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The Use of Intrathecal Tramadol as an Adjuvant in Subarachnoid Block to Extend the Duration of Analgesia

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ABSTRACT

Objective

To determine the effectiveness of tramadol as an adjuvant intrathecally in the subarachnoid block for extending the duration of pain relief. **Background:** Pain-free surgery and post-operative pain have always been a critical situation in post-operative care. The subarachnoid block, which is a commonly utilized regional anesthetic procedure, can also be improved by the use of adjuvants. The focus of our study is to investigate the impact of intrathecal tramadol in the subarachnoid block on extending postoperative analgesia. **Methodology:** The study is carried out at DHQ Hospital Gujranwala, Pakistan. It was a randomized clinical trial in which 150 patients were chosen and placed into 2 groups. Bupivacaine alone was administered to group A people. The second group, designated as the tramadol group, was administered intrathecal tramadol in addition to bupivacaine. **Results:** The tramadol group experienced a much longer period of analgesia than the bupivacaine alone group. The average amount of time that the tramadol group had analgesia was 153 ± 41.3 minutes, while the bupivacaine group experienced it for 117 ± 24.7 minutes. **Conclusion:** To increase the timespan of analgesia, our study concludes that tramadol can be safely and effectively employed in the subarachnoid block as an adjuvant.

INTRODUCTION

The issues of postoperative pain and pain-free surgery continue to be among the primary obstacles that patients face after undergoing inpatient or outpatient surgical procedures[1]. One of the most unfavorable outcomes of surgical procedures is postoperative pain, which, if not properly handled, can result in a prolonged recovery period and an extended stay in the hospital[2]. A wide variety of adverse acute and chronic outcomes may be brought about by postoperative pain that is not under control[3].

Wherever possible, regional anesthesia methods have been employed for both intraoperative anaesthesia and postoperative analgesia[4]. The goal of administering regional anesthesia is to alleviate or prevent pain by inserting an anesthetic into a peripheral nerve and then blocking its transmission[5]. The inherent benefits of regional anesthesia over general anesthesia are contributing to its rising popularity around the globe[6]. It reduces the likelihood of pulmonary aspiration, nausea, vomiting, airway damage, hypoxia, respiratory depression, and other problems that can arise with general anesthesia, which is why it is often used for orthopedic surgeries[7].

In this regard, spinal anesthesia has brought about a revolution in the field of anesthesia. In the case of lower abdominal procedures, it is the anesthetic method most often employed. It is better than general anesthesia for most of the lower limb and lower abdominal procedures. Due to its low failure rate, quick onset, thick blockage, and ease of administration, spinal anesthetic has seen an unprecedented increase in its use[3, 8, 9]. The subarachnoid block is widely used anesthetic technique for lower limb procedures because of the fact that it is less expensive and has a lower incidence of significant postoperative problems[10]. The pharmacologic characteristics of the substance determine which local anesthetic is used in the subarachnoid block. For the purpose of reducing pain during and after surgery, intrathecal injections of various medicines have been utilized. Among them, bupivacaine is by far the most popular. As a local anesthetic, bupivacaine is available in both hyperbaric and plain versions used for spinal anesthesia. There are three concentrations available: 0.25%, 0.5%, and 0.75%[11, 12].

The advancements in multimodal and Enhanced Recovery After Surgery (ERAS) protocols have made adjunct therapies more popular in treating and managing postoperative pain. Opioids were once the mainstay of postoperative pain treatment[13]. Because of their synergistic impact, adjuvants and additives are frequently used in conjunction with local

anesthetics for increasing the period of sensory-motor block while reducing the overall dose required[14]. Bupivacaine has been used with both opioids and non-opioid adjuvants in order to extend the duration of its effects, maintain stable hemodynamics, and provide prolonged postoperative analgesia[15]. The majority of opioids have been administered intrathecally as adjuvants[16]. In 1884, Koller anesthetized the conjunctiva with cocaine drops, marking the first documented use of a local anesthetic medication to deliver surgical anesthesia. As a result, cocaine became widely used in clinical settings, although the reports of harmful consequences and fatalities subdued the early excitement[17]. Using opioids, clonidine, dexmedetomidine and neostigmine with bupivacaine in spinal anesthesia has been shown to extend the time that pain relief lasts[16, 18].

