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Better Post Operative Caudal Analgesia With Tramadol Versus Clonidine Added To 0.25% Bupivacaine In Paedeatric Lower Abdominal Surgeries: A Prospective, Randomosed, Double Blind Clinical Study.

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Conflicts of Interest: Nil.

Abstract

In pediatric infra umbilical surgeries, caudal anaesthesia are a preferred mode, however, simple caudal anaesthesia produces analgesia for short duration with very little postoperative analgesia. Addition of some pharmacological agents with local anaesthetics enhances the duration and quality of analgesia. We in our study have compared the efficacy of Tramadol 1 mg/kg or Clonidine 1 mcg/kg with 1 ml/kg of Bupivacaine 0.25% in 60 cases of pediatric infra-umbilical surgeries at Jawaharlal Lal Nehru Medical College & Hospital, Bhagalpur, during the period August 2016 to April 2017.

Methods

In a randomized. Prospective, double blind study, 60 children from the age group of 1 to 3 years belonging to ASA physical status I and II scheduled for lower abdominal surgeries in different operation theatres of JLNMC&H were included. They were randomly assigned in to two groups. Group I (BT group) (n=30) receiving 1 ml/kg of Bupivacaine) 0.25% with Tramadol 1 mg/kg body weight and group II (BC group (n=30) receiving 1 ml/kg of Bupivacaine with 1 mcg/kg of Clonidine for caudal anaesthesia. Primary variable was the duration of analgesia and the secondary outcome of variables were motor block, sedation score time from caudal blocks to skin incision, emergence time and adverse effects.

Results

The mean duration of analgesia 632.45 ± 79.39 minutes in-group BT and 740.28 ± 48.25 minutes in-group BC. (p =0.0001). Difference between mean sedation score & mean emergence time between the two groups were statistically significant (p = 0.0001 and 0.0566 respectively). No significant differences were observed in the incidence of hemodynamic changes or adverse side effects.

Conclusion

Caudal Clonidine with Bupivacaine produces longer duration of postoperative analgesia compared to caudal Tramadol with Bupivacaine in lower abdominal pediatric surgeries with insignificant hemodynamic changes or comparative adverse side effects.

Keywords: Caudal analgesia, Bupivacaine, Clonidine, Tramadol, emergence.

Introduction

For lower abdominal pediatric surgeries, caudal anaesthesia is a preferred and commonly used technique. However, managing postoperative analgesia is important and troublesome aspects, which necessitatethe use either of an indwelling catheter for continuous infusion of

analgesic or systemic administration of some or of other narcotic analgesics: both of which modes carry substantial hazards and catastrophes. A caudal catheter is notorious for high incidence of catheter contamination from fecal proximity. So, now-a-days single shot analgesia technique(1) are practiced by adding different pharmacological agents(2), such as Tramadol(3), Dexmedetomidine(4), Clonidine(5)(6), Ephedrine and Fentanyl (7) with the local anaesthetics for safe intra-operative and postoperative analgesia in pediatric patients. Tramadol, a synthetic 4-phenyl-piperidine analogue of codeine, produces analgesia through different mechanism by enhancing inhibitory effects on pain transmission through spinal cord. Tramadol does not produce respiratory depression despite having analgesic potency almost equal to pethidine (8). On the other hand, Clonidine is a highly selective α2-adrenergic receptor antagonist, although degree of α2 receptor affinity is much lesser than Dexmedetomidine (9), but is costlier than Clonidine with higher degree of hemodynamic instability. Clonidine on the other hand produces prolong intra-operative and post operative analgesia with better hemodynamic stability. Its sympatholytic, analgesic and sedative effects and its remarkablely free from side effects, except for manageable hypotension and bradycardia makes it a better and cheaper additive with Bupivacaine for attaining peri and long duration postoperative analgesia for infra umbilical pediatric surgeries. Our results were in favor of Clonidine.

Methods

After Ethical Committee approval and detailed written consents obtained from the parents of each children, 60 pediatric patients between the age group of six months to six years of ASA physical status I & II posted for below umbilicus surgeries in surgical and orthopedic operation theaters of this institution were selected for this study. Patients having infection on the back, allergy of drugs, bleeding or coagulation disorder, history of developmental delay, sepsis, pre-existing neurological or spinal diseases and allergy to the study drugs were excluded from the study.

