

## A prospective randomized double blind Study of the effects of caudal clonidine and dexmedetomidine as an adjunct to caudal bupivacaine for postoperative analgesia in paediatric patients undergoing subumbilical surgery.

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**Abstract:** In this study, we compared the analgesic efficacy and safety of caudal dexmedetomidine and clonidine added to caudal bupivacaine for postoperative analgesia in children undergoing subumbilical surgeries. 90 patients aged 1 to 8 years scheduled for subumbilical surgeries were randomly allocated into three groups of 30 patients each. Group A received 1ml/kg of 0.25% bupivacaine with dexmedetomidine 2µg/Kg in normal saline 1 ml. Group B received 1ml/kg of 0.25% bupivacaine with clonidine 2µg/Kg in normal saline 1 ml and Group C received 1ml/kg of 0.25% bupivacaine with normal saline 1ml. All the patients in our study remained hemodynamically stable throughout the intraoperative and postoperative period. Addition of either dexmedetomidine 2µg/kg or clonidine 2µg/kg to 0.25% caudal bupivacaine significantly prolonged the postoperative analgesia time without increasing the incidence of side effects like nausea, vomiting, pruritis or urinary retention. Moreover dexmedetomidine did not offer significant advantage over clonidine as regards the duration of postoperative analgesia.

**Keywords:** bupivacaine, caudal, clonidine and dexmedetomidine

### I. Introduction

Pain after surgery is inevitable. Relieving pain is one of the fundamental responsibilities of anesthesiologist. The density of nociceptive nerve endings in the skin of newborn infants is similar to or greater than that in adults. The provision of adequate analgesia is necessary after any surgery and it is all more important in children<sup>[1]</sup>. Caudal block has become the most popular regional anaesthetic technique for use in children. It provides excellent analgesia during surgery as well as during postoperative period in subumbilical surgeries in children<sup>[2]</sup>. A number of non-opioid additives have been suggested to increase the quality and duration of analgesia by local anesthetics. The various non opioid additives include ketamine, midazolam, neostigmine, clonidine and more recently dexmedetomidine<sup>[3, 4]</sup>. Alpha 2 adrenergic receptor agonists like clonidine and dexmedetomidine have relevant physiological properties causing sedation and analgesia, reducing plasma catecholamine levels, attenuating the stress response to surgery and preventing shivering through alpha 2 adrenoreceptors in central nervous system<sup>[5]</sup>. Dexmedetomidine is a highly selective  $\alpha_2$  adrenergic agonist. It has a  $\alpha_2/\alpha_1$  selectivity ratio of 1600:1 compared with clonidine which has  $\alpha_2/\alpha_1$  selectivity ratio of 200:1, making it a complete  $\alpha_2$  receptor agonist<sup>[6]</sup>. The mechanism of action of dexmedetomidine is unique and differs from those of currently used sedatives<sup>[7]</sup>.

The present study was undertaken to the analgesic efficacy and safety of caudal dexmedetomidine and clonidine added to caudal bupivacaine for postoperative analgesia in children undergoing subumbilical surgeries.

### II. Material and Methods

After obtaining approval from ethical committee of the institute and informed parental consent, 90 patients of physical status ASA I and II of either sex, aged 1 to 8 years scheduled for subumbilical surgeries were prospectively enrolled in this study. During the preoperative visit, all patients were evaluated and assessed. No premeditation was given to any patient. In the operation theatre after connecting the patient to the monitors, an intravenous line was established. General anaesthesia was induced with standard doses of thiopental (4 to 6mg/kg) + Atracurium (0.5 mg/kg) to facilitate intubation and maintained with 0.5% to 1% of halothane and 66% Nitrous oxide in combination with 33% of oxygen, administered via laryngeal mask airway (LMA) or endotracheal tube. Muscle relaxation was achieved by the use of top up doses of atracurium. No intravenous or per rectal analgesic drugs were given to any patient intra operatively. Patients were randomly allocated into three groups of 30 patients each.

Group A received 1ml/kg of 0.25% bupivacaine with dexmedetomidine 2µg/Kg in normal saline 1 ml.  
 Group B received 1ml/kg of 0.25% bupivacaine with clonidine 2µg/Kg in normal saline 1 ml  
 Group C received 1ml/kg of 0.25% bupivacaine with normal saline 1ml.

