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COMPARISON OF THE EFFECTS OF INTRATHECAL TRAMADOL AS AN ADJUVANT WITH BUPIVACAINE IN PATIENTS UNDERGOING INFRA-UMBILICAL SURGERIES AT TERTIARY CARE HOSPITAL, KARACHI

Dr. Urooj Zafar[*1], Dr. Syed Nusrat Ali Jafri[2], Dr. Tabinda Qamar[3], Dr. Nasira Zobair[4], Dr. Arsala Hussain[5], Dr. Syed Hamid Ali[6], Dr. Rafia Afzal[7]

[*1]*Abbasi Shaheed Hospital (ASH), RMO, MBBS, MCPS, FCPS*
[2,3]*Abbasi Shaheed Hospital (ASH), RMO, MBBS, MCPS, MD*
[4,5]*Abbasi Shaheed Hospital (ASH), RMO, MBBS, MCPS*
[6]*Consultant, S.I.U.T, MBBS, FCPS*
[7]*Abbasi Shaheed Hospital (ASH), Senior Registrar, MBBS, FCPS*

[*1]smali255@yahoo.com, [2]nusrat_jafri@hotmail.com, [3]tabindaqamar84@gmail.com, [4]nasira.zobair@gmail.com, [5]drarsalahussain@gmail.com,[6]hamidsiut@gmail.com, [7]afzalrafia@gmail.com

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Corresponding Author: *
Dr. Urooj Zafar

Abstract

OBJECTIVE: *To compare the clinical outcomes of intrathecal administration of a Bupivacaine-Tramadol combination versus Bupivacaine alone in patients undergoing infra-umbilical surgeries under spinal anesthesia.*

METHODOLOGY: *This randomized controlled trial was executed at Abbasi Shaheed Hospital in Karachi, involving 100 subjects aged between 20 and 60 years who were scheduled for elective infra-umbilical surgical procedures. The participants were systematically assigned into two distinct groups: Group A received intrathecal bupivacaine exclusively, whereas Group B was administered bupivacaine in conjunction with tramadol. The primary outcomes assessed encompassed the onset time of both sensory and motor blockade, as well as the duration of analgesia. Data were subjected to analysis utilizing SPSS version 26, with a designated significance threshold set at $p<0.05$.*

RESULTS: *The mean ± SD ages of the two groups, i.e., Group A (bupivacaine alone) and Group B (tramadol-bupivacaine) were 41.82 ± 14.58 and 42.66 ± 13.72 years, respectively, and a proportion of them being males (68.0% and 74.0%). Mean sensory blockade (3.88 ± 1.69 v/s 3.10 ± 1.24; p=0.010), motor blockade (5.60 ± 1.12 v/s 5.10 ± 1.19; p=0.034) and duration of analgesia (5.38 ± 1.78 v/s 4.88 ± 1.63; p=0.147) while VAS was found as at 24 hrs (1.94 ± 0.84 v/s 1;98 ± 0.84; p=0.813).*

CONCLUSION: *The research indicates that the administration of intrathecal tramadol as an adjunct to bupivacaine significantly enhances the rapidity of both sensory and motor blockades in individuals undergoing infra-umbilical surgical procedures. Nevertheless, it does not yield a statistically significant extension in the duration of analgesia, nor does it alleviate postoperative pain scores when compared to bupivacaine administered independently. These findings substantiate*

the potential application of tramadol for expedited block onset without jeopardizing safety or the efficacy of analgesia

INTRODUCTION

Spinal anesthesia is considered a dependable, effective, and affordable technique that provides anesthesia for surgical procedures as well as relief from postoperative discomfort [1]. It also functions as a potent agent for managing intraoperative pain by suppressing autonomic, somatic, and endocrine system responses. In the past, 0.5% heavy bupivacaine was the preferred choice for spinal anesthesia after intrathecal lidocaine was phased out [2]. Bupivacaine is a combination of two enantiomers—dextrobupivacaine and levobupivacaine—forming a racemic mixture [3]. When properly administered, anesthesia that delivers a pain-free surgical and recovery experience contributes significantly to the anesthesiologist's satisfaction.

Untreated postoperative pain can lead to a variety of harmful acute and chronic consequences[4]. Postoperative pain and discomfort are inextricably related to the postoperative quality of life of surgical patients and easy postoperative course is very conducive to the surgical patients and makes the operation a comfortable experience for the surgeon as well [5].

Intrathecal opioids are widely used for effective postoperative pain control in various surgical settings; however, they are linked with an increased risk of respiratory depression [6]. Tramadol, unlike traditional centrally acting opioid analgesics, has a minimal respiratory depressant effect due to its significantly lower binding affinity—about 6000 times less—for μ receptors compared to morphine [6]. Additionally, it inhibits the spinal reuptake of serotonin and norepinephrine without any reported neural toxicity. Therefore, tramadol is considered a viable option for providing postoperative analgesia through central neuraxial administration without causing respiratory depression [7].

