Original Article

Caudal bupivacaine - midazolam for post operative analgesia in children

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Abstract

Background: *Adjuvant used with local anaesthetic agent in caudal is more effective for post operative analgesia in children .*

Aim and objective: *To find out the duration and quality of caudal analgesia in children undergoing genitourinary surgery by combination of bupivacaine and midazolam.*

Methods: *A total number of sixty patients ASA grade I&II were selected randomly as per inclusion & exclusion criteria in two groups. Thirty in each group. In group A, caudal block was given by bupivacaine-midazolam mixture and in group B, caudal block was given by bupivacaine in lateral decubitus position, just after completion of surgery before reversed from GA. In post operative period arterial blood pressure, heart rate, and duration of analgesia were recorded.*

Results: *There was no significant difference between the groups of blood pressure, heart rate, and pain score up to 30 min but after one hour of post operative period pain scores were significant($p<0.05$).*

Conclusion: *Midazolam improves the duration and quality of analgesic effect of bupivacaine.*

Key words: *bupivacaine,midazolam, caudal, genitourinary,analgesia.*

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Introduction

Caudal epidural is one of the most common regional techniques used for post-operative pain management in pediatric patients[1]. It is commonly used for procedures like urogenital, rectal, inguinal and lower extremity surgery [2].

Drugs which used commonly in caudal analgesia, are bupivacaine & lignocaine. Opioids may also be used as adjunct, although they are not recommended for day case surgery because of the risk of delayed respiratory depression. We want to use bupivacaine –midazolam combination to know the duration and quality of caudal analgesia. Antinociceptive effect, effective analgesic properties and safety of intrathecal-administered midazolam are well established in animals and human beings[3]. In-vitro autoradiography has shown that there is a high density of benzodiazepine (GABA-A) receptors in lamina-II of the dorsal horn in the human spinal cord, suggesting their possible role in pain modulation. The delta selective opioid antagonist naltrindol suppresses the antinociceptive effect of intrathecal midazolam, suggesting that intrathecal midazolam involved in the release of endogenous opioid acting at spinal delta receptors[4,5]. In1987, Goodchild and Serrao reported that benzodiazipines might have analgesic effects at spinal cord level in animal[4,5]. Recently it has been demonstrated the analgesic efficacy of intrathecal midazolam in human[4,5].

There have been some reports on the spinal application of midazolam in humans, which show no neurotoxic effect[4,5]. A single intrathecal injection of 2 mg midazolam did not cause any clinical neurological deficits and produce significant analgesia for 2 months in patients with chronic low back pain[6]. Intrathecal midazolam was also effective after leg surgery without any side effects[7].

So we can think that there is no neurotoxicity of caudal midozolam administration.

In addition to the effectiveness of intrathecal midazolam against somatic pain, an antinociceptive effect against visceral pain has been demonstrated in rabbits subjected to intestinal distention and in humans after caesarean section[8].

Intrathecal midazolam has been used in a continuous infusion for a long-term period with refractory neurogenic and musculoskeletal pain. In-vitro studies have suggested that clinically useful doses of intrathecal midazolam are unlikely to cause neurotoxic[9].

Intrathecal midazolam does not have the unwanted effects like pruritis, nausea and vomiting and respiratory depression as caused by intrathecal opoids[9].

The use of conventional dose of bupivacaine is associated with a high incidence of hypotension, prolonged motor recovery, nausea and vomiting and discharge time. It may be possible to minimize these unwanted outcomes by using small dose of bupivacaine combined with midazolam.

On the other hand low dose of bupivacaine may cause inadequate analgesia leading to discomfort during traction of peritoneum. This may be overcome by addition of midazolam to bupivacaine, which may prolong the duration of analgesia because of its antinociceptive action.

Method

After approval of Ethical Committee, 60 patients were selected randomly as per inclusion and exclusion criteria. Before taking the patient into the operation theatre, legal guardian of the patient was consulted about post-operative analgesia and consent for caudal analgesia was taken. Patients were allocated randomly into two groups, 30 patients in each group.

The same conventional GA was given to all patients. After completion of the surgery in group A patient caudal block was given by bupivacaine-midazolam mixture (0.125% bupivacaine 0.8 ml/kg, midazolam 0.08 mg/kg) and in group B patient caudal block was given by bupivacaine (0.125% bupivacaine 0.8 ml/kg) only. Caudal block was done in lateral decubitus position. Then patient was reversed in supine position.

Following parameters were recorded: - Time of caudal block, heart rate, blood pressure, duration of analgesia by first demand of analgesia of the patient.

Data was collected on pre-designed data collection sheet and was analyzed for statistical significance by Chi-square or student's t-test as appropriate. P value less than 0.05 was considered statistically significant.