The study drugs were prepared by an anesthesiologist who was not involved in the study. All study drugs were kept at room temperature and used within 30 minutes of preparation.

After induction of anaesthesia, patients were placed in lateral decubitus position. A short beveled 23 Gauge hypodermic needle was introduced in caudal epidural space under full aseptic precautions; single dose caudal block was performed. Skin incision was allowed after 15 minutes of caudal block. The aim was to record the blood pressure and heart rate just before and after surgical incision and then every five minutes till the end of surgery. An increase in systolic blood pressure and heart rate >15% of preincisional values was considered as failed block and rescue analgesia in the form of fentanyl 1-5 µg/kg bodyweight intravenously was administered and these cases were eliminated from the study. At the end of surgery, residual neuromuscular blockade was reversed with appropriate doses of neostigmine and atropine and patients were transferred to postoperative care unit (PACU). In the PACU, patients were monitored for one hour and following parameters were recorded at 30 minute interval: Heart rate, Systolic non-invasive blood pressure, Oxygen saturation (SpO<sub>2</sub>%). Patients were also assessed for pain at 30 minute interval upto one hour in PACU by using FLACC pain scale scoring.

**The FLACC Pain Scale**

Categories	Scoring		
	0	1	2
Face	Smile or no particular expression	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consol ability	Content, relaxed	Reassured by occasional touching, hugging or talking to, distractible	Difficult to console

This scale is used for assessment of pain in children. There are five parameters in this scale, each given a score of 0 – 2. Total score was taken to assess the pain.

Severity of pain	Pain Score
No pain	0
Mild pain	1-3
Moderate pain	4-7
Severe pain	8-10

After discharge from PACU, patients were again assessed for pain at 2 hours, 4 hours and at 6 hours and then every four hourly for 18 hours and then at 24 hours of postoperative period by ward nurse who was unaware of the caudal treatment received by the patients. The time from arrival in PACU to first time the FLACC score was ≥4, was recorded and noted as the duration of adequate caudal analgesia. Rescue analgesia was given in the form of rectal paracetamol (20mg/ kg/dose) if pain score was ≥4. The number of doses of rescue medication required and the time of first administration of rescue medication was also noted in all the three groups.

After completion of study the data was analyzed using SPSS version 17.0 computer software. Numerical variables were presented as mean and standard deviation (SD) and categorical variables were presented as percentages. One - way ANOVA was used for between – group comparisons of numerical variables. Chi square test was used for between – group comparisons of categorical variables. Student’s ‘t’ test was also used for analysis of difference of means for quantitative data. The tests were referenced for p values for their significance. Any P-value less than 0.05 (p < 0.05) was taken as statistically significant.

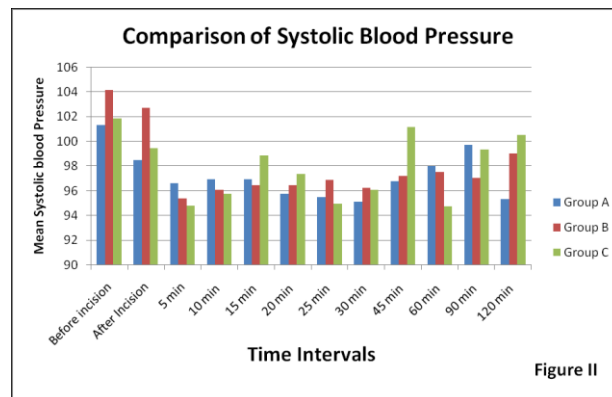
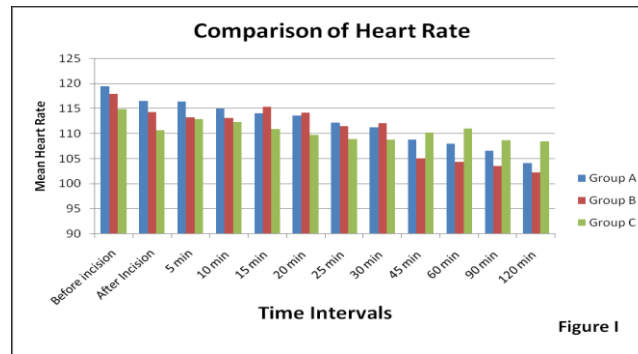
### III. Results