During the pre-anesthetic visit on the day before surgery, all parents were explained about the anesthetic technique and the Perioperative period. Patients were randomly assigned into two groups, comprising 30 patients in each group. An anesthetist not participating in the study prepared the drugs as par the patient's body weight in a syringe. Group Bupivacaine with preservative freeTramadol (BT-group) received 0.25% Bupivacaine 1 ml/kg with 1mg/kg Tramadol after making the volume to 0.5ml. Second group (BC-group) received Bupivacaine 1ml/kg with Clonidine 1 mcg/kg after making the volume to 0.5ml. In the operation theater monitoring of SpO_2, non-invasive blood pressure, continuous ECG, respiration and temperature were started. Premedication was done with Glycopyrolate (0.004mg/kg) and Propofol 3mg/kg, all given IV. After the patient wassedated,nitrous oxide and oxygen in 50%:50% ratio with Sevoflurane 4% and maintaining the airway with a face mask or a laryngeal mask airway. (After some times the percentage of sevoflurane was reduced to 1.5% till the end of operation).Patients were placed in a lateral position. Skin over the back of sacrum was disinfected using povidone iodine solution, and under aseptic precautions, single dose epidural injection was performed using a 23-gauge hypodermic needle. Needle position was confirmed by Whoosh-test (10) using 0.5ml of air. After negative aspiration of blood or cerebrospinal fluid, caudal medication was given as per the group assigned by an anesthetist not included in the study. The time of block was recorded and surgery was allowed to be started in 10 minutes, after testing the level of motor as well as sensory

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block. Oxygen was continued @50% mixed with 50% nitrous oxide and 1% of Sevoflurane occasionally. No other analgesics, narcotic or sedative were used in intra operative period. Time taken from administration to achievement of block was noted. Continuous monitoring of vital parameters likeheart rate, ECG, respiratory rate, NIBP and oxygen saturation were recorded before premedication, after premedication, induction, after incision and then at 10 minute interval during surgery. At the end of surgery, total surgical time was recorded. Side effects like shallow respiration, breath holding, apnea, bradycardia, hypotension, involuntary movements, nausea and vomiting were recorded. Hypotension (fall in blood pressure < 20percentage of base line) was delt with IV bolus of fluid. Bradycardia (Heart rate <20percentage of base line) was treated with IV Atropine and recorded.Respiratory depression (respiratory rate <10/minute and SpO2<92%) was treated with supplemental oxygen. The primary objective was duration of analgesia, defined as the time between administration of block to facial and limb activity and crying and FLACC score(10) reaching to ≥4.

categories	scorings		
	0	1	2
Face	No particular expression or smile	Occasionally grimace or frown, withdrawn disinterested	Frequent to constant frown, quivering chin, clenching jaw
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
consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

(Each of the five categories, Face(F), Legs(L), Activity(A), Cry(Cr) and Consolability(C) is scored from 0-2, which results in a total score between 0-10.

Secondary objectives were duration of motor block, sedation and emergence time & adverse side effect. After conclusion of surgery all vital parameters were noted and patients shifted to post-anesthesia-care-units for further observation for number of supplementaryanalgesia, nausea, vomiting, hypotension, bradycardia, respiratory depression and urinary retentionfor 24 hours were recorded and treated accordingly. Nausea and vomiting was treated with IV ondansetron. Pain status and degree of sedation was evaluated using FLACC pain score with its 0-10 score range, recorded every three hours for 24 hours. Patients were treated with loading dose of paracetamol suppository 30mg/kg, given when the FLACC score went >4. This dose of paracetamol suppository was reduced to

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15mg/kg every 6 hours if required. Time of requirement of rescue medication and total number of medications during the 24 hours were recorded. Motor block was assessed on awakening by using a modified Bromage-scale (11) consisting of 6 points,

Table: 2: (Modified Bromage Scale).

score	criteria
1	Complete block (unable to move feet or knee)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knee)
4	Detectable weakness of hip flexion while supine(full flexion of knees)
5	No detectable weakness of hip flexion while supine)
6	Able to perform partial knee bend.

