

Anelgesic Efficacy of Intra-Thecal Tramadol as a Spinal Adjunct to 0.5% Heavy Bupivacaine in Lower Abdominal Surgery

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Article received: July 30 2020

Article accepted: Sep 1 2020

ABSTRACT:

Introduction: Hyperbaric Bupivacaine is the most widely used local anesthetic. A number of adjuvants have been used with local anesthetic agents in order to improve the quality and duration of analgesia and anesthesia. This study was carried out to assess the efficacy of intrathecal Tramadol as a spinal adjunct to prolong the duration of spinal anesthesia in lower abdominal surgeries.

Materials and Methods: Sixty patients aged between 18 to 80 years, were randomly divided into two groups - Tramadol and Placebo group. Spinal anesthesia was given by using 25 Gauge Quinke spinal needle in sitting position with midline approach. Patients belonging to Tramadol group received 3 ml of 0.5% Bupivacaine along with 0.5 ml of Tramadol (25mg) and patients belonging to Placebo group received 3 ml of 0.5% Bupivacaine along with 0.5 ml of Normal Saline. In the postoperative ward, duration of analgesia was assessed by the time when first rescue analgesia was given. Visual Analogue Scale for pain was noted at the time of rescue analgesia. The total amount of opioid consumed over 24 hour postoperative period was noted. Hemodynamic like heart rate, systolic, diastolic and mean arterial blood pressures were also noted. Data were analyzed using independent t-test for continuous variables and chi-square test for categorical variables, p value <0.05 was considered significant.

Results: The two groups were comparable with respect to age, weight, sex, ASA grading and duration of surgery. Mean duration of effective analgesia was 231.53 ± 22.00 min in Tramadol group and 125.40 ± 8.86 min in Placebo group ($p = 0.001$). The mean total amount of opioid consumption in 24 hours postoperative period was 145.00 ± 30.31 mg in Tramadol group and 171.67 ± 36.39 mg in Placebo group ($p = 0.003$). Mean of Heart rate, systolic, diastolic and mean arterial blood pressures were not significant between the two groups. Incidence of nausea and vomiting was statistically significant between the two groups with a p value of 0.010. Hypotension and bradycardia was statistically not significant between the two groups.

Conclusion: Tramadol was effective adjuvant to hyperbaric bupivacaine for intrathecal use to increase the duration of spinal anesthesia in patients undergoing lower abdominal surgeries.

Keywords: Analgesic, Spinal Anesthesia, Tramadol.

Spinal anesthesia is a form of a regional anesthesia in which local anesthetic drug is injected into subarachnoid space.¹ It greatly expands the anesthesiologist's armamentarium, providing alternatives to general anesthesia when appropriate. This may also be used combined with general anesthesia or afterward for postoperative analgesia and also for the management of acute and chronic pain.² The popularity of spinal anesthesia is due to the fact that the block has well defined end points and the anesthesiologist can produce a reliable block with a single injection.³

Regional anesthesia is the preferred technique for most of the lower abdominal and lower limbs surgeries. It provides the patient to remain awake and avoids the problems associated with airway manipulation. This technique is simple to perform, virtually devoid of systemic effects and can produce profound and reproducible surgical anesthesia. By altering even a small amount of drug, we can produce varying levels of anesthesia.

According to International Association for the Study of Pain (IASP), pain can be categorized according to several variables, including its duration, pathophysiologic mechanisms (physiologic, nociceptive, neuropathic), and clinical context (postsurgical, malignancy related, neuropathic, degenerative). Nociceptive pain has also been termed inflammatory because peripheral inflammation and inflammatory mediators play major roles in its initiation and development. Postoperative pain is a type of acute nociceptive pain.² Beside this, it is also considered as a transient, reversible type of neuropathic pain.³

Postoperative pain has to be controlled for many reasons. Different techniques have been tried to relieve the postoperative pain associated with surgeries. The cost-effective and reliable technique is to use anaesthetic procedure which can be effective for surgery as well as for postoperative period.