90 patients were recruited in the study. All the groups were comparable with respect to age, body weight and duration of surgery. The three groups were comparable with regard to baseline hemodynamic variables. (TABLE 1)

**Table – 1: Demographic data and baseline Hemodynamic parameters**

Parameter	Group A Mean± SD	Group B Mean± SD	Group C Mean± SD	P value
Age (years)	5.0±2.14	4.3±2.16	3.7±2.5	0.082 (NS)
Weight (kgs)	17.76±3.98	17.73±5.66	15.17±6.5	0.102 (NS)
Duration of Surgery (min)	39.0±7.6	38.0±7.8	39.0±9.43	0.58 (NS)
Heart Rate (beats/min.)	117.23±10.12	114.66±10.7	113.33±12.27	0.421(NS)
Systolic Blood Pressure (mmHg)	104.43±10.74	102.66±10.36	105.03±9.55	0.561(NS)

In the study, hemodynamic effects with regards to heart rate and systolic blood pressure showed a benign profile and no clinically relevant change was observed in these variables at various study stages. (Figure I and Figure II)



The two groups( Group A & Group C )did not differ significantly on statistical analysis upto 4 hours of postoperative period with reference to total pain scores achieved at different postoperative intervals when assessed at 30 minutes, 1 hour, 2 hours and at 4 hours of postoperative period ( $p > 0.05$ ). None of the patients in two groups had moderate or severe pain i.e. FLACC score  $\geq 4$  upto 4 hours. The two groups when compared with reference to total pain scores, the difference was found to be statistically significant ( $p < 0.05$ ). (TABLE 2)

**Table – 2: Comparison of FLACC scores at various intervals in Postoperative period between Dexmedetomidine + Bupivacaine (Group A) and Bupivacaine (Group C)**

		Group A		Group C		p value	χ <sup>2</sup>
		N	%	n	%		
30 min FLACC	No pain	23	76.66	22	73.33	0.766	0.08
	Mild pain	7	23.33	8	26.66		
	Moderate pain	0	0.00	0	0.00		
1 hour FLACC	No pain	10	33.33	9	30.00	0.781	0.077
	Mild pain	20	66.66	21	70.00		
	Moderate pain	0	0.00	0	0.00		
2 hour FLACC	No pain	9	30.00	6	20.00	0.37	0.8
	Mild pain	21	70.00	24	80.00		
	Moderate pain	0	0.00	0	0.00		
4 hour FLACC	No pain	5	16.66	3	10.00	0.44	0.56
	Mild pain	25	83.33	27	90.00		
	Moderate pain	0	0.00	0	0.00		
6 hour FLACC	No pain	4	13.33	3	10.00	0.02	7.10
	Mild pain	19	63.33	10	33.33		
	Moderate pain	7	23.33	17	56.66		
10 hour FLACC	No pain	3	10.00	1	3.33	0.03	6.85
	Mild pain	18	60.00	10	33.33		
	Moderate pain	9	30.00	19	63.33		
14 hour FLACC	No pain	0	0.00	0	0.00	0.03	4.34
	Mild pain	17	56.66	9	30.00		
	Moderate pain	13	43.33	21	70.00		
18 hour FLACC	No pain	0	0.00	0	0.00	0.03	4.44
	Mild pain	16	53.33	8	26.66		
	Moderate pain	14	46.66	22	73.33		
24 hour FLACC	No pain	0	0.00	0	0.00	0.39	0.73
	Mild pain	20	66.66	23	76.66		
	Moderate pain	10	33.33	7	23.33		

No pain = FLACC 0; Mild pain = FLACC 1-3; Moderate pain = FLACC 4-7; n = Number of patients; % = Percentage