The drug tramadol is readily available and is often used as an adjuvant[19]. Tramadol, an analogue of codeine based on synthetic 4-phenylpiperidine, operates via a distinct mechanism. It primarily stimulates μ-opioid receptors but also slightly increases activity at δ and κ receptors. By reducing the uptake of serotonin and norepinephrine from nerve endings, it stimulates spinal pain suppression through a non-opioid mechanism and, when paired with peripheral regional nerve blocks, it increases the efficacy of regional anesthetics. Because of its relatively small μ receptor affinity, it has a significantly lower respiratory depressive impact compared to opioids[20, 21]. It was discovered in a study that the tramadol administration (20 milligrams) along with bupivacaine (0.5 percent) through the intrathecal route could extend the duration of analgesia following surgical procedures. Twenty milligrams of tramadol and fifteen milligrams of 0.5% hyperbaric bupivacaine produced much longer-lasting analgesia than intrathecal bupivacaine alone, according to the study[22].

There is a lack of study in Pakistan about the use of tramadol in the subarachnoid area. Though, it is frequently used as an intravenous analgesic and has a significant number of beneficial outcomes and very few adverse effects. Our research aims to improve spinal anesthesia by introducing tramadol as a safe adjuvant for regular use.

MATERIALS AND METHODS

The study was conducted at DHQ Hospital Gujranwala, Pakistan with the goal to assess the safety and effectiveness of tramadol adjuvant via intrathecal route in the SAB for increasing the extent of analgesia. It is a randomized clinical trial. This research includes 150 patients of status ASA I and ASA II. They are placed into two groups. Group A patients (n=75) received bupivacaine alone while the Group B (n=75) received tramadol along with bupivacaine in the

subarachnoid block. Ethical guidelines were kept in consideration while investigating our research. Patients' privacy and confidentiality remained intact. Consent forms were obtained from all of the participants of study.

Patients aged between 25 and 75 years were enlisted and undergone research. No statistical significant difference was present among participants' demographical variables. This study excluded participants who had contraindications to spinal anesthesia or a history of hypersensitivity to the medications. Prior to the surgical procedure, patients were maintained in a state of fasting for a duration of 6 to 7 hours and were closely monitored. The patients' vital signs were assessed and noted down prior to the administration of spinal anesthetic. An intravenous (IV) line was successfully established. Ringer lactate RL was given to each of the patients before anesthesia is induced. While the patient was seated, a Quincke spinal needle of 25 gauge was inserted at the level of the third and fourth vertebrae to administer anesthesia. Patients in group A were given 12.5 milligrams of 0.5-percent bupivacaine, and group B patients received 25 milligrams of tramadol along with the 12.5 milligrams of 0.5-percent bupivacaine.

Table I: Demographical data of both groups

Variables	**Group A (n=75)**	**Group B (n=75)**	**P value**
Age (Yrs.)	44.45 ± 14.82	44.86 ± 13.04	0.856
Gender distribution Male Female	 37 (49.3%) 38 (50.7%)	 39 (52%) 36 (48%)	 0.744

A pin prick test in the mid-clavicular line was performed after every minute to check the sensory block until it hit the T10 level. The Sensory block was assessed then after every 2 minutes using the same procedure until the peak sensory block level (PSBL) is achieved. Patients were asked about quality of analgesia at the end of surgery. The time at which the initial request for an analgesic dose was made was used as the designated time limit for that group, and rescue analgesia was administered accordingly. Post-operatively, the initial 24-hours administration of analgesia was properly documented.

Using SPSS, data was analyzed properly. Data was presented as percentage for qualitative factors and mean ± standard deviation for the quantitative parameters. Chi-square tests were used for nonparametric data and Student's unpaired t-tests for parametric data. Statistical significance was 0.05 or less.