Very young children who could not understand commands, were stimulates by tapping. Level of sedation was assessed Ramsey sedation scale (12) at 30 minutes until the sedation score became 1 in all patients.

Table: 3: (Ramsey sedation scale).

Scale	**(If Awake)**
Ramsey 1	Anxious, agitated, restless
Ramsey 2	Cooperative, oriented, tranquil
Ramsey 3	Responsive to command only
	(If Asleep)
Ramsey 4	Brisk response to light glabellar tap or loud auditory stimulus
Ramsey 5	Sluggish response to light glabellar tap or loud auditory stimulus
Ramsey 6	No response to light glabellar tap or loud auditory stimulus

The criteria for transferring the patents from operation theater and post-anesthesia-care-units was , an awake patient, moving all limbs, patent airway, normal respiratory pattern, normal oxygen saturation, stable hemodynamic, normothermic and pain free. Data thus obtained were entered in to a computer-basedspreadsheet for analysis using SPSS statistical software. Numerical values like age, weight, HR and BP were presented as mean and standard deviations. Categorical variables like sex and adverse events were presented as % frequency. Student T-test and Chi-square was used for testing numerical values. The value P<0.05 was considered statistically significant.

Statistical Analysis

The data were analysed using statistical software " SPSS 12.0" and mean (SD) and median (range) of various parameters were calculated. Correlating various distances and patient factors were calculated using "Correlation regression analysis software" . "Standard tests of significance" was applied to find out the "p" value. P < 0.05 was considered to be significant.

Results

The two study groups (n= 30) were similar with regard to paediatric variables, like age, sex, weight and duration of surgery. Type of surgery included hypospedius repair, orchidopexy, and orchidectomy, inguinal hernia repair Ander's nailing of femer or tibea (Table 1). Mean duration of analgesia were 678.50 ± 82.35 minutes and 795.85 ± 76.45 minutes in group BT and group BC respectively (p=0.0001). Thus, the mean duration of analgesia was higher in group BC, where Clonidine was added to Bupivacaine.

Table 4: (Demographic profile)

Demographic parameters	Group BT (n=30)Bupivacaine plus Tramadol.	Group BC (n=30)Bupivacaine plus Clonidine.	P value

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Age (years)	3.73 ± 2.48	3.55 ± 2.37	> 0.05
Sex (male/female)	29/1	28/2	> 0.05
Weight (kg)	8.59 ± 3.86	8.67 ± 4.18	> 0.05
Surgical procedures			
Hypospedius repair	4	3	> 0.05
Orchidopexy	4	4	> 0.05
Orchidectomy	1	1	> 0.05
Inguinal hernia repair	21	22	> 0.05
Duration of Surgery (minutes)	40 ± 9.7	39 ± 7.8	> 0.05
mean Heart Rate (beats per minute)	132.18 ± 15.6	128-09 ± 18.9	>0.05
Mean systolic blood pressure (mm Hg)	105.64 ± 9.8	102.59 ± 8.76	>0.05
Values are expressed in mean± standard deviation; p value < 0.05 is significant.			

Table: 5 (Caudal block character)

	Group BT (n=30)	Group BC (n=30)	P value
	Bupivacaine plus Tramadol.	Bupivacaine plus Clonidine.	
Duration of Analgesia (minutes)	678.50 ± 82.35	795.85 ± 76.45	**<0.05**
Sedation (minutes)	243.23 ± 61.38	346.55 ± 64.29	**<0.05**
Duration of motor block(minutes)	153.45 ± 80.34	172.64 ± 92.34	> 0.05
Duration of spontaneous eye opening (hour)	3	4	> 0.05
Time of first administration of rescue analgesia(hr)	12	18	**<0.05**
Values are expressed in mean± standard deviation; p value < 0.05 is significant.			

Table-5 shows that the duration of analgesia is longer when Clonidine is used as additive to Bupivacaine as Tramadol.Thoughsedation is also prolong, but it is considered beneficial for paediatric patients if no other unmanageable other side effects are absent.

Table: 6 (Rescue analgesia in 24 hours)

Number of rescue analgesia in 24 hours			
1 dose	13	23	**<0.05**
2 doses	16	7	**<0.05**
3 doses	1	0	**<0.05**
4 doses	0	0	
5 doses	0	0	
Values are expressed in mean± standard deviation; p value < 0.05 is significant.			