The FLACC score between groups B and C did not differ significantly on statistical analysis upto 4 hours of postoperative period with reference to total pain scores achieved at different postoperative intervals when assessed at 30 minutes, 1 hour, 2 hours and at 4 hours of postoperative period ( $p > 0.05$ ). None of the patients in two groups had moderate or severe pain i.e. FLACC score  $\geq 4$  upto 4 hours. The two groups when compared with reference to total pain scores, the difference was found to be statistically significant ( $p < 0.05$ ). (TABLE 3)

**Table – 3: Comparison of FLACC scores at various intervals in Postoperative period Between Clonidine + Bupivacaine (Group B) and Bupivacaine alone (Group C)**

		Group B		Group C		p value	χ <sup>2</sup>
		N	%	n	%		
30 min FLACC	No pain	23	76.66	22	73.33	0.76	0.08
	Mild pain	7	23.33	8	26.66		
	Moderate pain	0	0.00	0	0.00		
1 hour FLACC	No pain	8	26.66	9	30.00	0.77	0.08
	Mild pain	22	73.33	21	70.00		
	Moderate pain	0	0.00	0	0.00		
2 hour FLACC	No pain	7	23.33	6	20.00	0.75	0.08
	Mild pain	23	76.66	24	80.00		
	Moderate pain	0	0.00	0	0.00		
4 hour FLACC	No pain	7	23.33	3	10.00	0.16	0.18
	Mild pain	23	76.66	27	90.00		
	Moderate pain	0	0.00	0	0.00		

6 hour FLACC	No pain	2	6.66	3	10.00	0.02	7.10
	Mild pain	21	70.00	10	33.33		
	Moderate pain	7	23.33	17	56.66		
10 hour FLACC	No pain	2	6.66	1	3.00	0.05	5.3
	Mild pain	18	60.00	10	33.33		
	Moderate pain	10	33.33	19	63.33		
14 hour FLACC	No pain	0	0.00	0	0.00	0.049	3.26
	Mild pain	16	53.33	9	30.00		
	Moderate pain	14	46.66	21	70.00		
18 hour FLACC	No pain	0	0.00	0	0.00	0.49	3.26
	Mild pain	15	50.00	8	26.66		
	Moderate pain	15	50.00	22	73.33		
24 hour FLACC	No pain	0	0.00	0	0.00	0.55	0.34
	Mild pain	21	70.00	23	76.66		
	Moderate pain	9	30.00	7	23.33		

No pain = FLACC 0; Mild pain = FLACC 1-3; Moderate pain = FLACC 4-7; n = Number of patients; % = Percentage

The two groups( Group A & Group B) were compared with reference to total pain scores at various intervals postoperatively i.e. at 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 10 hours, 14 hours, 18 hours and at 24 hours as depicted in the table (TABLE 4). The difference between the two groups at all these intervals was found to be statistically insignificant ( $p > 0.05$ ), showing that the two groups were having similar quality of pain relief when compared at various intervals in the postoperative period.

**Table – 4: Comparison of FLACC scores at various intervals in Postoperative period Between Dexmedetomidine + Bupivacaine (Group A) and Clonidine + Bupivacaine (Group B)**

	Group A		Group B		p value	$\chi^2$	
	N	%	n	%			
30 min FLACC	No pain	23	76.66	23	76.66	1.00	0.0 0
	Mild pain	7	23.33	7	23.33		
	Moderate pain	0	0.00	0	0.00		
1 hour FLACC	No pain	10	33.33	8	26.66	0.57	0.3 1
	Mild pain	20	66.66	22	73.33		
	Moderate pain	0	0.00	0	0		
2 hour FLACC	No pain	9	30.00	7	23.33	0.55	0.3 0
	Mild pain	21	70.00	23	76.66		
	Moderate pain	0	0.00	0	0.00		
4 hour FLACC	No pain	5	16.66	7	23.33	0.51	0.4 0
	Mild pain	25	83.33	23	76.66		
	Moderate pain	0	0.00	0	0.00		
6 hour FLACC	No pain	4	13.33	2	6.66	0.68	0.7 6
	Mild pain	19	63.33	21	70.00		
	Moderate pain	7	23.33	7	23.33		
10 hour FLACC	No pain	3	10.00	2	6.66	0.88	0.2 5
	Mild pain	18	60.00	18	60.00		
	Moderate pain	9	30.00	10	33.33		
14 hour FLACC	No pain	0	0.00	0	0.00	0.79	0.0 6
	Mild pain	17	56.66	16	53.33		
	Moderate pain	13	43.33	14	46.66		
18 hour FLACC	No pain	0	0.00	0	0.00	0.79	0.0 6
	Mild pain	16	53.33	15	50.00		
	Moderate pain	14	46.66	15	50.00		
24 hour FLACC	No pain	0	0.00	0	0.00	0.78	0.0 7
	Mild pain	20	66.66	21	70.00		
	Moderate pain	10	33.33	9	30.00		

