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Original Research Article

A Clinical Comparative Study between Intrathecal Midazolam and Tramadol with 0.5% Hyperbaric Bupivacaine for Patients Undergoing Infraumbilical Surgeries

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Abstract

Background: Adjuvants are added to 0.5% heavy bupivacaine to improve the quality of spinal anesthesia and prolong the duration of motor and sensory blockade.

Tramadol, a centrally acting opioid analgesic, has minimal respiratory depressant effect as it has 6000-fold less affinity for μ receptors compared to morphine whereas midazolam occupies benzodiazepine receptor that modulates γ-amino butyric acid (GABA), a major inhibitory neurotransmitter in the brain.

Methodology: A prospective randomized study was conducted among 70 patients who were posted for various elective infraumbilical surgical procedures. They were randomly divided by the closed envelope method into two groups of 35 patients each, Group M (Midazolam) and Group T (Tramadol). Subarachnoid block was performed using a 27-gauge Quincke spinal needle with intrathecal hyperbaric bupivacaine with adjuvants. Onset and duration of the sensory and motor blockade along with post-operative analgesia were assessed.

Results: The onset of sensory and motor blockade was comparable as there was no statistical significance. There was a statistically significant difference in sensory blockade prolongation in the tramadol group, whereas motor blockade was significantly less in the tramadol group than in midazolam. Both the groups had stable hemodynamics both intraoperatively and postoperatively. The midazolam group shows sedation as a significant side effect.

Conclusion: We conclude that adjuvant tramadol is better than midazolam when used along with intrathecal bupivacaine.

Keywords: Spinal anesthesia, Bupivacaine, Tramadol, Midazolam.

Introduction

Spinal Anaesthesia is the most common technique used for infra-umbilical surgeries as it is very economical and comparatively easy to perform. Many adjuvants are added to local intrathecal anesthetic to improve the quality and duration of subarachnoid block and also to prolong analgesia postoperatively.

Tramadol, a centrally acting opioid analgesic with 6000-fold less affinity for mu receptors in comparison to morphine, also has a minimal respiratory depressant effect. It inhibits serotonin and norepinephrine reuptake in the spinal cord. Higher doses of tramadol intrathecally can cause pruritis, nausea, vomiting, and respiratory depression.[1]

Anti-nociceptive action of midazolam is well known. It binds with gamma-aminobutyric acid-A receptors in the spinal cord which results in good analgesia. Hypnotic, sedative, amnesic, and anticonvulsant effects are mediated by α1 GABA receptors. Anxiolysis and centrally acting muscle relaxant properties are mediated by α2 GABA receptors.[2]

Methodology

After obtaining ethical committee clearance, this study was conducted at Kempegowda Institute of Medical Sciences and Hospital, Bangalore. After taking informed consent, seventy patients of either gender belonging to American society of Anesthesiology (ASA) physical status 1 & 2, aged between 20 to 60 years, were scheduled for elective infra umbilical surgeries for the prospective randomized study.

Study Duration: February 2021-august-2021(6 months)

Patients were divided into two groups by the closed envelope method after a routine preoperative evaluation.

Group **M** (Midazolam): 35 patients

Group **T** (Tramadol): 35 patients

Exclusion criteria included patient refusal for spinal anesthesia, gross spinal deformities, history of peripheral neuropathy and infection at the site of injection, coagulopathy, and history of allergy to local anesthetics.

A thorough pre-anesthetic evaluation was done on the previous evening of surgery. Premedication with Tab pantoprazole 40 mg at night before surgery and on the morning of the surgery & Tab Alprazolam 0.5 mg at night before surgery was given. After shifting to the operating room, routine monitors were used: Electrocardiogram (ECG), Heart Rate (HR), Blood pressure (NIBP) & Oxygen saturation (SpO2). An appropriately sized peripheral cannula was secured. Intravenous infusion of Ringers Lactate (RL) at 10 ml/kg over 15 minutes was started. Vital parameters were observed throughout the procedures at specific time intervals.

In this study, 3 ml of the solution of local anesthetic along with 0.5 ml of the adjuvant (midazolam/tramadol) was injected into the intrathecal space and a surgical operation involving the infraumbilical region was performed. Onset and duration of sensory and motor blockade were recorded for all cases, Pain intensity score was evaluated based on the VAS during recovery as well as 0,6,12 and 24 hours after the surgery. Trained nurses who were blinded to the study verified the dose of analgesics needed within 24 hours after the surgery.

