 3 (TREND OF SEDATION SCORE)

	Group A(L)		Group B(Lccau)		Group C(LcIV)		p-Value b/w	p-Value b/w	p-Value b/w	p-Value b/w
	Mean	SD	Mean	SD	Mean	SD				
Ene of surgery	5.0	0.0	5.0	0.0	5.0	0.0				
15min	2.6	1.3	2.9	0.8	2.7	1.1	.542	0.7441	0.4158	0.2772
30min	2.6	0.7	2.3	0.5	2.5	o.7	.182	0.5840	0.1908	0.0622
45min	2.0	0.2	2.0	0.0	2.2	0.3	.364	0.5616	0.1608	0.3256
1hr	2.0	0.0	2.0	0.0	2.0	0.0				
2hr	2.0	0.0	2.0	0.0	2.0	0.0				
3hr	2.0	0.0	2.0	0.0	2.0	0.0				
4hr	2.0	0.0	2.0	0.0	2.0	0.0				
5hr	2.0	0.0	2.0	0.0	2.0	0.0				
6hr	2.0	0.0	2.0	0.0	2.0	0.0				
7hr	2.0	0.0	2.0	0.0	2.0	0.0				
10hr	2.0	0.0	2.0	0.0	2.0	0.0				
12hr	2.0	0.0	2.0	0.0	2.0	0.0				

TABLE 4(TREND OF CHIPPS SCORE)

	Group A(L)		Group B(Lccau)		Group C(LcIV)		p-Value b/w Gps	p-Value A v/s C	p-Value B v/s C	p-Value A v/c B
	Mean	SD	Mean	SD	Mean	SD				
End of surgery	0.0	0.0	0.0	0.0	0.0	0.0				
15min	0.8	1.4	0.2	0.5	0.7	1.4	.070	0.7121	0.0543	0.0176
30min	0.3	0.7	0.1	0.4	0.5	1.0	.080	0.2374	0.0300	0.2842
45min	0.0	0.2	0.0	0.0	0.0	0.2	.608	1.0000	0.3256	0.3256
1hr	0.0000	0.0	0.0000	0.0	0.0000	0.0				
2hr	0.0000	0.0	0.0000	0.0	0.0000	0.0				
3hr	0.3333	0.8	0.0333	0.2	0.0333	0.2	0.36	0.0662	1.0000	0.0662
4hr	0.5333	1.0	0.0333	0.2	0.1667	0.7	.031	0.1231	0.3491	0.0145
5hr	0.6667	1.1	0.0000	0.0	0.3000	0.8	.005	0.1357	0.0476	0.0018
6hr	0.6000	0.9	0.0333	0.2	0.1667	0.4	.000	0.0152	0.0900	0.0012
7hr	0.5000	1.0	0.0000	0.0	0.4668	0.8	.022	0.8910	0.0041	0.0136
8hr	0.2333	0.6	0.0000	0.0	0.4333	0.8	.017	0.2762	0.0070	0.0323
9hr	0.8333	1.4	0.1333	0.3	0.4667	0.9	.021	0.2196	0.0563	0.0104
10hr	0.6667	1.2	0.0000	0.0	0.5667	1.2	.025	0.7544	0.0168	0.0063
11hr	0.6667	1.3	0.0000	0.0	0.1667	0.5	.005	0.0540	0.0573	0.0086
12hr	0.6000	1.4	0.0000	0.0	0.1667	0.7	.037	0.1427	0.2313	0.0264

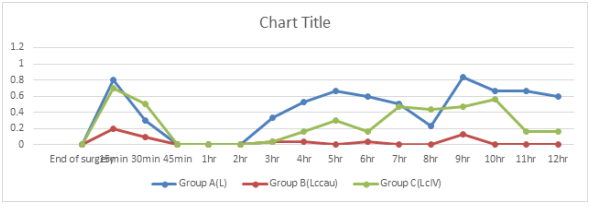

TABLE 5(Indicating the duration if surgery and analgesia and number of rescue analgesics)