No pain = FLACC 0; Mild pain = FLACC 1-3; Moderate pain = FLACC 4-7; n = Number of patients; % = Percentage

When groups A and C were compared, the difference in the mean duration of postoperative analgesia between the two groups was found to be statistically significant ( $p < 0.05$ ). Similarly, when the groups B and C were compared, the difference between the mean duration of postoperative analgesia was found to be statistically significant between the two groups ( $p < 0.05$ ). However, the difference in the mean duration of postoperative analgesia was found to be statistically insignificant when group A was compared to group B ( $p > 0.05$ ). (TABLE 5)

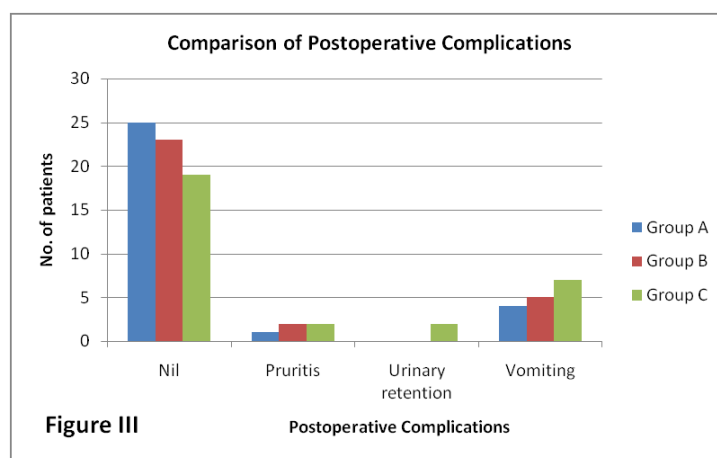
**Table – 5: Comparison of Mean Duration of Postoperative Analgesia between the Three Studied Groups**

Group	Mean	Minimum	Maximum
A	14.43±2.58	10.00	18.00
B	13.53±2.01	10.00	18.00
C	6.06±1.85	4.00	10.00

P - value:	A vs. C	0.0001
	B vs. C	0.0001
	A vs. B	0.137

Group A = Dexmedetomidine + Bupivacaine; Group B = Clonidine + Bupivacaine; Group C = Bupivacaine alone

The three groups were compared for postoperative complications and the difference between the groups was found to be statistically insignificant ( $p > 0.05$ ). (Figure III)



#### IV. Discussion

Caudal block is one of the most common regional anaesthetic technique used in children. It is considered safe and simple procedure but its main disadvantage is its relatively short duration of action even with use of long acting agents such as bupivacaine<sup>[8]</sup>. The successful use of epidural clonidine in adults leads to its evaluation in paediatric caudal block. The resulting studies have consistently shown caudal clonidine to increase the duration of postoperative analgesia.<sup>[9,10]</sup> On the other hand dexmedetomidine compared to clonidine is much more selective alpha-2 adrenoreceptor agonist which might permit its application in relatively high doses for sedation and analgesia without unwanted vascular effects from activation of alpha-1 receptors.<sup>[11]</sup>

All the three groups were homogenous with reference to age, sex, body weight and duration of surgery and anaesthesia. Mean age of patients was  $5.0 \pm 2.14$  years in group A,  $4.3 \pm 2.6$  years in group B and  $3.7 \pm 2.5$  years in group C respectively. Mean weight of patients was  $17.7 \pm 3.9$  kgs in group A,  $17.7 \pm 5.6$  kgs in group B and  $15.1 \pm 6.5$  kgs in group C respectively.