Results

Observation of the present study was analyzed in the light of comparison among the subject groups, each group having n=30. All results are expressed as mean ± standard error of mean (SEM). The studied groups became statistically matched for age (p=0.871), weight (p=0.796), duration of surgery (p=0.016), pulse rate (p=0.096), systolic blood pressure (p=0.932), diastolic blood pressure (p=0.503) and SpO_2 (p=0.237),and pain score($p<0.05$).

Table-I

Demographic data

Groups	Age (year)	Weight (Kg)	Duration of surgery(Min.)
	Mean ± SEM	Mean ± SEM	Mean ± SEM
Group A	4.209 ± 0.206	12.90 ± 0.354	48.45 ± 1.199
Group B	4.200 ± 0.221	12.800 ± 0.414	45.50 ± 0.874
P	0.871	0.796	0.016

Values were expressed as mean ± SEM. Analysis was done by student's t- test. There was no significant changes.

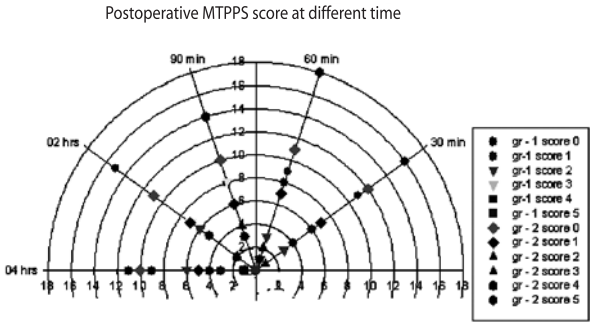

Fig.-1. *Modified TPPPS score in different time period.*

Table- II

Changes of heart rate.

Groups	Pre - operative	After Induction	After Caudal	End of Surgery	½ hr POP	1hr POP	1 ½ hr POP	2 hr POP	4 hr POP	6 hr POP	8 hr POP	12 hr POP
A	103.00	140.15	140.65	103.60	104.95	102.40	102.50	108.25	111.60	104.00	111.44	109.85
	± 1.76	±2.24	±1.80	±1.75	±1.95	±4.90	±5.14	±2.14	±2.62	±5.37	±1.87	±1.97
B	102.35	102.50	103.40	98.15	103.45	103.00	102.90	99.60	104.00	98.60	104.20	100.00
	±2.28	±2.24	±2.27	±5.10	±1.74	±2.00	±1.68	±4.6	±1.66	±4.64	±1.85	±5.15
P	0.945	0.665	0.377	0.467	0.611	0.947	0.994	0.158	0.019	0.539	0.022	0.137

Values were expressed as mean ± SEM. Analysis was done by student's t-test. There was no significant change in heart rate between groups.

Table-III

Changes in systolic blood pressure

Groups	Pre-operative	After Induction	After Caudal	End of Surgery	½ hr POP	1hr POP	1 ½ hr POP	2 hr POP	4 hr POP	6 hr POP	8 hr POP	12 hr POP
A	29.00	79.75	79.85	80.00	78.70	77.30	79.30	81.90	81.90	80.90	81.10	79.20
	±10.95	±11.59	±13.03	11.08	±11.62	±11.53	±11.55	±10.59	±11.96	±10.40	±10.90	±10.55
B	77.60	77.60	77.60	77.65	77.85	77.85	77.85	79.65	79.35	79.30	79.15	79.60
	±13.17	±13.18	±13.18	13.18	±12.44	±12.44	±12.44	±12.35	±11.92	±11.89	±12.30	±12.62
P	0.932	0.845	0.718	0.717	0.958	0.927	0.899	0.630	0.804	0.825	0.872	0..985

Values were expressed as mean ± SEM. Analysis was done by student's t- test. There was no significant change in systolic blood pressure between groups. Mean systolic blood pressure (SBP) in group A was 79.00 ± 10.95 and in group B was 77.60 ± 13.17, (P= 0.932). Mean values of systolic BP varied from 77.30 ± 11.53 to 81.90 ± 10.59 in-group A and 77.60 ± 13.17 to 79.63 ± 12.35 in-group B. Systolic blood pressure did not vary significantly in different time period between groups . (Table-III)

Table-IV

Changes of diastolic blood pressure.

Groups	Pre - operative	After Induction	After Caudal	End of Surgery	½ hr POP	1hr POP	1 ½ hr POP	2 hr POP	4 hr POP	6 hr POP	8 hr POP	12 hr POP
A	42.25	42.15	42.33	42.95	40.60	39.25	40.60	40.10	40.65	41.65	42.10	42.25
	±9.66	±10.01	±9.49	±8.127	±5.78	±6.98	±6.16	±6.86	±5.05	±4.55	±5.05	±4.20
B	46.50	46.50	45.70	44.75	44.90	44.85	45.25	46.20	46.80	46.95	48.10	47.60
	±30.96	±30.96	±14.20	14.45	±15.05	±15.09	±14.78	±13.96	±13.62	±13.73	±14.36	±14.76
P	0.503	0.428	0.665	0.928	0.518	0.363	0.442	0.397	0.202	0.301	0.228	0.290