Despite its advantages, adverse effects such as pruritus, nausea, vomiting, urinary retention, activation of herpes labialis, and unpredictable respiratory depression have prompted healthcare providers to explore lower intrathecal doses of tramadol. This is intended to achieve effective and prolonged pain relief while avoiding these complications [8]

Similar results were reported by Bandreddy et al in its comparisons of the effect of this (Bupivacaine Tramadol) combination versus placebo for intrathecal anesthesia in TURP surgery with its results showing that the time required for rescue analgesia was significantly longer in the Bupivacaine Tramadol group (312.56 ± 137.42 min versus 256.97 ± 130.46 minutes), although the onset of sensory blockade was slower in the combination group (8.44 ± 2.35 min versus 6.53 ± 1.65) [9].

Another study by Gupta et al also compared the effectivity of intrathecal Bupivacaine Tramadol (20mg) combination when compared with Bupivacaine alone and observed that the combination was associated with decreased mean time of onset of sensory blockade (5.13 ± 0.86 versus 6.06 ± 1.13) and mean time of onset of motor blockade (6.72 ± 1.79 versus 8.15 ± 1.53) [10].

At present, no such study is conducted in Pakistan on the comparison of clinical effects of intrathecal use of Bupivacaine-Tramadol mixture versus Bupivacaine alone in patients of infra-umbilical surgeries. Tramadol is a commonly used agent as intravenous analgesic with good responses and its role as an intrathecal adjuvant is yet to be explored in this region. This research also aims at investigating whether the combination of intrathecal tramadol with bupivacaine can enhance the quality of spinal anesthesia when compared to bupivacaine alone. This information will help guide dosing, and as simple drugs are more often prescribed, it is likely to set the approach for routine use of the combination in in infra-umbilical surgery. Ultimately, this study will provide the scientific basis for improved anesthesia regimens specific to our population.

METHODOLOGY

The randomized controlled trial was performed in the Department of Anesthesia, Abbasi Shaheed Hospital, Karachi. The sample of 100 patients, 20-60 years of age, ASA physical status I or II, underwent elective infra-umbilical surgery. Exclusion criteria were increased intracranial pressure, severe hypovolemia, coagulation disorders, height below 150

cm, local infection at the site of the spinal injection, allergy to trial drugs, emergency operation or pregnancy or lactation. The subjects were divided into two groups by random method Group A bupivacaine alone 50 patients and Group B bupivacaine with tramadol 50 patients, by non-probability consecutive sampling manner.

Baseline demographics were completed after consent had been obtained in writing. Heart rate, non-invasive arterial blood pressure and oxygen saturation measurements were recorded pre-induction of spinal anesthesia and at regular intervals during the operation in the OR. Venous access was established with an 18-gauge intravenous cannula, and the patients were preloaded with Ringer's Lactate (10 ml/kg) before spinal anesthesia induction. Spinal anesthesia was performed in the sitting position in the space of the L3-L4 vertebrae with a 25 G Quincke needle, using the aseptic method. Group A received 2 ml (10 mg) of 0.5% hyperbaric bupivacaine and 1 ml normal saline and in Group B, 2 ml (10 mg) of 0.5% hyperbaric bupivacaine+1 ml (25 mg) tramadol was given.

The main superordinate ones were analgesia, sensory and motor blockade after IT injection of the study drugs. Efficacy related to analgesia was evaluated using time to first rescue analgesia, defined as interval from intrathecal injection to the time that the rescuer analgesia was needed after intrathecal injection for patients with a Visual Analogue Scale (VAS) score greater than 4. Block initiation time was defined as the time from injection until the patient achieved sensory blockade at the T10 level as confirmed by loss of sensation to pinprick at that level. Motor block was evaluated by the interval between injection time and the occurrence of Bromage Grade II motor block, a motor block that is only partial and would affect movement of lower limb without a normal tone.

Vital signs were also monitored throughout the operative procedure. Visual Analog Scale was applied postoperatively at 15-minute intervals for the first 2 hours, 30-minute intervals in the next 4 hours, and hourly during the following 16 hours. If the patient had a VAS score >4, rescue analgesia was applied and the time to the first rescue analgesia was recorded.

"SPSS software version 26.0 was employed for statistical analysis. To compare outcomes and complications between groups, the independent samples t-test and Chi-square test were utilized, with a significance threshold set at 5% ($P < 0.05$)."