Heart rate, systolic blood pressure and oxygen saturation ( $SpO_2\%$ ) by pulse oximetry were recorded at various intervals in perioperative period starting from baseline values upto the time when the patients were discharged from recovery room. The groups when compared with reference to mean heart rate and mean systolic blood pressure at various intervals perioperatively, the difference was found to be statistically insignificant ( $p$  value  $> 0.05$ ). None of the patients in any group developed bradycardia (heart rate  $< 60$ /min) or hypotension (systolic arterial pressure  $< 70$  + twice the age in years associated with altered peripheral perfusion). No significant respiratory depression was reported in any patient in this study and none of the patients had a  $SpO_2$  value of  $< 95\%$  on pulse oximetry).

Our observations correlate with Klimsha et al<sup>[12]</sup> who found no significant hemodynamic effects in their patients receiving either 1 or  $2 \mu\text{g}/\text{kg}$  of caudal clonidine. A.M. El-Hennawy et al<sup>[13]</sup> also found no significant difference in the magnitude of hemodynamic changes in perioperative period when either dexmedetomidine  $2 \mu\text{g}/\text{kg}$  or clonidine  $2 \mu\text{g}/\text{kg}$  was added to caudal bupivacaine 0.25% in paediatric patients undergoing subumbilical surgeries.

Quality of postoperative analgesia was assessed by using FLACC pain scale scoring at 30 minutes interval upto 1 hour in the recovery room, thereafter at 2 hours, 4 hours, 6 hours and subsequently every 4 hourly upto 18 hours and then at 24 hours of postoperative period.

We found from our observation that upto 4 hours of postoperative period all the patients in our study had adequate caudal analgesia (FLACC score < 4). Subsequently the number of patients with adequate caudal analgesia declined in all the three groups but the decline was more rapid in group C as compared to group A or B. Group C patients achieved significantly higher FLACC scores compared to groups A and B.

Our results are in correlation with the study conducted the A.M. El-Hennawy [13] who in their study observed better quality of analgesia in groups receiving either dexmedetomidine or clonidine combined with bupivacaine compared to groups receiving 0.25% bupivacaine alone.

Duration of postoperative analgesia (time of maintaining adequate caudal analgesia FLACC <4) was 14.4±2.5 hour in group A, 13.5±2.6 hour in group B and 4.6±1.8 hour in group C. When group C was compared to group A or group B with reference to postoperative analgesia time it was found that the mean duration of postoperative analgesia was shorter in group C as compared to group A or group B and the difference was found to be statistically significant (p < 0.05). However the difference between group A and B was found to be statistically insignificant (p > 0.05).

Our results are similar to the study of I. Saadawy et al [14] who reported longer duration of postoperative analgesia and better quality of sleep after administration of caudal dexmedetomidine (2 µg/kg) plus bupivacaine (0.25%) as compared when bupivacaine (0.25%) was given alone. This was confirmed by longer interval to first request of rescue analgesics and significantly lowers consumption of rescue analgesics in postoperative period.

In our study we observed that during 24 hour of postoperative period 21 patients in group C received rescue analgesic doses as compared to 8 patients in group A and 10 patients in group B. It was observed that analgesic requirement in group C was significantly higher as compared to groups A and B and the difference was found to be statistically significant (p < 0.05). However the difference in the requirement of rescue analgesics was insignificant between groups A and B.

Our results are in correlation with the study of A.M. El-Hennawy [13] who observed less use of analgesics in postoperative period in groups receiving either caudal dexmedetomidine or clonidine combined with bupivacaine in comparison with the group receiving bupivacaine alone.

The incidence of postoperative complications like nausea, vomiting, and urinary retention was comparable between the groups in our study (p > 0.05). Aruna Parameswari et al [15] also observed that no significant increase in incidence of pruritis, urinary retention after administration of caudal clonidine with bupivacaine 0.25%.

In conclusion we found that the addition of both dexmedetomidine and clonidine offered better quality of postoperative analgesia as compared to bupivacaine alone. Moreover dexmedetomidine did not offer significant advantage over clonidine as regards the duration of postoperative analgesia.

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