Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(3) (Part - I): 852-860
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6319.24

Evaluation of low dose Bupivacaine with Tramadol as an Alternative to Conventional dose of Bupivacaine in Spinal Anaesthesia for TURP

Sushma Bandreddy[1], Ravi Madhusudhana[2]

[1]Post Graduate Resident, [2]Professor, Department of Anaesthesiology, Sri Devaraj Urs Medical College, Kolar, Karnataka 563101, India.

Abstract

Context: SAB is safe and effective technique for TURP, offers advantage of easy identification of TURP syndrome, bladder perforations but, associated with hemodynamic changes like hypotension and bradycardia in geriatric patients with coexisting cardiac and respiratory diseases. Hence the study had been undertaken with low dose bupivacaine in combination with tramadol. *Aims:* To evaluate the efficacy of very low dose bupivacaine with tramadol as an alternative to conventional dose of bupivacaine in TURP surgeries. *Settings and Design:* Randomised double blind prospective study. *Methods and Material:* 64 patients scheduled for TURP surgeries, aged 55-75 years with ASA-PS I and II were recruited and randomly divided into 2 groups. Group I-injection bupivacaine 0.5 ml (2.5 mg)+ preservative free tramadol 1 ml (50 mg) diluted with 0.5 ml NS intrathecally. Group II-injection bupivacaine 2 ml (10 mg) intrathecally. *Statistical analysis used:* Data analysis: SPSS 22 version software; Categorical data: frequencies and proportions; Continuous data:mean+ SD. Tests of significance: Chi-square test and independent t test. p value < 0.05: statistically significant. *Results:* Attainment of sensory blockade in group I was slow ie., 8.44 ± 2.35 min compared to that in group II ie., 6.53 ± 1.65 min and the two segment regression is faster in group I ie., 65.38 ± 20.52 min compared that of group II ie., 86.78 ± 36.88 min which were statistically significant. The time for rescue analgesia was significantly higher in group I ie., 312.56 ± 137.42 min compared to group II ie., 256.97 ± 130.46 min. The degree of motor blockade was less in group I. There were no significant changes in heart rate and SpO_2, but the fall in MAP in group II was significant compared to that in group I. *Conclusions:* 50 mg preservative free Tramadol added to intrathecal bupivacaine 2.5 mg offers adequate anaesthesia, stable hemodynamics, early ambulation and prolongs analgesia.

Keywords: Bupivacaine; Spinal Anaesthesia; Tramadol.

How to cite this article:

Sushma Bandreddy, Ravi Madhusudhana. Evaluation of low dose Bupivacaine with Tramadol as an Alternative to Conventional dose of Bupivacaine in Spinal Anaesthesia for TURP. Indian J Anesth Analg. 2019;6(3):852-860.

Introduction

Spinal anaesthesia is a very safe and effective technique for TURP procedures [1]. Advantages with spinal anaesthesia include rapid onset of anaesthesia and muscle relaxation [2]. In TURP procedures spinal anaesthesia offers added advantage of an awake patient with easy identification of complications associated with TURP procedure [3]. Bupivacaine has emerged as a safe drug for spinal anaesthesia administration, it offers prolonged anaesthesia and duration of analgesia.

Corresponding Author: Ravi Madhusudhana, Professor, Department of Anaesthesiology, Sri Devaraj Urs Medical College, Kolar, Karnataka 563101, India.

E-mail: ravijaggu@gmail.com

Received on 05.03.2019, **Accepted on** 04.04.2019

Spinal anaesthesia is associated with hemodynamic changes like hypotension and bradycardia. TURP procedure is usually done in geriatric patients who will be having limited cardiopulmonary reserve and hence they may not be able to tolerate hypotension [4].

Objectives of the Study

To assess the synergistic effect and safety of combination of low dose bupivacaine with tramadol in subarachnoid block for TURP surgeries compared to conventional dose of bupivacaine, regarding

- Onset and duration of sensory blockade.
- Degree of motor blockade
- Haemodynamic parameters
- Time for rescue analgesia
- Any adverse effects associated with drugs.

Materials and Methods

Study Design: This study was a randomized double blind prospective study.