RESULTS

The initial characteristics of participants in groups A and B are outlined in Table I, with each group consisting of 50 individuals. The mean age was 41.82 ± 14.58 years in Group A and 42.66 ± 13.72 years in Group B. Group A exhibited a higher average Body Mass Index (BMI) of 27.96 ± 5.28 kg/m² compared to Group B's 26.88 ± 4.67 kg/m². In Group A, 34 participants (68.0%) were male and 16 (32.0%) were female, whereas Group B comprised 37 males (74.0%) and 13 females (26.0%).

Table II outlines the outcome comparisons and adverse events between Groups A and B. A statistically significant difference was observed in the mean duration required for sensory block onset: Group B had a time of 3.10 ± 1.24 minutes, and Group A had 3.88 ± 1.69 minutes ($P = 0.010$). The time to achieve motor block was notably shorter in Group B (5.13 ± 1.19 min) than in Group A (5.60 ± 1.12 min, $P = 0.034$). Analgesia duration was slightly extended in Group A (5.38 ± 1.78 hours) relative to Group B (4.88 ± 1.63 hours), although this difference lacked statistical significance ($P = 0.147$).

No significant group differences were detected in visual analogue scale (VAS) scores at 2, 6, and 24 hours. However, at the 12-hour mark, Group A reported lower pain scores than Group B (2.10 ± 0.93 vs. 2.72 ± 1.05, $P = 0.002$).

Regarding adverse effects, hypotension occurred in 22.0% of Group A and 14.0% of Group B. Nausea was noted in 26.0% and 16.0% of participants in Groups A and B, respectively. Fever and shivering were more prevalent in Group A (10.0% and 6.0%) than in Group B (6.0% and 18.0%). However, all these differences in rate of complications did not reach statistical significance.

Table I: Baseline characteristics of the patients (n=100)	
Variables	**Groups**

		A (n=50)	B (n=50)
Age in years, Mean ± SD		41.82 ± 14.58	42.66 ± 13.72
BMI in kg/m², Mean ± SD		27.96 ± 5.28	26.88 ± 4.67
Gender	Male, *n* (%)	34 (68.0)	37 (74.0)
	Female, *n* (%)	16 (32.0)	13 (26.0)

Table II: Comparison of Outcomes and Complications Between the Groups (n=100)

Mean Onset time		Groups			P-Value
		A (n=50)	B (n=50)	95% C. I	
Sensory Blockade in mins, Mean ± SD		3.88 ± 1.69	3.10 ± 1.24	0.188~~1.372	0.010*
Motor Blockade in mins, Mean ± SD		5.60 ± 1.12	5.10 ± 1.19	0.039~~0.961	0.034*
Duration of Analgesia in hr, Mean ± SD		5.38 ± 1.78	4.88 ± 1.63	-0.179~~1.179	0.147
Visual Analogue Scale (VAS)	At 2 hr	2.88 ± 1.28	3.14 ± 1.22	-0.760~~0.240	0.304
	At 6 hr	3.12 ± 1.36	3.42 ± 1.37	-0.843~~0.243	0.276
	At 12 hr	2.10 ± 0.93	2.72 ± 1.05	-1.014~~ -0.226	0.002*
	At 24 hr	1.94 ± 0.84	1.98 ± 0.84	-0.375~~0.295	0.813
Complications, *n* (%)					
Hypotension		11 (22.0)	7 (14.0)	0.611~~4.912	0.298
Nausea		13 (26.0)	8 (16.0)	0.689~~4.941	0.220
Fever		5 (10.0)	3 (6.0)	0.393~~7.713	0.357
Shivering		3 (6.0)	9 (18.0)	0.074~~1.147	0.061

DISCUSSION

The aim of the present study was to assess and compare the clinical efficacy of IT administration of bupivacaine-tramadol mixture and bupivacaine alone for infra-umbilical surgeries. Primary variables noted were onset of sensory and motor block, analgesia time and post-operative pain using VAS at different time points.

We noted a statistically faster onset of both sensory (3.10 ± 1.24 and 3.88 ± 1.69; p=0.010) and motor blocks (5.10 ± 1.19 and 5.60 ± 1.12; p=0.034) for the group treated with bupivacaine-tramadol compared with the bupivacaine group. These results are consistent with the survey by Bozdar et al. [11] who compared tramadol and buprenorphine as intrathecal adjuvants to bupivacaine and found similar onset of sensory (3.4 ± 2.84 vs 3.0 ± 0.48; p=0.005) and motor blockade (5.6 ± 0.48 vs 5.0 ± 1.84; p=0.005) in the tramadol group. Similarly, Siddiq et al. [12] Faster onset for both blockades in the buprenorphine group than the tramadol group was also reported by them, further stressing the possibility that tramadol could facilitate a faster onset when used as an adjuvant.