RESULTS

The tramadol group experienced a much longer period of analgesia as compared to the bupivacaine group as shown in the table II. The average amount of time that the tramadol group had analgesia was 153 ± 41.3 minutes, while the bupivacaine group experienced it for 117 ± 24.7 minutes. The group that received tramadol, as shown in that table II below, experienced an average time of 1.7 ± 0.87 minutes to attain the peak sensory block level, and the group that received bupivacaine alone reported a time of 2.8 ± 1.4 minutes.

Table II: Spinal block characteristics among both groups

Variables	Group A	Group B	P value
Time for first analgesia request (minutes)	117 ± 24.7	153 ± 41.3	< 0.001
Time for peak sensory block level (minutes)	2.8 ± 1.3	1.7 ± 0.87	< 0.001
Peak sensory block level T10 T9 T8 T7 T6	 9 14 24 26 2	 7 14 20 25 9	0.278
Quality of anesthesia Excellent Good Fair Poor	 27 16 26 6	 32 31 11 1	0.02

The tramadol group also attained a much higher level of sensory block. More than fifty percent of people who received tramadol reached sensory block levels greater than T8. Table-II exhibits percentages sensory block level in patients of both groups. In addition, the quality of the anesthetic was evaluated between both groups. It is seen that more patients in Group B have excellent quality anesthesia compared to Group A, where more patients have fair quality anesthesia.

DISCUSSION

A breakthrough in postoperative analgesia began with the finding of opioid receptors.[23]. In order to alleviate the pain (both chronic and acute), opioids are commonly prescribed as therapeutic medicines[24]. A higher degree blockade and longer postoperative analgesia can be achieved by injecting opioids intrathecally, either alone or in conjunction with local anesthetic. Adjuvants have included many opioids (e.g., morphine, buprenorphine, hydromorphone, fentanyl, sufentanil, tramadol) and non-opioid medications (e.g., clonidine, ketamine, neostigmine, and midazolam). Fentanyl is the intrathecal opioid that is most often utilized in day cases[25, 26].

Recent research indicates that tramadol may also work as a local anesthetic for less invasive procedures[27]. After an epidural injection of tramadol, the patient will continue to experience clinical analgesia for up to 10 hours. It exhibits the terminal elimination half-life of 5 to 6 hours[28]. The centrally acting opioid tramadol's analgesic effects are well-known. Using tramadol epidurally has been demonstrated in clinical trials to offer longer-lasting analgesia avoiding typical opioid adverse reactions[22].

Nagpal et al. carried out a research according to which bupivacaine along with tramadol in a supraclavicular brachial plexus block accelerates the onset of the block and prolongs the continuance of the motor blockade. Additionally, it put off the need for the initial dosage of painkiller to be delivered postoperatively without creating any adverse effects, in contrast to the group that received tramadol through systemic administration and the control group[21].

Another study by Baraka et al. found that epidural tramadol can offer long-lasting postoperative analgesia without clinical respiratory depression[29].

Delilkan and Vijayan concluded that administering tramadol hydrochloride via the epidural route effectively relieved postoperative pain. The results demonstrated its efficacy in providing pain relief after surgery[30].

Tramadol, in conjunction with bupivacaine, has been shown in a number of studies to be an effective analgesic and anesthetic adjunct during spinal anesthesia. Hussain A. performed an investigation on the intrathecal tramadol effects on orthopedic patients, which found that the drug greatly prolonged the duration of pain relief and generated little side effects[31].

The research conducted by Chakraborty et al. provides support for our findings. They discovered that compared to intrathecal bupivacaine alone, the combination of twenty milligrams of tramadol and 15 milligrams of 0.5% hyperbaric bupivacaine produced increased durations of analgesia[22].

Regmi and Sapkota performed a study. In this study, it was found that 0.25% Bupivacaine can be mixed with 1 mg/kg tramadol to make caudal analgesia last longer in children who are having lower extremity surgery or lower abdominal avoiding the number of adverse effects[32].