Values were expressed as mean ± SEM. Analysis was done by student's t -test. There was no significant change in diastolic blood pressure between groups.Mean diastolic blood pressure was 42.25-± 9.66 in-group A and 46.50 ± 13.96 in-group B (P = 0.503). Diastolic blood pressure in-group A varied from 39.25 ± 6.98 to 42.75 ± 8.12 and from 44.90 ± 15.05 to 47.70 ± 14.67 in group B. Diastolic blood pressure did not vary significantly between groups in different time period.(Table-IV)

Table-V
Postoperative MTPPS score at different time.

Group	Score	At 30 min		At 1 hr		At 90 min		At 2 hr		At 4 hr	
		No of Pt		No of Pt		No of Pt		No of Pt		No of Pt	
A	0	20		18		16		15		10	
	1	10		10		12		13		15	
	2	0		2		2		2		3	
	3	0		0		0		0		2	
	4	0		0		0		0		0	
	5	0	P=0.249	0	P=0.023	0	P=0.008	0	P=0.000	0	P=0.006
B	0	18	X^2=5.40	17	X^2=11.38	15	X^2=17.28	15	X^2=30.97	10	X^2=24.76
	1	12		10		12		11		12	
	2	0		3		3		4		5	
	3	0		0		0		0		3	
	4	0		0		0		0		0	
	5	0		0		0		0		0	

Intensity of pain in different time period was measured using modified TPPPS score. Shown in (Figure-1, Table-V).At 30 min pain score was insignificant(p=0.249) but at one hour to four hours 30 min interval there were significant difference between the groups ie, (p=0.023), (p=0,008),(p=0.000),(p=0.006) respectively.

Table VI
Rescue pethidine required first time in minute

Group	Number of Pt.	Mean ± SEM	P
A	30	210.00 ± 30.00	<0.05
B	30	150.00 ± 30.00	

Rescue pethidine required first time was 210.00 ± 30.00 in group A and 150.00 ± 30.00 in group B. (Table-VI)

Discussion

Prolongation of analgesic effect of bupivacaine by caudal route is a desired goal for anaesthetiologist. In this study we used caudal midazolam along with 0.125% plain bupivacaine to achieve that goal.

Bupivacaine is the local anaesthetic with longest duration of action currently available. When we used for analgesia in children in a dose of 2.0-2.5 mg/kg, it lasts for 2-3 hrs., most of the children undergoing sub umbilical operation require further analgesia during postoperative period[10] which influenced many authors to search for means to prolong the duration of caudal analgesia.

Many drugs including epinephrine, morphine[11], clonidine[11], ketamine[11], and tramadol[12, 13] have been co-administered with caudal bupivacaine to maximize and extend the duration of analgesia. Morphine extends the duration of analgesia but frequent association of delayed respiratory depression, itching, vomiting, and postoperative retention of urine has limited its use[14]. Behavioral side effects are reported with use of ketamine and increased incidence of vomiting was observed with use of tramadol[12, 13].

Midazolam is being investigated for use with bupivacaine caudally for postoperative pain control. Antinociceptive effect, effective analgesic properties and safety of intrathecal- midazolam are well established in animals and human beings[3].

There have been some reports on the spinal application of midazolam in humans, which show no neurotoxic effect[4,5]. A single intrathecal injection of 2 mg midazolam did not cause any clinical neurological deficits and produce significant analgesia for 2 months in patients with chronic low back pain[6]. Intrathecal midazolam was also effective after leg surgery without any side effects[7].

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Intrathecal midazolam does not have the unwanted effects like pruritis, nausea and vomiting and respiratory depression as caused by intrathecal opoids[9].

The use of conventional dose of bupivacaine is associated with a high incidence of hypotension, prolonged motor recovery, nausea and vomiting and discharge time. It may be possible to minimize these unwanted outcomes by using small dose of bupivacaine combined with midazolam.

On the other hand low dose of bupivacaine may cause inadequate analgesia leading to discomfort during traction of peritoneum. This may be overcome by addition of midazolam to bupivacaine, which may prolong the duration of analgesia because of its antinociceptive action.

In our study we used Midazolam along with Bupivacaine at the end of the surgery through caudal route in childrens undergone genitourinary surgery.

Our observation showed that there were no significant changes in heart rate, blood pressure and oxygen saturation in both groups. We also observed no untoward event in either of the groups.

Our result shows that caudal midazolam along with bupivacaine prolongs the postoperative analgesic action.

In group A, duration of analgesia is 210 ±30 minutes and in group B, duration of analgesia is 150 ± 30minutes.

So, Conclusion is that midazolam improves the duration and quality of analgesic effects of bupivacaine without any side effects.

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