Comparative Study between Dexmedetomidine versus Nalbuphine as an Adjuvant to Bupivacaine in Caudal Anesthesia in Children undergoing Inguinal Hernia Repair Surgery

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Abstract: Background: Anesthesia primarily aims to relief patient's pain, agony and discomfort associated with the surgical procedure. Postoperative pain control is a cornerstone in management of anesthesia, various methods are used to control postoperative pain in children, one of the most reliable, popular and safe techniques is the caudal block which provides proper analgesia for lower abdominal surgical procedures with one disadvantage which is the short lived duration of action of the single shot caudal block. **Objectives:** The aim of this the study is to compare the efficacy of adding dexmedetomidine versus nalbuphine to local anesthetic in children undergoing inguinal hernia repair surgery. **Patients and methods:** After obtaining informed written consent from parents or guardian, and obtaining approval from Research Ethics Committee of anesthesiology department, the study was conducted in Nasser institute for research and treatment hospital. This prospective randomized controlled, double blind clinical trial was conducted on 60 patients were randomly divided into 2 study groups as simple randomization by computer-generated random numbers. Each group contains 30 patients: ***Group D*** (Dexmedetomidine group): Bupivacaine+ Dexmedetomidine, ***group N*** (Nalbuphine group): Bupivacaine + Nalbuphine. **Results:** There was no significant difference in the two groups with regard to age and sex. The mean age was 4.23±1.50 years in Group N and 4.17±1.53 years in Group D. In both the groups' males were more, this could be due to inclusion of surgery. Regarding heart rate and blood pressure, all the patients were monitored at regular intervals. The mean baseline heart rate was similar in both groups before the administration of caudal block. The mean baseline rate was 124.10±3.5 beats per minute in Group N and 123.90±3.4 beats per minute in Group D. There was significant fall in heart rate after caudal by 20 minutes which showed 114.60±2.62 beats per minute in Group N and 112.30±3.58 beats per minute in Group D. This fall in heart rate continued until end of surgery without clinical significance. **Conclusion:** The results of this clinical trial had demonstrated that addition of dexmedetomidine to caudal local anesthetic bupivacaine produced longer duration of postoperative analgesia in pediatric patients undergoing inguinal hernia repair surgery than in nalbuphine group with no side effects.

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1. Introduction

Anesthesia primarily aims to relief patient's pain, agony and discomfort associated with the surgical procedure.

Postoperative pain control is a cornerstone in management of anesthesia, various methods are used to control postoperative pain in children, one of the most reliable, popular and safe techniques is the caudal block which provides proper analgesia for lower abdominal surgical procedures with one disadvantage which is the short lived duration of action of the single shot caudal block ***(Lloyd and Thomas, 1990).***

Various adjuvants have been used to prolong the duration of action of the single shot caudal block, such as opioids, ketamine and α2 agonists ***(Vetter et al., 2007).***

Dexmedetomidine (DEX) is a selective α2 adrenergic agonist with analgesic and anxiolytic properties, it is a safe and effective adjuvant to many anesthetic techniques such as intrathecal or epidural ***(Carollo et al., 2008).***

Its effects are resulting from activation of α2 adrenergic receptors, and depending on their location; their stimulation in the central nervous system (CNS) result in inhibition of calcium influx in the nerve terminals with subsequent inhibition of the neurotransmitter release thus facilitating analgesia ***(Haselman, 2008).***

Nalbuphine is a mixed κ-agonist and μ-antagonist opioid of the phenanthrene group; it is related in its chemical structure to the opioid antagonist naloxone and oxymorphone. It leads to stimulation of spinal and supraspinal opioid receptors

which leads to good analgesia with minimal sedation, minimal nausea and vomiting, less respiratory depression and stable cardiovascular functions ***(De Souza et al., 1988).***

Its safety and efficacy has been established in the clinical field and its safety and efficacy also established via the epidural route ***(Wang et al., 1988).***

Nalbuphine being an agonist antagonist opioid is less likely to cause side effects such as pruritus, respiratory depression, urinary retention, excessive sedation, because of its action at kappa receptors.

The aim of this trial was to compare the duration of post-operative analgesia, sedation and any side effects of single shot caudal epidural dexmedetomidine versus nalbuphine mixed with bupivacaine in children undergoing hernia repair.