Hyperbaric, isobaric and hypobaric local anesthetics drug can be injected in subarachnoid block. In our hospital we use 0.5% heavy Bupivacaine. Various additives can be added with intrathecal injection of local anesthetics to enhance the effect of spinal anesthesia such as, Opioids (Fentanyl, Sufentanyl, Alfentanyl, Morphine, Pethidine and Tramadol), Clonidine, Neostigmine, Ketamine and Midazolam

Medical Journal of Pokhara Academy of Health Sciences Vol. 3 Issue 2
can be added with 0.5% heavy Bupivacaine

Spinal anesthesia with hyperbaric Bupivacaine is very common and popular method. The identification of opioid receptors has provided new horizons in pain management. Yaksh and Rudy, in 1976, were the first investigators to demonstrate direct opioid analgesia at the spinal cord level.⁴ The discovery of opioid receptors and endorphins in spinal cord soon led to the use of spinal opiates. Morphine was the first opioid administered intrathecally to augment neuraxial blocks.⁵ Side effects like respiratory depression and pruritis has led to development of non-opioid analgesics with less side effects.⁶ Intrathecal Tramadol is being extensively studied as an alternative to neuraxial opioids for pain management and has been proven to be a potent analgesic devoid of most of the opioid related side effects.⁷ Intrathecal opioid administration has been demonstrated to provide effective postoperative analgesia at the cost of an increased risk for respiratory depression.

MATERIALS AND METHODS

This is a randomized prospective double-blind comparative and interventional study done in National Academy of Medical Sciences (NAMS), Bir Hospital and Paropakar Maternity and Women's Hospital, Kathmandu, Nepal during the study period of 12 months from 2012-2013. There were total 60 patients which were included for the study, 30 patients in each group. Inclusion criteria for the patient was as ASA physical status grades of I-II and scheduled for elective lower abdominal surgery with age group between 18 yrs to 80 yrs. Patients who refused the procedure or study were excluded from the study. Any contraindication to spinal anesthesia, history of Coagulopathy, patient on anti platelets therapy, patient with spinal deformity, failure of the procedure, patient with any psychiatric illness that could affect the reliability of clinical assessment, allergy to the study drug and any emergency surgery were excluded from the study.

Approval was obtained from the Institutional Review Board (IRB), NAMS and Research Committee of Paropakar Maternity and Women's Hospital. Patient fulfilling the inclusion criteria were recruited in the study after obtaining written and informed consent. Preoperative evaluation was done with thorough history, physical examination and relevant laboratory investigations. The patients

were randomly divided into two study groups by lottery method as Group AT and Group BS which were drawn by anesthesia assistant not involved in the study.

In group AT (n=30), patients received 3 ml of 0.5% hyperbaric Bupivacaine (15 mg) plus 0.5 ml Tramadol (25 mg), total volume of 3.5 ml intrathecally. In group BS (n=30), patients received 3 ml of 0.5% hyperbaric Bupivacaine (15 mg) plus 0.5 ml of normal saline, total volume of 3.5 ml intrathecally. Principle investigator and the patients were blinded to the study drugs. Assessment of the patient during study period was done by the blinded principle investigator.

In the operation theatre, all the patients had intravenous access with 18 G IV cannula. All patients were hydrated with 500 ml Normal Saline. Then subarachnoid block was performed with 25 G Quincke needle in sitting position at L3-L4 level. Preservative free Tramadol was used (Centradol, 1 ml = 50 mg, batch no TAM 111, Tablets India Limited). The study drug was injected over 10-15 secs after obtaining free flow of CSF. Following that, the patients were immediately placed supine. The level of subarachnoid block was assessed by pin prick along the midclavicular line bilaterally from cephalad to caudal direction. Operative positioning was done after fixation of subarachnoid block. Patient were excluded from the study if the spinal anesthesia failed for which they were given general anesthesia.

Standard monitoring was done which included: pulse oximetry (SpO₂), non invasive blood pressure (NIBP), heart rate (HR), and electrocardiography (ECG) using patient monitor. Pulse and NIBP were measured and recorded every two minutes for the first 10 minutes and then every 15 minutes interval up to 100 minutes. SpO₂ and ECG were monitored continuously throughout the operative period.

Inj. Pethidine 0.5 mg/kg IV was administered as needed for intraoperative breakthrough pain. Hypotension was defined as 20% decrease in systolic blood pressure from the baseline or less than 90 mmHg which was promptly treated with IV fluid bolus and if hypotension persisted, it was treated with 6 mg of injection Mephentermine bolus. HR < 45 beats/min was treated with Atropine 0.3 mg IV as needed.

The degree of pain was assessed by using Visual Analogue Scale (VAS) and duration of analgesia

by the first use of a rescue analgesic after the intrathecal administration of the drug. Total amount of opioid consumed during 24 hours was noted. Injection Pethidine 50 mg intramuscular was given postoperatively for pain management when patients complained of pain and VAS score \geq 4.