	Group A(L)		Group B(Lccau)		Group C(LcIV)		P-Value b/w Gps	P-Value A v/s C	P-Value B v/s C	P-Value A v/s B
	Mean	SD	Mean	SD	Mean	SD				
Duration of surgery	40.0	16.1	44.0	19.4	45.5	19.4	.490	0.2376	0.7657	0.3877
Duration of analgesia	342.8	110.6	671.3	82.3	461.4	125.6	.000	0.0003	0.0000	0.0000
No of rescue analgesics	1.4	0.6	0.1	0.3	0.9	0.3	P<0.05	0.0010	0.0000	0.0000

DISCUSSION

The concept of postoperative pain relief and its utilization in the pediatric age group has improved dramatically over the recent years. Multimodal analgesia is proving to be effective mean of prevention and control of pain in all age groups. Presently techniques of co-analgesia are mainly based on four classes of analgesics, namely local anaesthetics, opioids, NSAID's and acetaminophen. As opioids pose the risk of respiratory depression, and oral medications after general anaesthesia may leads to vomiting and aspiration in children. A multimodal approach with inclusion of a regional technique is being preferred nowadays.

Caudal anaesthesia is one of the most popular and safe regional anaesthesia technique used in paediatric surgery to provide adequate intraoperative and postoperative analgesia. One of the major limitations of the single shot caudal block is relative shorter duration of analgesia; various additives such as morphine, fentanyl, tramadol, dexmedetomidine, clonidine with local anaesthetics have been used to increase the duration and quality of caudal block.

We inferred from this study that caudal clonidine prolonged the duration of postoperative analgesic effects of caudal levobupivacaine and reduced the requirement of rescue analgesics. The duration of analgesia in our study, after administration of caudal clonidine was recorded 671 minutes as compared to 461 minutes after intravenous clonidine. Similar findings were observed by **Bajwa et al.**,Singh J et al and Archana Koul et al., they all observed significant prolongation of postoperative analgesia duration after caudal administration of clonidine. This effect might be due to the spinal mode of action of caudal clonidine rather than its systemic absorption. However Jian –Ping Cao et al,found no difference in duration of analgesia, whether clonidine was administered by caudal or systemic route. This variability might be due to difference in doses of clonidine, local anaesthetics, use of various premedication and different scale of pain assessment.

Clonidine, an alpha-2 agonist has been shown to produce analgesia without causing significant respiratory depression after systemic, epidural or spinal administration in children.[21]Alpha-2 receptors are located primarily on afferent terminals centrally and peripherally, but are also found on the spinal cord and within brainstem nuclei known to be involved in analgesia, several studies suggest that clonidine's analgesic effects are more pronounced after neuraxial administration.[22]Still,the precise mechanism of action has not been completely clarified.

We observed that number of rescue analgesic requirement was least in caudal clonidine group, while maximum in plain levobupivacaine group,these findings are in accordance with studies done by Archana Koul et al. And Locatelli et al, while Jian –Ping Cao et al reported similar rescue analgesics requirement with systemic and caudal clonidine administration.

Systemic as well as caudal clonidine has been associated with sedation by causing stimulation of the locus ceruleus, a nucleus of the medulla involved in the sleep wake cycle. A delayed sedation after neuraxial administration of clonidine might be due to the cephalad migration of the drug in cerebrospinal fluid. Sedation is found to be favourable effect in children, as it reduces requirement of sedatives and anxiolytics in post operative period. In our study,the mean sedation scores were comparable in all three groups.Similar finding was observed by Archana Koul et al,they are concluded that no sedation was observed with the use of caudal clonidine 2mcg/kg.In our study all patients were stable haemodynamically and no incidence of untoward effects like pruritis,urinary retension and respiratory depression were reported.

CONCLUSION

Caudal clonidine with levobupivaicaine provided prolonged duration of postoperative analgesia as compared to intravenous clonidine with caudal levobupivacaine without causing any significant side effects in children undergoing subumbilical surgeries.

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