Aim of the Study

The aim of this the study is to compare the efficacy of adding dexmedetomidine versus nalbuphine to local anesthetic in children undergoing inguinal hernia repair surgery.

Patients and Methods

After obtaining informed written consent from parents or guardian, and obtaining approval from Research Ethics Committee of anesthesiology department, the study was conducted in Nasser institute for research and treatment hospital. This prospective randomized controlled, double blind clinical trial was conducted on 60 patients were randomly divided into 2 study groups as simple randomization by computer-generated random numbers. Each group contains 30 patients:

Group D (Dexmedetomidine group): Bupivacaine+ Dexmedetomidine.

Group N (Nalbuphine group): Bupivacaine + Nalbuphine.

Inclusion criteria:

- American Society of Anesthesiology grade I, II (ASA I-II).
- Patients of either sex.
- Aged 2-6 years old.
- Normal CBC and coagulation profile.
- Scheduled for inguinal hernia repair surgery not exceeding 2 hours.

Exclusion criteria:

- Local infection at the site of puncture.
- Patient refusal (parental or guardian consent).
- Patients having any neurologic deficit.
- Patients having history of hematological disorders, including coagulation abnormality.
- Patients with severe hepatic impairment.
- Patients with severe cardiac or respiratory system affection.
- Patient has a known allergy to study drug or additions.
- Congenital abnormality of the sacrum.

Patient preparation:

Routine preoperative investigations including complete blood picture, renal function tests, liver function tests and coagulation profile were done. All patients were fasting according ASA guidelines; 2 hours for clear fluids, 4 hours for breast milk and 6 hours for milk formula or light meals. Also, all patients were premedicated with oral midazolam 0.5 mg/kg on 20 ml clear juice 20 minutes pre-operatively. Standard monitoring devices including electrocardiogram, finger tip pulse oximetry, and non-invasive blood pressure (NIBP) used to measure the hemodynamic variability.

Anesthetic technique:

On arrival to the operating room, continuous monitoring with ECG, non-invasive blood pressure and pulse oximetry were started. Baseline mean arterial blood pressure, heart rate and arterial oxygen saturation were recorded.

Then general anesthesia were induced by using inhalation of 8% sevoflurane in 100% oxygen, intravenous line were inserted and tracheal intubation by appropriate size endotracheal tube were facilitated by intravenous atracurium 0.5 mg/kg. Anesthesia were maintained using 2% isoflurane in 50% oxygen and 50% air with controlled mechanical ventilation to keep end tidal carbon dioxide between 30-35 mmHg. Thereafter, patients were positioned in a lateral decubitus and under complete aseptic technique caudal injection were done using 25 G needle, proper placement of the needle was confirmed by whooshing test ***(Lewis et al., 1992)***. After negative aspiration for blood or cerebrospinal fluid; patients of group (D) were received dexmedetomidine (Precedex 100 µg/ml, Hospira®) 2 µg/kg in 1ml/kg plain bupivacaine 0.25% maximum volume 20 ml and patients of group (N) were received nalbuphine (Nalufin® ampoules 20 mg/ml, Amoun pharmaceutical, Egypt) 0.2 mg/kg in 1ml/kg plain bupivacaine 0.25% maximum volume 20 ml. the caudal block were performed by anesthetist who was blinded to the drug given.

After 15 minutes from caudal anesthesia If tachycardia occurred > 20% of baseline, we consider failed block and we were given fentanyl intra venous 2 µg/kg. Mean arterial blood pressure (MAP), heart rate (HR) and oxygen saturation (SpO2) were documented at baseline, after induction, immediately after caudal anesthesia and every 5 minutes for the first 20 minutes then every 10 minutes thought the procedure till the end of surgery.

By the end of surgery inhalational anesthesia were discontinued and the residual muscle relaxant effect were antagonized with neostigmine 0.05 µg/kg, given with atropine 0.02 mg/kg, and the endotracheal tube were removed after return of his spontaneous

breathing and opening his eyes then the patient were transferred to the post anesthesia care unit (PACU), all care givers; anesthetist, surgeon, PACU nurse, as well as patients' parents or guardians were unaware of caudal drug given. In the PACU, pain scores were evaluated by the "Face, Leg, Activity, Cry, Consolability" FLACC pain scale ***(Merkel et al., 2010)***; FLACC pain scale is a measurement used to assess pain in children between the ages of 2 months and 7 years or in individuals who are unable to communicate their pain. The scale is scored in a range of 0–10, with 0 representing no pain while 10 is the worst pain. This was done immediately after recovery and every half an hour for 6 hours. The scale has five criteria, which are each assigned a score of 0, 1 or 2.