According to Dalvi and Patil's study, sensory and motor blockade lasts longer when 25 µg of fentanyl is added to 2.5 milliliters of 0.5% hyperbaric bupivacaine, as opposed to when 25 mg of tramadol is added to the same amount of 0.5% hyperbaric bupivacaine, which contradicts our initial findings[26].

The findings of Zahid et al. provided a considerable boost to our investigation. According to the findings of their research, it was demonstrated that anesthesia duration was considerably extended in the group that was administered tramadol, which was 181.56 ± 12.42 minutes, and it was 120.93 ± 15.54 minutes in the group that was administered bupivacaine alone. This research generated results that were quite comparable to our research[3].

The quality of the blockade is greatly improved and, more critically, the length of the blockade is prolonged for surgery when 25 milligrams of tramadol and 12.5 milligrams of 0.5% bupivacaine are added to a subarachnoid block. However, it is necessary to do further study that includes multiple doses and an extended follow-up period in order to find out the best dose of tramadol for administration through intrathecal route and to evaluate its optimal safety profile.

CONCLUSION

Considering the findings of our research, it has been shown that tramadol can be utilized with safety and effectiveness in the subarachnoid space for the purpose of increasing the duration of analgesia. Tramadol appears to be an excellent option for intraoperative anesthetic and post-operative analgesia when administered through the intrathecal route. 25 milligrams of tramadol is a safe dose that has very little risk of adverse reactions, additional research should be made in order to enhance the anesthesia quality and patient care, and to provide patients with an experience that is free of pain.

REFERENCES

1. Mitra, S., et al., *New Advances in Acute Postoperative Pain Management.* Current Pain and Headache Reports, 2018. **22**(5): p. 35.
2. Wels, D., *Management of postoperative pain.* South african family practice, 2012. **54**(3): p. S25-S28.
3. Zahid, F., H.M. Tarar, and M.T.M. Tariq, *Intrathecal tramadol as an adjuvant in subarachnoid block to prolong the duration of analgesia.* Pakistan Armed Forces Medical Journal, 2017. **67**(4): p. 534-39.
4. Grandhe, R., J. Wig, and L. Yaddanapudi, *Evaluation of bupivacaine-clonidine combination for unilateral spinal anaesthesia in lower limb orthopedic surgery.* Journal of Anaesthesiology Clinical Pharmacology, 2008. **24**(2): p. 155-158.
5. Folino, T.B. and S.K. Mahboobi, *Regional Anesthetic Blocks*. 2023, StatPearls Publishing, Treasure Island (FL).
6. Khanduri, K., *Regional anaesthesia techniques for orthopaedic surgery.* Medical journal armed forces India, 2008. **64**(2): p. 108-110.
7. Kamel, I., M.F. Ahmed, and A. Sethi, *Regional anesthesia for orthopedic procedures: What orthopedic surgeons need to know.* World J Orthop, 2022. **13**(1): p. 11-35.
8. Kolawole, I.K. and B.O. Bolaji, *Subarachnoid block for lower abdominal and lower limb surgery: UITH experience.* Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria, 2002. **11**(4): p. 153-155.
9. Joshi-Khadke, S., et al., *Efficacy of spinal additives neostigmine and magnesium sulfate on characteristics of subarachnoid block, hemodynamic stability and postoperative pain relief: A randomized clinical trial.* Anesth Essays Res, 2015. **9**(1): p. 63-71.
10. Malhotra, A., et al., *Efficacy of premixed versus succedent administration of fentanyl and bupivacaine in subarachnoid block for lower limb surgeries: A randomised control trial.* Indian J Anaesth, 2020. **64**(Suppl 3): p. S175-s179.
11. Shafiei, F.T., R.K. McAllister, and J. Lopez, *Bupivacaine.* 2018.
12. Heng Sia, A.T., et al., *Hyperbaric Versus Plain Bupivacaine for Spinal Anesthesia for Cesarean Delivery.* Anesthesia & Analgesia, 2015. **120**(1): p. 132-140.
13. Mitra, S., et al., *New advances in acute postoperative pain management.* Current pain and headache reports, 2018. **22**: p. 1-11.
14. Swain, A., et al., *Adjuvants to local anesthetics: Current understanding and future trends.* World J Clin Cases, 2017. **5**(8): p. 307-323.
15. Liu, S.S. and S.B. McDonald, *Current issues in spinal anesthesia.* The Journal of the American Society of Anesthesiologists, 2001. **94**(5): p. 888-906.
16. Routray, S.S., et al., *Comparison of Intrathecal Clonidine and Fentanyl as Adjuvant to Hyperbaric Bupivacaine in Subarachnoid Block for Lower Limb Orthopedic Surgery.* Anesth Essays Res, 2017. **11**(3): p. 589-593.
17. Wiles, M. and M. Nathanson, *Local anaesthetics and adjuvants–future developments.* Anaesthesia, 2010. **65**: p. 22-37.
18. Gupta, A. and U. Saha, *Spinal anesthesia in children: A review.* J Anaesthesiol Clin Pharmacol, 2014. **30**(1): p. 10-8.
19. Allene, M.D., et al., *The effectiveness of adding tramadol versus fentanyl as an adjuvant to bupivacaine on brachial plexus block: A double blind, randomized controlled trial.* International Journal of Surgery Open, 2020. **24**: p. 85-90.
20. Ghazaly, H.F., et al., *Fentanyl versus tramadol as an adjunct to bupivacaine in ultrasound-guided supraclavicular brachial plexus blockade: pros and cons.* Anaesthesia, Pain & Intensive Care, 2021. **25**(4): p. 450-457.
21. Nagpal, V., et al., *Comparative study of systemically and perineurally administered tramadol as an adjunct for supraclavicular brachial plexus block.* Journal of Anaesthesiology Clinical Pharmacology, 2015. **31**(2): p. 191-195.