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Table 6 shows that rescue analgesia needed in 24 postoperative hours were significantly lesser in clonidine group as compared to tramadol group.

Table 7: Ramsay sedation score during first six postoperative hours.

Time	Median range	
	Group BT	Group BC
End of surgery	2 (1-3)	3 (2-3)
At 1 hour	1 (0-2)	2 (2-2)
At 2 hour	1 (0-2)	2 (202)
At 3 hour	1 (0-2)	1 (0-2)
At 4 hour	0 (0-1)	1 (0-2)
At 5 hour	0 (0-1)	0 (0-1)
At 6 hour	0 (0-1)	0 (0-1)
At 24 hours	0	0

Table: 7, shows that the sedation scores in the clonidine groups were higher than tramadol group in the first 4 hours of postoperative period but patients were arousible on little stimulation.

Discussion

Clonidine was first used as epidural additive in 1984 inadults successfully which led to its evaluation in paediatric caudal block to increase the duration of postoperative analgesia. The analgesic action of intrathecal or epidural clonidine results from direct stimulation of pre and post synaptic α2-adrenoceptors in the dorsal horn grey matter of spinal cord, thereby inhibiting the release of nociceptive neurotransmitters (13).This effect correlates with the concentration of Clonidine in the Cerebro-spinal fluid and not in the plasma (14).Studies have shown that caudal clonidine increase the duration of postoperative analgesia in children aged 1-7 years undergoing subumblical surgery (15). Caudal clonidine does appear to have a dose dependent sedative effect in children. Lee and Robin (16) demonstrated a longer duration of postoperative sedation following caudal bupivacaine with clonidine 2 μg/kg (5-21 hours) (mean 9.8 hours) and this increased duration of sedation was not only the sedative effect of clonidine, but more importantly reflected superior analgesia.On the other hand, Tramadol has also been successfully administered epidurally for the same purpose. Addition of Tramadol to Bupivacaine produces a dose related increase in postoperative analgesia duration. (16). Best results were found with Tramadol 1 mg/Kg and Bupivacaine 0.25%by Batra et al(17) and our results were similar to them. Prosser et al (18) reported the addition of Tramadol 2mg/kg without any additional gain. Tramadol is one of the few drugs that is administered in the same dose both epidurally and intravenous. Gunes et al (19) concluded that caudal tramadol (2mg/kg) provides better and long lasting postoperative analgesia (>24 hrs) than intravenous Tramadol (2mg/kg) (2 hrs). Tramadol has been reported to depress the spinal nociceptive receptors, indicating that, similar to morphine, it acts at spinal level (20).The mean duration of analgesia in our study was 3-19 hours (mean11 hours ± 1.5) hours in Tramadol group while Prosser et al(18) shows this mean duration as 10 hours and was almost comparable to our study. This duration was 16 hours(mean 14 ± 2 hours) in clonidine group, result of which are slightly lower than that of Cook et al(21) who used the same amount of clonidine with duration of 16.5 hours, while Cook B, Doyle E et al (22) found it to be only 10-12 hours. This difference may be explained in part by difference in difference in study design or the variable nature of analgesia provided by clonidine as reported in other studies.So, we got enhanced duration of postoperative analgesia with Clonidine group as compared to other groups.Average duration of sedation in Tramadol group was 4 hours ± 1 hour while Clonidine group showed this duration as 6 hours ± 1 hour. This is significant but

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this enhanced sedation time was considered better as far as a paediatric patient is involved. The most frequently reported side effect of epidural Tramadol or Clonidine is nausea. In our study we found an insignificant incidence of nausea and vomiting with this dose schedule in both the groups and were easily overcome by simple medications.

Conclusion

Using clonidine 1 µg/kg as additive to 0.25% bupivacaine 1 ml/kg for caudal anaesthesia in subumblical surgery in children provided longer duration of analgesia and reduced requirement of rescue analgesic in the postoperative period in comparison to Tramadol 1 mg/kg with bupivacaine 0.25% for the same purpose. Thus clonidine with bupivacaine is a safer and cost effective method of caudal block in children.

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Conflict of interest: Nil.

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