Instructions

Patients who are awake:

- Observe for at least 2-5 minutes.
- Observe legs and body uncovered.
- Reposition patient or observe activity; assess body for tenseness and tone.
- Initiate consoling interventions if needed.

Patients who are asleep:

- Observe for at least 5 minutes or longer.
- Observe body and legs uncovered.
- If possible reposition the patient.
- Touch the body and assess for tenseness and tone.

Each category is scored on the 0-2 scale which results in a total score of 0-10.

Assessment of Behavioral Score:

0 = Relaxed and comfortable

1-3 = Mild discomfort

4-6 = Moderate pain

7-10 = Severe discomfort/pain

(Voepel-Lewis et al., 2010)

Others were noted:-

- Whenever pain score > 4 a rescue analgesic will be given (paracetamol 10 ml/kg IV).
- Time to first request of analgesia.
- Total analgesic requested.
- Any side effects such as nausea and vomiting, hypotension (MAP 20% decrease from baseline), bradycardia (HR 20% decrease from baseline) and respiratory depression (SpO2 < 92%) were also evaluated and recorded. The primary outcome was the time to first analgesic request (i.e. pain score <4), the secondary outcome was to assess FLACC score, hemodynamic and demographic data.

Statistical Analysis:

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 22. P-values less than 0.05 were considered as statistically significant.

3. Results

Table (1) shows no statistical significant difference **(p-value > 0.05)** between studied groups as regard age.

Table (2) shows no statistical significant difference **(p-value > 0.05)** between studied groups as regard sex.

Table (1): Comparison between studied groups as regard age.

		Nalbuphine (N = 30)	Dexmedetomidine (N = 30)	P-value
Age (years)	**Mean**	4.23	4.17	0.9
	±SD	1.50	1.53	

Table (2): Comparison between studied groups as regard sex.

		Nalbuphine (N = 30)	Dexmedetomidine (N = 30)	P-value
Sex	**Male**	17 (56.7%)	19 (63.3%)	0.6
	Female	13 (43.3%)	11 (36.7%)	

Table (3): Comparison between studied groups as regard intra-operative heart rate (HR).

		Nalbuphine (N = 30)	Dexmedetomidine (N = 30)	P-value	
Baseline	**Mean ±SD**	124.10 3.5	123.90 3.4	0.8	NS
After induction	**Mean ±SD**	123.8 3.7	123.6 3.9	0.8	NS
After caudal	**Mean ±SD**	123.5 4.4	123.1 4.1	0.7	NS
HR 5	**Mean ±SD**	122.3 2.9	122 3.1	0.7	NS
HR 10	**Mean ±SD**	121.1 3.8	120.8 4.0	0.8	NS

HR 15	**Mean ±SD**	118.7 5.1	117.9 3.6	0.5	NS
HR 20	**Mean ±SD**	114.60 2.62	112.30 3.58	**0.02****	**S**
HR 30	**Mean ±SD**	113.70 3.25	109.9 3.47	**0.002****	**S**
HR 40	**Mean ±SD**	111.60 2.54	109.8 2.40	**0.007****	**S**
HR 50	**Mean ±SD**	109.90 3.23	107.7 1.88	**0.002****	**S**
HR 60	**Mean ±SD**	108.70 3.19	106.10 2.43	**0.002****	**S**
HR 70	**Mean ±SD**	105.60 2.04	103.80 1.97	**0. 01****	**S**
HR 80	**Mean ±SD**	103.70 1.99	102.30 2.09	**0. 01****	**S**

p-value > 0.05 is considered non statistical significant (NS).
**: p-value < 0.05 is considered significant (S).

This table shows statistical significant decrease in intra-operative heart rate (**p-value < 0.05)** in Group D than Group N at (20, 30, 40, 50, 60, 70 and 80 min) and no statistical significant difference **(p-value > 0.05)** between studied groups as regard intra-operative heart rate at (baseline, after induction, after caudal, 5, 10 and 15 min).

Table (4): Comparison between studied groups as regard intra-operative mean arterial blood pressure (MAP).