22. Chakraborty, S., J. Chakrabarti, and D. Bhattacharya, *Intrathecal tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after major gynecological surgeries.* Indian J Pharmacol, 2008. **40**(4): p. 180-2.
23. Gilbert, P.E. and W.R. Martin, *The effects of morphine and nalorphine-like drugs in the nondependent, morphine-dependent and cyclazocine-dependent chronic spinal dog.* J Pharmacol Exp Ther, 1976. **198**(1): p. 66-82.
24. Paul, A.K., et al., *Opioid Analgesia and Opioid-Induced Adverse Effects: A Review.* Pharmaceuticals (Basel), 2021. **14**(11).
25. Cosgrave, D., et al., *Intrathecal opioids.* Pain tutorial.[online], 2017.
26. Dalvi, N.P. and N. Patil, *Comparison of effect of intrathecal fentanyl-bupivacaine and tramadol-bupivacaine combination on postoperative analgesia in lower abdominal surgeries.* Journal of Research & Innovation in Anesthesia, 2010. **1**(2): p. 35-40.
27. Altunkaya, H., et al., *The Postoperative Analgesic Effect of Tramadol When Used as Subcutaneous Local Anesthetic.* Anesthesia & Analgesia, 2004. **99**(5): p. 1461-1464.
28. Prosser, D., et al., *Caudal tramadol for postoperative analgesia in pediatric hypospadias surgery.* British journal of Anaesthesia, 1997. **79**(3): p. 293-296.
29. Baraka, A., et al., *A comparison of epidural tramadol and epidural morphine for postoperative analgesia.* Canadian Journal of Anaesthesia, 1993. **40**(4): p. 308-313.
30. Delilkan, A. and R. Vijayan, *Epidural tramadol for postoperative pain relief.* Anaesthesia, 1993. **48**(4): p. 328-331.
31. Hussain, A., et al., *Intrathecal Tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after lower limb orthopedic Surgeries.* Indian J Appl Res, 2016. **6**: p. 4-6.
32. Regmi, U.K. and S. Sapkota, *Efficacy of tramadol as an adjuvant to bupivacaine for caudal analgesia in children: a randomised controlled trial.* Journal of Society of Anesthesiologists of Nepal, 2017. **4**(1): p. 11-15.