As to the duration of analgesia, there was no statistical difference in our study (5.38 ± 1.78 vs. 4.88 ± 1.63; p=0.147). These findings are consistent with those of Siddiq et al. [12], who observed no difference in the length of analgesia between bupivacaine-tramadol (4.51 ± 2.84) and bupivacaine-buprenorphine (4.94 ± 4.1; p=0.52). In contrast, Bozdar et al. [11] found that based on dose and response within the two groups, analgesia time was a statistically significantly longer for the tramadol group (5.24 ± 5.3 versus 4.98 ± 4.9; p=0.05).

With regard to postoperative pain, assessed by VAS scores, there was no significant difference between the two groups at 2 hours (2.88 ± 1.28 vs. 3.14 ± 1.22; p=0.304), 6 hours (3.12 ± 1.36 vs. 3.42 ± 1.37;

p=0.276) and 24 hours (1.94 ± 0.84 vs. 1.98 ± 0.84; p =0.813), as well as 48 hours post operation (1.82 ±0.59 vs.1.76 ± 0.58; p =0.319). However, there was a statistically significant difference at 12 h (2.10 ± 0.93 vs. 2.72 ± 1.05; p=0.002) in favour of lower scorer in bupivacaine-only group. In comparison, Bozdar et al. [11] found significantly different VAS scores at 2, 6, and 12 hours in favor of tramadol, but not at 24 hours. Siddiq et al. [12] also reported lower VAS scores in group buprenorphine at 2 and 12 hours, vouching the superiority of buprenorphine over tramadol at some time intervals.

Under such chancy scenarios as these, our different average therapeutic effect for VITP may be attention to these average differences at different studies, and support that each drug should be chosen based on patient characters and surgical conditions. For example, Meena et al. [13] proved the effectiveness of tramadol as a chloroprocaine adjuvant, with positive sensory block and analgesic results. However, such an analgesic profile was not markedly extended when compared to other drugs. Similarly, Poovathai et al. [14] compared intrathecal tramadol with magnesium sulphate and reported that although intrathecal tramadol satisfactorily controlled shivering, it was not superior for prolongation of analgesia.

In contrast, other intrathecal adjuvants such as midazolam and fentanyl, studied by Nayak and Ninave [15] potentiated post-operative analgesia to a greater extent with bupivacaine. Shravani et al. [16] too found dexmedetomidine and dexamethasone to be superior as an adjuvant for infra-umbilical surgeries in children. Furthermore, Nadaf et al. [17] further established that different doses of intrathecal bupernorphine resulted in longer duration of analgesia and better quality of block.

The findings of our study and those in the literature [11–17] suggest that, although the intrathecal tramadol may accelerate the onset of anesthesia, its effect on the duration of analgesia and pain score isn't monotonous and less effective than that of other adjuvants such as buprenorphine, midazolam, and dexmedetomidine.

This randomized controlled trial was well done; few limitations, however, need to be highlighted. One of major limitation is that being non-probability consecutive type of sampling, may bring selection bias, and findings may not be generalized to the wider population. Moreover, there was the study design that not considered some the potential influence such as the difference of anxiety level between patients, intraoperative stress response, pain threshold, that may have an effect on parameters like VAS and the analgesic requirements.

A further limitation is that the follow-up duration is only 24 hours and which suffice for evaluation of short-term analgesic effects, but may not last long enough to capture late-onset adverse events or long lasting analgesic effects of TEA. In addition, the s did not report longer term follow-up, so conclusions regarding sustained efficacy and patient satisfaction cannot be made.

Notwithstanding these limitations, the study has several strengths. The randomization of patients and the uniform anesthesia administration procedure contributed to comparison of patients between the two groups. The employment of a fixed dose of bupivacaine and tramadol, and standardised intraoperative and postoperative monitoring also contributed to the internal validity of this study.

Recommendation Future research should include a randomized probability sampling method and procedures, because generalisability can be increased. Furthermore, increasing the sample size and mixing the patient population and prolonging the postoperative follow-up period and other patient reported outcomes like satisfaction and functional recovery would give a complete picture of clinical efficacy of tramadol as adjuvant to spinal anaesthesia.

CONCLUSION

The research indicates that the administration of intrathecal tramadol as an adjunct to bupivacaine significantly enhances the rapidity of both sensory and motor blockades in individuals undergoing infra-umbilical surgical procedures. Nevertheless, it does not yield a statistically significant extension in the duration of analgesia, nor does it alleviate postoperative pain scores when compared to bupivacaine administered independently. These findings substantiate the potential application of tramadol for expedited block onset without jeopardizing safety or the efficacy of analgesia.

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