		Nalbuphine (N = 30)	**Dexmedetomidine (N = 30)**	**P-value**	
Baseline	**Mean ±SD**	88.70 3.16	88.50 2.53	0.9	NS
After induction	**Mean ±SD**	88.50 4.26	88.20 3.73	0.9	NS
After caudal	**Mean ±SD**	88.30 2.26	87.90 2.73	0.8	NS
MAP 5	**Mean ±SD**	86.50 3.26	85.90 2.63	0.8	NS
MAP 10	**Mean ±SD**	83.00 3.86	82.8 3.06	0.9	NS
MAP 15	**Mean ±SD**	82.20 5.22	81.90 3.37	0.7	NS
MAP 20	**Mean ±SD**	81.70 5.66	80.00 2.19	**0.03****	**S**
MAP 30	**Mean ±SD**	81.40 4.62	79.10 2.71	**0.01****	**S**
MAP 40	**Mean ±SD**	80.00 3.34	78.70 2.77	**0.007****	**S**
MAP 50	**Mean ±SD**	79.90 2.16	78.60 2.81	**0.001****	**S**
MAP 60	**Mean ±SD**	79.70 3.19	78.50 2.57	**0.04****	**S**
MAP 70	**Mean ±SD**	79.50 3.67	78.10 1.92	**0.03****	**S**
MAP 80	**Mean ±SD**	78.40 3.28	77.60 1.83	**0.03****	**S**

p-value > 0.05 is considered non statistical significant (NS).
**: p-value < 0.05 is considered significant (S).

This table shows statistical significant decrease in mean intra-operative blood pressure (**p-value < 0.05)** in Group D than Group N at (20, 30, 40, 50, 60, 70 and 80 min) and no statistical significant difference **(p-value > 0.05)** between studied groups as regard

mean intra-operative blood pressure at (baseline, after induction, after caudal, 5, 10 and 15 min).

Table (5): Comparison between studied groups as regard intra-operative SPO2.

		Nalbuphine (N = 30)	Dexmedetomidine (N = 30)	P-value	
Baseline	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
After induction	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
After caudal	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
SPO2 0	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
SPO2 5	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
SPO2 10	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
SPO2 15	**Mean ±SD**	99.00 0.00	99.00 0.00	1	**NS**
SPO2 20	**Mean ±SD**	99.00 0.00	99.00 0.00	1	**NS**
SPO2 30	**Mean ±SD**	99.00 0.00	99.00 0.00	1	**NS**
SPO2 40	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
SPO2 50	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
SPO2 60	**Mean ±SD**	98.90 0.31	98.90 0.31	1	**NS**
SPO2 70	**Mean ±SD**	99.00 0.00	99.00 0.00	1	**NS**
SPO2 80	**Mean ±SD**	99.00 0.00	99.00 0.00	1	**NS**

This table shows no statistical significant difference **(p-value > 0.05)** between studied groups as regard intra-operative SPO2.

Table (6): Comparison between studied groups as regard post-operative heart rate (HR).

		Nalbuphine (N = 30)	Dexmedetomidine (N = 30)	P-value	
HR 0	**Mean ±SD**	101.00 3.84	100.30 2.67	**0.002****	**S**
HR 30	**Mean ±SD**	101.20 3.84	100.400 2.67	**0.03****	**S**
HR 1	**Mean ±SD**	101.30 4.96	100.50 3.00	**0.03****	**S**
HR 1.5	**Mean ±SD**	101.30 4.12	100.70 2.81	**0.02****	**S**
HR 2	**Mean ±SD**	101.40 4.12	100.90 2.80	**0.04****	**S**
HR 2.5	**Mean ±SD**	101.70 3.84	101.10 2.23	0.9	**NS**
HR 3	**Mean ±SD**	101.80 4.22	101.30 3.46	0.8	**NS**
HR 3.5	**Mean ±SD**	101.90 3.50	101.50 3.47	0.8	**NS**
HR 4	**Mean ±SD**	102.30 2.95	101.70 3.68	0.9	**NS**
HR 4.5	**Mean ±SD**	102.50 2.89	101.80 4.05	0.7	**NS**
HR 5	**Mean ±SD**	102.80 2.57	102.40 3.76	0.9	**NS**
HR 5.5	**Mean ±SD**	103.80 2.52	102.90 3.02	0.6	**NS**
HR 6	**Mean ±SD**	103.90 2.69	103.00 2.37	0.8	**NS**

p-value > 0.05 is considered non statistical significant (NS). **: p-value < 0.05 is considered significant (S).