Statistical Method:

Data entry and statistical analysis were performed using Microsoft Excel 2007 and SPSS 17. Chi-square test was used for comparing proportions like sex, ASA physical status and incidence of adverse effects. Student's t-test was used for comparing continuous parametric data like age, weight, duration of surgery, heart rate, blood pressure, post operative analgesia duration and total opioid consumption in post operative period. The p value less than 0.05 was taken as significant.

RESULTS

A total of 60 patients of ASA I and II were included in the study. The mean age was 54.10 ± 13.51 years in Tramadol group and 52.37 ± 11.20 years in Placebo group. There was no statistically significant difference in the age distribution ($p = 0.59$). The weight distribution of the patients in both Tramadol group and Placebo group were comparable. There was no statistically significant difference in the weight distribution ($p = 0.24$). Similarly the time of onset of block in both Tramadol and Placebo group were comparable and no statistically significant differences noted ($p = 0.53$). Similarly there was no statistically differences noted for the duration of surgery in both groups, as seen in Table 1.

Table 1: Comparison of demographic variables between the two groups

Demographic Variables	Tramadol Group (Mean \pm SD)	Placebo Group (Mean \pm SD)	p value
Age (yrs)	54.10 \pm 13.51	52.37 \pm 11.21	0.59
Weight (kg)	52.23 \pm 6.36	54.23 \pm 6.88	0.24
Time of onset of block (min)	3.33 \pm 1.37	3.93 \pm 1.94	0.53
Duration of surgery (min)	130.33 \pm 28.58	125.25 \pm 28.97	0.49

There was significant increase in duration of analgesia in Tramadol group as compared to Placebo group ($p = 0.001$). The mean duration of postoperative analgesia was 231.53 ± 22.01 minutes in Tramadol group and 125 ± 8.87 minutes in Placebo group.

The total consumption of Injection Pethidine in postoperative period was 145 ± 30.31 mg in Tramadol group and 171 ± 36.39 mg in Placebo group. There was a significant increase in opioid consumption in postoperative duration in 24 hours in placebo group than in Tramadol group and it was statistically significant with a p value of 0.003.

Table 2: Comparison of Post – operative Inj. Pethidine Requirement between two groups

Variable	Tramadol Group (Mean \pm SD)	Placebo Group (Mean \pm SD)	p value
First rescue analgesic time (min)	231.53 ± 22.01	125.40 ± 8.87	0.001
Total analgesic requirement in 24 hrs (mg)	145.00 ± 30.31	171.67 ± 36.39	0.003

The VAS Score at the time of 1st rescue analgesia between the two groups was assessed. In Tramadol group, 18 patients had VAS score of 4, 10 patients had VAS score of 5, 1 patient had VAS score of 6 and 1 patient had VAS score of 1 at the time of 1st rescue analgesia. In Placebo group, 7 patients had VAS score of 4, 18 patients had VAS score of 5, 3 patients had VAS score of 6 and 2 patients had VAS score of 7 at the time of 1st rescue analgesia. The VAS score of 4 among the two groups was statistically significant with a p value of 0.008. The VAS score of 5 among the two groups was not statistically significant with a p value of 0.069. The VAS score of 6 and 7 among the two groups were not statistically significant with a p value of 0.61 and 1.0 respectively.

Table 3: Comparison of VAS score at 1st rescue analgesia time between the groups

VAS score	Tramadol Group	Placebo Group	P value
4	18 (60.00 %)	7 (23.33 %)	0.008
5	10 (33.33 %)	18 (60.00 %)	0.069
6	1 (3.33 %)	3 (10.00 %)	0.61
7	1 (3.33 %)	2 (6.66 %)	1.0
Total	30	30	

In Tramadol group, out of 30 patients, 17 of them had experience side effects among them 11 of them had nausea and vomiting, 2 of them had hypotension and 4 of them had bradycardia. Similarly in Placebo group out of 30 patients enrolled, 9 of them experiences side effects, out of 9 patients, 2 of them had nausea and vomiting, 1 of them had hypotension and 6 of them had bradycardia. Incidence of nausea and vomiting was more common in Tramadol group than in placebo group, as 11 patient in Tramadol group had nausea and vomiting while 2 patient in placebo group, which was statistically significant ($p = 0.010$). Similarly incidence of hypotension and bradycardia between the two groups was not statistically significant with a p value of 1.00 and 0.50 respectively.