Statistical Analysis

Data collected was entered in an MS Excel sheet. The descriptive and analytical statistics were performed using the Statistical Package of Social Sciences (SPSS) version 22 software. Percentages, means, and standard deviations (SD) were computed for descriptive purposes. Student

t-test was used to compare the mean age, BMI, and outcome variables between the study groups. Visual analog scores at different intervals were also compared between the groups using the student t-test. The Chi-Square test was used to compare frequency distributions between the two groups. A p-value less than 0.05 was considered statistically significant.

Results

Demographic Data

Table 1: Comparison Between the Groups Regarding the Mean of Baseline Variables

	Group	N	Mean	Std. Deviation	P Value
Age (years)	Group-M	35	33.86	8.73	0.063
	Group-T	35	37.54	7.56	
BMI (KG/M^2)	Group-M	35	25.01	1.94	0.112
	Group-T	35	24.32	1.60	

Student t test * statistically significant

The mean age (Years) among the GROUP-M was 33.86±8.73 and while it was 37.54±7.56 among the GROUP-T. The difference was not statistically significant (p=0.063). The mean BMI (kg/m^2) among the GROUP-M was 25.01±1.94, while it was 24.32±1.60 among the GROUP-T. the difference was not statistically significant (p=0.112).

Table 2: Comparison between the Groups Regarding the Mean of Outcome Variables

Sensory Onset (Mins)	Group-M	35	2.817	0.6181	0.762
	Group-T	35	2.766	0.7495	
Time To Maximum Sensory Blockade (In Mins)	Group-M	35	6.66	1.589	0.001*
	Group-T	35	4.89	0.832	
Motor Block Onset(Mins)	Group-M	35	4.29	0.667	0.128
	Group-T	35	4.83	6.671	
Maximum Motor Blockade Onset (Mins)	Group-M	35	5.409	0.1721	0.001*

Student t test * statistically significant

The mean Sensory onset between GROUP-M and GROUP-T was not statistically significant (p=0.762). The mean time to maximum Sensory blockade (in mins) among the GROUP-M was 6.66±1.589 and while it was 4.89±0.832 among the GROUP-T. The difference was statistically significant (p=0.001). The mean motor block onset (mins) among the GROUP-M and GROUP-T was not statistically significant (p=0.128). The mean time to maximum motor blockade onset (mins) among the GROUP-M was 5.409±0.1721 and while it was 7.514±1.0109 among the GROUP-T. The difference was statistically significant (p=0.001).

Table 3: Duration of Motor and Sensory Blockade

Duration Of Analgesia(Mins)	Group-M	35	199.77	2.819	0.001*
	Group-T	35	254.29	33.103	
Duration Of Motor Blockade (Mins)	Group-M	35	192.49	12.708	0.005*
	Group-T	35	188.69	19.964	

The mean duration of analgesia(mins) among the GROUP-M was 199.77±2.819 and while it was 254.29±33.103 among the GROUP-T. The difference was statistically significant (p=0.001). The mean duration of motor blockade (mins) among the GROUP-M was 192.49±12.708 and while it was 188.69±19.964 among the GROUP-T. The difference was statistically significant (p=0.005).

Table 4: Comparison between the Groups Regarding the Frequency of Complications

		Complications				Total
		AB	Bradycardia	Hypotension	Sedation	
Group	GROUP-M	23	1	3	8	35
	GROUP-T	33	1	1	0	35
Total		56	2	4	8	70