This table shows no statistical significant decrease in post-operative heart rate **(p-value > 0.05)** between studied groups at (2.5, 3, 3.5,4, and 4.5, 5, 5.5 and 6 hours) and statistical significant decrease in post-operative heart rate **(p-value < 0.05)** in Group D than Group N at (0 min, 30 min, 1, 1.5 and 2 hours).

Table (7): Comparison between studied groups as regard post-operative mean arterial blood pressure (MAP).

		Nalbuphine (N = 30)	Dexmedetomidine (N = 30)	P-value	
MAP 0	**Mean ±SD**	79.60 2.59	78.60 3.07	**0.01****	**S**
MAP 30	**Mean ±SD**	79.70 3.84	78.60 1.83	**0.005****	**S**
MAP 1	**Mean ±SD**	80.40 3.84	79.30 2.04	**0.006****	**S**
MAP 1.5	**Mean ±SD**	80.60 2.85	79.50 1.59	**0.01****	**S**
MAP 2	**Mean ±SD**	80.90 2.73	79.90 2.29	**0.005****	**S**
MAP 2.5	**Mean ±SD**	81.20 2.80	80.70 2.96	0.9	**NS**
MAP 3	**Mean ±SD**	81.30 3.43	80.90 2.84	0.8	**NS**
MAP 3.5	**Mean ±SD**	81.50 3.79	81.00 2.58	0.8	**NS**
MAP 4	**Mean ±SD**	81.70 2.44	81.10 2.58	0.9	**NS**
MAP 4.5	**Mean ±SD**	82.90 1.70	82.20 1.12	0.7	**NS**
MAP 5	**Mean ±SD**	83.70 1.29	82.80 0.68	0.9	**NS**
MAP 5.5	**Mean ±SD**	83.80 1.27	82.90 1.02	0.6	**NS**
MAP 6	**Mean ±SD**	83.90 1.21	83.10 1.31	0.8	**NS**

p-value > 0.05 is considered non statistical significant (NS).
**: p-value < 0.05 is considered significant (S).

This table shows no statistical significant decrease in mean post-operative blood pressure (**p-value > 0.05)** between studied groups at (2.5, 3, 3.5,4, and 4.5, 5, 5.5 and 6 hours) and statistical significant decrease in mean post-operative blood pressure **(p-value < 0.05)** in Group D than Group N at (0 min, 30 min, 1,1.5 and 2 hours).

Table (8): Comparison between studied groups as regard post-operative SPO2.

		Nalbuphine (N = 30)	Dexmedetomidine (N = 30)	P-value	
SPO2 0	**Mean ±SD**	98.60 0.67	98.60 0.67	1.0	NS
SPO2 30	**Mean ±SD**	97.90 0.84	97.90 0.84	1.0	NS
SPO2 1	**Mean ±SD**	96.50 1.04	96.50 1.04	1.0	NS
SPO2 1.5	**Mean ±SD**	97.00 1.51	97.20 1.19	0.6	NS
SPO2 2	**Mean ±SD**	96.50 0.82	96.60 0.67	0.6	NS
SPO2 2.5	**Mean ±SD**	96.50 1.04	96.50 1.04	1.0	NS
SPO2 3	**Mean ±SD**	96.40 1.04	96.60 0.93	0.4	NS
SPO2 3.5	**Mean ±SD**	96.30 1.37	96.40 1.22	0.8	NS
SPO2 4	**Mean ±SD**	96.40 1.30	96.40 1.30	1.0	NS

SPO2 4.5	**Mean ±SD**	96.70 1.29	96.70 1.29	1.0	NS
SPO2 5	**Mean ±SD**	96.70 0.92	96.70 0.92	1.0	NS
SPO2 5.5	**Mean ±SD**	96.40 0.50	96.40 0.50	1.0	NS
SPO2 6	**Mean ±SD**	94.70 0.79	95.10 0.96	0.08	NS

This table shows no statistical significant difference **(p-value > 0.05)** between studied groups as regard post-operative SPO2.

Table (9): Comparison between studied groups as regard post-operative FLACC.