DISCUSSION

Postoperative analgesia has always been a matter of great concern. Regional block techniques and various medications as adjuvants have been tried for the relief of pain, intrathecal Tramadol being one of them. In recent years, the use of intrathecal narcotics has become widespread, at the cost of an increased risk for respiratory depression. Tramadol is a centrally acting analgesic that has minimal respiratory depressant effects as it had 6000 fold decreased affinity for μ receptors compared to Morphine.⁸

Addition of adjuncts to hyperbaric Bupivacaine may change the baricity of Bupivacaine, but the volume of adjunct being small (0.5 ml), it may not change the distribution of drugs in the CSF. Although there was invitro study which suggested that baricity of local anesthetic drug change with addition of spinal adjuncts but there are no clinical studies which suggest the change in baricity to small volume of adjunct influenced the distribution of spinal block as stated by Gunaydin B et al.⁹

We added 25 mg of Tramadol (0.5 ml) in 15 mg hyperbaric Bupivacaine (3 ml) intrathecally for lower abdominal surgeries and found significant increase in duration of analgesia in Tramadol group as compared to Placebo group. The mean duration of analgesia was 231.53 ± 22.01 mins in Tramadol group and 125.40 ± 8.86 mins Placebo group which was statistically significant ($p = 0.001$). Similar findings were observed in study done by Chakraborty S et al, Mankeshwar H J et al, Mustafa M G et al and Khoon A et al.¹⁰⁻¹³ In the study done

by Chakraborty S. et al¹⁰ 20 mg (0.2 ml) Tramadol was added intrathecally along with 15mg (3 ml) 0.5% hyperbaric Bupivacaine in Group A and 0.2 ml of Normal Saline was added along with 15 mg (3 ml) 0.5% hyperbaric Bupivacaine in Group B, in patients scheduled for Wardmayo's operation and Fothergill's operation. They found significantly prolonged duration of postoperative analgesia in Tramadol group. The duration of analgesia was 210 ± 10.12 mins in Bupivacaine only group and in Tramadol group; it was 380 ± 11.82 mins, which was found to be significant ($p < 0.05$). Similarly, Mankeshwar H J et al¹¹ conducted a study in patients undergoing elective gynecological surgery under spinal anaesthesia; Group I ($n = 50$) patients received 0.5 ml Normal Saline and Group II ($n = 50$) patients received 25mg Tramadol intrathecally along with local anaesthetic. They found that intrathecal Tramadol prolonged the duration of analgesia by 5 hrs, 95% CI (4.39-5.61) ($p < 0.0001$).

Similarly in a study done by Khoon A et al¹³ intrathecal Tramadol along with Bupivacaine was used for TURP. Dose of Tramadol were 30 mg, 40 mg and 50 mg along with 2.5 ml of 0.5% Bupivacaine in three different groups. The post operative analgesia duration was 14.69 ± 5.5 hrs, 18.18 ± 6.18 hrs and 19.45 ± 4.66 hrs in three groups respectively. This study showed dose dependent increased in duration of analgesia. Similarly in our study there was increase in post operative analgesia duration but in our study the postoperative analgesia duration was short than their duration. This may be due to the fact that they had used large doses 30 mg, 40 mg and 50 mg but we had used small dose of 25 mg Tramadol with Bupivacaine.

Alhasheimm J A et al¹⁴ compared the intrathecal effects of 25 mg Tramadol (0.5 ml) and Placebo N/S (0.5 ml) with that of 15 mg 0.5% hyperbaric Bupivacaine (3 ml) on post operative pain after transurethral resection of prostate. This study showed that the time to 1st rescue analgesic duration in Tramadol group was 7.6 hours and that in Placebo group was 6.3 hours. There was no different in analgesia duration with addition of Tramadol as compared to Placebo group. In our study addition of Tramadol as adjuncts increased the postoperative analgesia duration by 231 ± 22.01 mins in Tramadol group. This may be due to that, in their study they had taken only TURP cases but in our study we had taken lower abdominal surgeries requiring spinal anesthesia like TURP, TAH, VAH, interval

appendectomy, and inguinal hernia. Due to this there may be different variations in pain perception by the patients as well as the intensity of pain also differs in different procedures.