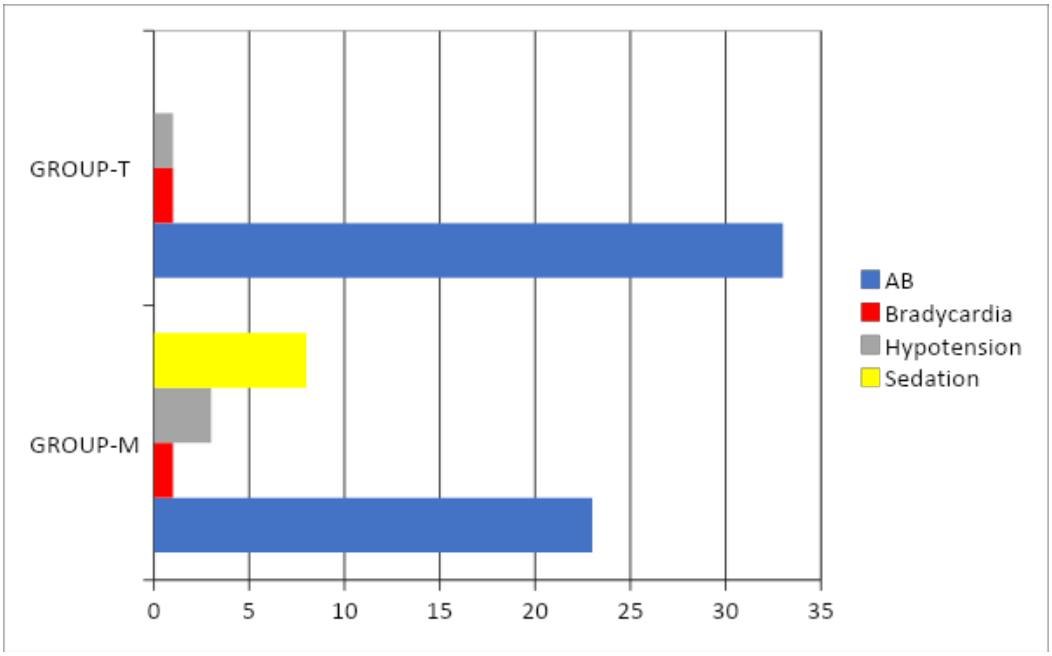

Figure 1: Comparison of side effects between the two groups

In group M 8 cases out of 23 had sedation. Sedation was seen as a significant side effect in group M compared to group T.

Discussion

Bupivacaine is the most commonly used drug for spinal anesthesia in lower abdominal surgeries. It is an amide local anesthetic with pka of 8.2, is a potent local anesthetic, and is more lipid soluble agent. Its mechanism of action is by binding to the preferentially open or inactive sodium channels and it is metabolized by the microsomal P-450 enzymes in the liver. It provides an adequate level of motor blockade and effective postoperative analgesia in the early postoperative period.[3]

The peritoneum and intestine have innervations as high as the T_4 level. Therefore, any level of the sensory block below T_4 may cause visceral pain and discomfort. In some cases, a maximum height of the sensory block may not be attained if intrathecal 0.5% hyperbaric

bupivacaine is used alone, thus the need to add intrathecal opioid as an adjuvant for management of visceral pain and discomfort.[4]

Tramadol is a centrally acting opioid. It binds to the μ-receptor and to a lesser extent to the δ- and κ-opioid receptors and is 5 to 10 times less potent than morphine as an analgesic. By inhibition of neuronal reuptake of norepinephrine and serotonin, it enhances the function of spinal descending inhibitory pathways. Lower incidence of cardiovascular and respiratory depression as compared to other opioid agonists.[5]

Midazolam is known for its antinociception action The benzodiazepine-GABA receptor complex is the reason for spinal mediated analgesia and the segmental analgesia produced by intrathecal midazolam. This receptor is distributed in the grey matter of cervical, thoracic and sacral regions of the spinal cord. Intrathecal midazolam interrupts the somatic nociceptive afferent pathway of pain but does not block the abdominal visceral nociceptive afferent pathway of pain.[6]

In our study**,** the two groups group M and group T were comparable with respect to age, BMI, and duration of surgery. The duration of analgesia in group M was 199.77+/-2.819, whereas in group T was 254.29+/-33.103 as shown in table 3. The duration of the motor blockade in group M was 192.49+/-12.708 whereas in group T was 188.69+/-19.964. Patients in the tramadol group (group T) had a significantly longer sensory block than the midazolam group (group M), midazolam group had a significantly longer motor blockade than the tramadol group (group T). The mean time to maximum Sensory blockade (in mins) among the GROUP-M was 6.66±1.589 and while it was 4.89±0.832 among the GROUP-T. Thus, the onset of sensory blockade was earlier in the tramadol group than in the midazolam group. Patients were monitored with parameters of heart rate, and BP, during the intraoperative period and also post-operatively for up to 12 hours. In both groups, patients were hemodynamically stable. In the postoperative period, visual analog scores were recorded for 12 hours post-surgery. VAS score was comparable for both groups. Sedation was seen as a significant side effect in the midazolam group than in the tramadol group while other side effects were comparable. Mohamed Abdel Raheem *et al.*,[3]have shown in their study that intrathecal tramadol provides very good and prolonged postoperative analgesia without significant side effects compared to intrathecal midazolam. Our study results were in accordance with the above study.

Conclusion

In the comparison of intrathecal midazolam 2.5mg (0.5ml) to intrathecal tramadol 25mg (0.5ml) with 3ml of 0.5% hyperbaric bupivacaine, it was seen that tramadol and midazolam in terms of onset of sensory and motor blockade were similar, but tramadol prolongs the duration of sensory analgesia and whereas midazolam prolongs the duration of motor blockade. Both provide good intraoperative and postoperative stability and midazolam additionally showed sedation as a significant side effect.

Hence, we conclude that intrathecal tramadol along with bupivacaine provides better postoperative analgesia without prolonged motor blockade in comparison to intrathecal midazolam along with bupivacaine.

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