		Nalbuphine (N = 30)	**Dexmedetomidine (N = 30)**	**P-value**	
FLACC 0	**(0)**	12 (40%)	21 (70%)	**0.02***	**S**
	(1)	18 (60%)	9 (30%)		
FLACC 1	**(0)**	9 (30%)	18 (60%)	**0.02***	**S**
	(1)	21 (70%)	12 (40%)		
FLACC 1.5	**(0)**	3 (10%)	3 (10%)	**0.03***	**S**
	(1)	21 (70%)	27 (90%)		
	(2)	6 (20%)	0 (0%)		
FLACC 2	**(1)**	15 (50%)	27 (90%)	**0.001***	**S**
	(2)	15 (50%)	3 (10%)		
FLACC 2.5	**(1)**	6 (20%)	15 (50%)	**0.02***	**S**
	(2)	24 (80%)	15 (50%)		
FLACC 3	**(1)**	0 (0%)	3 (10%)	**0.01***	**S**
	(2)	24 (80%)	27 (90%)		
	(3)	6 (20%)	0 (0%)		
FLACC 3.5	**(2)**	21 (70%)	30 (100%)	**0.001***	**S**
	(3)	9 (30%)	0 (0%)		
FLACC 4	**(2)**	21 (70%)	30 (100%)	**0.001***	**S**
	(3)	9 (30%)	0 (0%)		
FLACC 4.5	**(2)**	3 (10%)	15 (50%)	**0.001***	**S**
	(3)	27 (90%)	15 (50%)		
FLACC 5	**(2)**	0 (0%)	6 (20%)	**0.01***	**S**
	(3)	27 (90%)	24 (80%)		
	(4)	3 (10%)	0 (0%)		
FLACC 5.5	**(3)**	21 (70%)	30 (100%)	**0.001***	**S**
	(4)	9 (30%)	0 (0%)		
FLACC 6	**(3)**	21 (70%)	30 (100%)	**0.001***	**S**
	(4)	9 (30%)	0 (0%)		

*: p-value < 0.001 is considered highly significant (HS).
**: p-value < 0.05 is considered significant (S).

Group D shows statistically significant difference **(p-value < 0.05)** compared to Group N as regard post-operative FLACC (0, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5 and 6 hours).

4. Discussion

Caudal block is a technique that is relatively easy to become familiar with. It is generally used for intraoperative or postoperative analgesia in infra-umbilical surgery, including some kinds of surgery for lower extremity, in children under 7 years of age ***(Dalens and Truchon, 2009).***

In our study, we selected children under 7 years of age as patients older than this, thickening of the sacrococcygeal ligament makes it difficult to identify the sacral hiatus, and so block is not often performed at the hiatus ***(Dalens and Truchon, 2009).***

The sacral vertebrae plate is less ossified at birth, and sacral vertebrae are connected by cartilage; the plate undergoes progressive ossification and union and becomes a single structure after puberty ***(Bogduk and Twomey, 1987).***

Also, in our study we selected caudal block under general anesthesia as Awaken infants and

children are likely to move away from the touch, needle placement and even the cold US probe. This may increase the risk of nerve injury during needle placement ***(Ivani et al., 2015).***

In 2015, the Joint Committee of European Society of Regional Anesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine suggested that high-level evidence for the safety of central neuraxial block in small children is still not available. However, they also concluded that, based on evidence category B2 (observational studies with associative statistics) and B3 (non-comparative observational studies with descriptive statistics), the performance of pediatric regional block under deep sedation/general anesthesia is acceptable in terms of safety and could be a standard of care ***(Ivani et al., 2015).***

Caudal anesthesia is established to be safe in preterm infants (born at a gestational age > 37 weeks), because the procedure is technically simple to perform, the success rate is high, and complications are rare and minor ***(Giaufre et al., 1996).***

It is suggested that awake caudal block may be stressful for the child, is associated with a significant failure rate and requires experienced performers ***(Williams et al., 2001).***

In caudal block, the most used local anesthetic agent is bupivacaine, because it is readily available, has a long duration of action and its side effects are very well known ***(Congedo et al., 2009).***

Any drug used as an adjunct must be preservative-free as they may cause local nerve damage. Their purpose is to prolong the duration of analgesia, or to improve the quality of the blocks by reducing unwanted side-effects. Clonidine is an a2-adrenoceptor agonist, used previously as an anti-hypertensive and sedative in children. Clonidine stimulates the descending norepinephric medullo-spinal pathway, which inhibits the release of nociceptive neurotransmitters in the dorsal horn of the spinal cord ***(Hager et al., 2002).***