In our study, the total opioid consumption in 24 hours post operative period was 145.00 ± 30.371 mg in Tramadol group and 171.67 ± 36.397 mg in Placebo group, which was statistically significant ($p = 0.003$). Also the VAS score of 4 at the time of 1st rescue analgesia in Placebo group was statistically significant than in Tramadol group with a p value of 0.008. The 23% of the patients in Placebo group scored lower value of VAS 4 at the time of 1st rescue analgesia and the difference was statistically significant ($p = 0.008$) when compared to 60% of patients receiving the same VAS score in Tramadol group. This means Tramadol group had lower VAS score for pain at the time of analgesia demand than in Placebo group. Similarly, 60% of patients in Placebo group (18 patients) scored higher value of VAS score 5 at the time of 1st rescue analgesia but the difference was not statistically significant ($p = 0.069$) when compared to 33% of patients receiving the same VAS score in Tramadol group (10 patients). Alhasheimm J A et al¹⁴ compared the intrathecal effects of Tramadol and Placebo with that of 0.5% Bupivacaine heavy 3 ml on post operative pain after transurethral resection of prostate. Total Morphine consumption was 9.1 ± 5.5 mg in Tramadol group and 10.6 ± 7.9 mg in Placebo group which was not significant in consumption of opioid between the groups in 24 hours postoperative period. This may be due to that in their study they have taken only TURP cases but in our study we have taken different lower abdominal surgeries. Similarly in a study conducted by Malik A I et al¹⁵ to determine the effectiveness and duration of post operative pain relief after local infiltration of Tramadol in comparison with Bupivacaine in adult hernia surgery. They concluded that locally infiltrated Tramadol provided an improved post operative analgesia in comparison to Bupivacaine and decreased the requirements of post operative analgesics with early patient mobility and discharge. Similarly in a study done by Mustafa M G¹² total analgesic consumed was 2 gm of Paracetamol in Tramadol group and 1 gm mg Paracetamol in Nalbuphine group which was not significant.

Regarding side effects of intrathecal Tramadol in our study, the incidence of nausea and vomiting were more in the Tramadol group as compared

to Bupivacaine only group. In Tramadol group, 11 patients had nausea and vomiting (36.66%) while only 2 patients in sole Bupivacaine group developed nausea and vomiting (6.66%), which was statistically significant ($p = 0.010$). This nausea and vomiting may be attributed due to the effect of Tramadol and not due to effect of hypotension after subarachnoid block as incidence of hypotension was similar in both group ($p = 1.00$). There were no such episodes of nausea and vomiting in studies by Chakraborty S et al¹⁰ and Mankeshwar H J et al.¹¹ Khoon A et al¹³ determine the optimal dose required for intrathecal Tramadol on post operative analgesics and to evaluate the side effects of the various Tramadol dose, 1st group received 30 mg Tramadol, 2nd group received 40 mg Tramadol and 3rd group received 50 mg Tramadol along with 2.5 ml 0.5% hyperbaric Bupivacaine. The incidence of nausea and vomiting were 13.8 % in 1st group, 17.2 % on 2nd group and 34.5% on 3rd group. The incidence of nausea and vomiting in our study was more in Tramadol group than in Placebo group with an incidence of 36.66% and 6.66% respectively. In spite of using low dose of Tramadol 25 mg, our study showed the increased incidence of nausea and vomiting. This may be because they considered incidence of vomiting only but we considered the incidence of nausea and vomiting. The incidence of vomiting might be lower if we considered both nausea and vomiting separately.

LIMITATIONS

- This study involved patients with wide range of age, from 18 – 80 yrs.
- This study involved patients with different diagnosis and surgical procedures, so intensity of pain vary accordingly which may influence effective duration of spinal anesthesia.
- Level of block obtained is not analyzed.

CONCLUSION

This study concludes that 25 mg Tramadol (0.5 ml) when used with 15 mg of 0.5% hyperbaric Bupivacaine (3 ml) intrathecally significantly prolongs postoperative analgesia duration after lower abdominal surgery. It also decreases the post operative opioids consumption in 24 hr postoperative period. Intraoperative haemodynamics are stable upto 100 minutes after subarachnoid block. There is statistically significant nausea and vomiting in Tramadol group as compared to Placebo group.

RECOMMENDATIONS

- Position during the surgery should be of similar type.
- VAS score should be assessed at regular interval throughout the postoperative period.
- Intraoperative fluids should be considered.

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