Ketamine is an NMDA receptor antagonist that binds to the subset of the glutamate receptor. These receptors are found at both the CNS and spinal cord level. At spinal cord level, it decreases the activity of dorsal horn neurons involved in the nociceptive pathway. Clonidine 1–2 mg / kg and ketamine 0.5–1 mg / kg increase the duration of analgesia by 5–10 h when combined with bupivacaine 0.1–0.25% or ropivacaine 0.08–0.2 % ***(Hager et al., 2002).***

The combination of ketamine and clonidine is reported to provide satisfactory analgesia for up to 20 h. Both agents, at a higher dose, are associated with a greater risk of sedation, apnea, hallucination (particularly neonates and infants) or nausea ***(Hager et al., 2002).***

Morphine 50 mg / kg, or diamorphine 30 mg / kg, may increase the duration of analgesia by up to 24 h. However, they commonly produce unpleasant side-effects (e.g. nausea and pruritus) and have a theoretical risk of late onset respiratory depression. The potential risk of these additives seems unjustified for relatively minor day case surgery ***(De Beer and Thomas, 2003).***

However, fentanyl does not prolong the duration of analgesia but significantly increases the incidence of nausea and vomiting. In infants > 6 months, these additives should not be used because concerns over spinal cord toxicity and the risk of apnea remain unanswered ***(De Beer and Thomas, 2003).***

Dexmedetomidine, potentiates the action of local anesthetics without increasing the incidence of side-effects and compared to clonidine it's a highly selective α2 adrenergic receptor agonist, and this facilitates its use in larger doses for analgesia and sedation without the fear of inadvertent effects on the hemodynamics ***(Yoshitomi et al., 2008).***

Nalbuphine is a mixed agonist-antagonist opioid which has antagonist effect at mu receptor and agonist at kappa receptors. There are few reports of neuraxial administration of nalbuphine, but no reports of neurotoxicity. Previous studies also have shown that epidural or intrathecal use of nalbuphine produces a significant analgesia accompanied by minimal itching and respiratory depression ***(Salama, 2015).***

This study was undertaken to assess the efficacy of dexmedetomidine with bupivacaine compared to nalbuphine with bupivacaine in pediatric patients undergoing inguinal hernia repair surgeries under caudal analgesia.

In the present study, there was no significant difference in the two groups with regard to age and sex. The mean age was 4.23±1.50 years in Group N and 4.17±1.53 years in Group D. In both the groups' males were more, this could be due to inclusion of surgery.

Regarding heart rate and blood pressure, all the patients were monitored at regular intervals.

The mean baseline heart rate was similar in both groups before the administration of caudal block. The mean baseline rate was 124.10±3.5 beats per minute in Group N and 123.90±3.4 beats per minute in Group D.

There was significant fall in heart rate after caudal by 20 minutes which showed 114.60±2.62 beats per minute in Group N and 112.30±3.58 beats per minute in Group D. This fall in heart rate continued until end of surgery without clinical significance.

In the post-operative, heart rate showed statistical significant decrease in Group D from HR 0 min post-operative was 100.30±2.67 beats per minute

until HR 2 hours post-operative was 100.90±2.80 beats per minute, compared to Group N at HR 0 min post-operative was 101.00±3.48 beats per minute until HR 2 hours post-operative was 101.40±4.12 beats per minute, after that there was no significant decrease in heart rate of clinical significance till 6 hours post-operative.

The mean baseline of MAP was 88.70±3.16mmHg in Group N and 88.50±2.53mmHg in Group D.

There was a gradual significant fall in MAP after caudal by 20 minutes which showed 81.70±5.66 mmHg in Group N and 80.00±2.19 mmHg in Group D. This fall in MAP continued until end of surgery without clinical significance, MAP was similar to heart rate in the post-operative period.

Arora MK and co-workers reported hemodynamic effect in the form of hypotension. In their study hypotension treated in 6 out of 30 patients with inotropes ***(Mahesh et al., 2005).***

Another study by *El-Hennaway et al.* investigating if addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children- found that the magnitude of haemodynamic changes between the groups was comparable, and therapeutic interventions were not required ***(El-Hennawy et al., 2009).***

A randomized double blind study done by *Bhaskar et al.* comparing caudal dexmedetomidine and fentanyl for postoperative analgesia showed that the hemodynamics (HR & ABP) were comparable and statistically insignificant in both study groups ***(Bhaskar et al., 2014).***

Khaled investigated efficacy and safety of dexmedetomidine added to caudal bupivacaine in pediatric major abdominal cancer surgery & found that regarding the HR & MAP there was a statistically significant difference in the group that received the bupivacaine – dexmedetomidine mixture when compared with the group that received bupivacaine alone. However, the hemodynamic changes were of no clinical significance ***(Khaled, 2014).***

Saleh et al. investigated effect of nalbuphine as an adjuvant on levobupivacaine induced caudal analgesia in children undergoing surgical procedures, and found that there was no statistically significant difference among the two groups as regards HR and MAP at different times ***(Saleh et al., 2015).***

Cho et al. conducted a study to explore the effect of 1 μg/kg dexmedetomidine combined with high-volume/low-concentration caudal ropivacaine in children undergoing ambulatory orchiopexy. It was found that dexmedetomedine, *α*2-agonist, decreases the MAP and HR dose- dependently however, and these adverse effects appear to be less prominent in children compared with adults. The HR was significantly reduced at 10 min of surgery in the dexmedetomidine group compared with the Control group, but MAP changes were similar in both groups ***(Cho et al., 2015).***

The antihypertensive effect of dexmedetomidine results from stimulation of α2 inhibitory neurons in the medullary vasomotor center of the brainstem, which leads to a reduction in norepinephrine turnover and sympathetic outflow from the central nervous system to the peripheral tissues. Bradycardia is caused by an increase in vagal tone resulting from central stimulation of parasympathetic outflow, as well as reduced sympathetic drive. Dexmedetomidine has an 8-fold greater affinity for α2 receptors as compared to clonidine. It is more selective for α2a receptors that are responsible for sedative and analgesic effects of such drugs. Our study confirms the finding of hemodynamic changes ***(Anand et al., 2011).***

At no time in this study, there was a decrease in RR and fall in SpO2 requiring oxygen supplementation. Similar findings were demonstrated by *Upadhyay et al.* ***(Upadhyay et al., 2005).***

This confirms results from previous studies that α2 agonists have no clinical respiratory effects ***(Ramsay and Kuterman, 2004).***

Also in our study there was a significant reduction in the FLACC score in Group D at 0 min, 30min, 1, 2, 3, 4 and 6 hours postoperatively in comparison with Group N. Our results regarding postoperative pain relief are in agreement with *El-Hennawy et al.* When dexmedetomidine and clonidine were administered, both in a dose of 2 μg/ kg as adjuvant with 0.25% bupivacaine caudally, they found that the duration of analgesia was significantly prolonged in the group receiving the bupivacaine–dexmedetomidine mixture (analgesia time was 16 hours) over the group receiving bupivacaine alone (analgesia time was 5 hours) ***(El-Hennawy et al., 2009).***

Neogi et al. compared clonidine 1 μg/kg and dexmedetomidine 1 μg/kg as adjuncts to ropivacaine 0.25% for caudal analgesia in pediatric patients and concluded that addition of both clonidine and dexmedetomidine with ropivacaine administered caudally significantly increased the duration of analgesia. The mean duration of analgesia was 6.32 ± 0.46 hours in the ropivacaine group, 13.17 ± 0.68 hours in the clonidine group, and 15.26 ± 0.86 hours in the dexmedetomidine group ***(Neogi et al., 2010).***

Also the FLACC score was significantly reduced in the dexmedetomidine with ropivacine group ***(Neogi et al., 2010).***

Saadawy et al. have demonstrated that the addition of dexmedetomidine 1 μg/kg to bupivacaine 2.5 mg/mL (1 mL/kg) significantly improved the

efficacy of caudal analgesia with less use of postoperative analgesics ***(Saadawy et al., 2009).***

Conclusion

To summarize caudal block is a simple, safe, and effective method of providing anesthesia and post-operative pain relief in patients undergoing inguinal hernia repair surgeries. The results of this clinical trial had demonstrated that addition of dexmedetomidine to caudal local anesthetic bupivacaine produced longer duration of postoperative analgesia in pediatric patients undergoing inguinal hernia repair surgery than in nalbuphine group with no side effects.

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