Source of Data: Sixty four Patients admitted for elective TURP Surgeries, were selected for the study under spinal anaesthesia at the Tertiary care centre, during the period from January 2017 to June 2018.

The study was approved by the ethics committee of the institute and valid written informed consent was taken from all the patients. Patients were randomly divided into 2 groups. Randomization was done by simple computer generated randomization.

Method of collection of data

Inclusion criteria: All patients of ASA physical status I and II aged between 55 to 75 years weighing more than 50 kg, posted for elective TURP surgeries under spinal anaesthesia were included in this study.

Exclusion criteria: Infection at site of spinal anaesthesia, bleeding diathesis, patients with history of known allergy to any drugs especially bupivacaine and tramadol, uncontrolled hypertension, cardiac disease, uncontrolled diabetes mellitus, cerebrovascular and neurological disease, renal and hepatic disease, bronchial asthma, drug and alcohol abuse.

Sampling Procedure: After obtaining informed consent, 64 patients were randomly divided into two groups of 32 each. Randomization was done by computer generated table.

All patients were examined a day before surgery and routine investigations were done. Patients were kept fasting overnight after 10:00 pm and received tab. ranitidine 150 mg orally and tab. alprazolam 0.25 mg orally as premedication at night before surgery.

All the patients were preloaded with intravenous (IV) 500 ml of normal saline after securing IV access with 18G cannula. Monitoring included heart rate, blood pressure, ECG and SpO_2. Baseline vital signs were noted.

All the patients were randomly divided into two groups, I and II. Patients were unaware of the group of spinal drug administered. A second anaesthesiologist who was not involved in the study prepared the spinal solution and the anaesthesiologist performing the block was blind to the spinal solution administered. Under strict aseptic precautions, spinal anaesthesia was performed at L3-L4 interspace through a midline approach in lateral position using 26G Quincke Babcock spinal needle. Patients in group I received injection hyperbaric (0.5%) bupivacaine 0.5 ml (2.5 mg) combined with preservative free injection tramadol 1 ml (50 mg) and diluted with 0.5 ml normal saline, total volume made upto 2 ml. Patients in group II received injection hyperbaric (0.5%) bupivacaine 2 ml (10 mg).

The time of intrathecal injection of drug was considered as 0 and the following parameters were observed.

1. Sensory blockade – time taken to attain highest dermatomal level and two segment regression.
2. Motor blockade – bromage score at the time of highest dermatomal level.
3. Time to rescue analgesia.
4. Haemodynamic parameters.
5. Any adverse effects like hypotension, bradycardia, nausea, vomiting, pruritus and shivering associated with drugs.

Sensory blockade was tested with cold swab every 2 min after the subarachnoid block and motor blockade was assessed by modified Bromage scale [5]. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SpO_2 and respiratory rate were recorded every 5 min for 30 min and then every 10 mins throughout the intraoperative period and also at the completion of surgery. The vital signs were recorded at period intervals in post operative period. Pain was assessed using Visual analogue scale [6].

Statistical Analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was presented in the form of frequencies and proportions. Chi-square

was the test of significance. Continuous data was represented as mean and standard deviation. Independent t test was the test of significance to identify the mean difference between two groups. p value < 0.05 was considered as statistically significant.

Sample Size was estimated by using the mean duration of analgesia in hours from pilot study. Mean duration of analgesia in group I was 10 ± 5.78 hours and in group II was 6.2 ± 2.28 hours. Using the values at 95% Confidence limit and 90% power sample size of 29 was obtained in each group. With 10% nonresponse sample size of 29 + 2.9 ≈ 32 cases was the sample size for each group. Hence, 32 patients were included in each group.

Results

It was a prospective clinical randomized controlled double blind study with 64 patients divided randomly into 2 groups of 32 patients each.

Group I – received injection hyperbaric bupivacaine 0.5 ml (2.5 mg) combined with preservative free injection tramadol 1 ml (50 mg) and diluted with 0.5 ml normal saline, total volume made upto 2 ml.

Group II – received injection hyperbaric bupivacaine 2 ml (10 mg).

They were evaluated for onset of sensory blockade, degree of motor blockade, duration for two segment regression, hemodynamic variations, side effects of the drugs if any and time for rescue analgesia.

Statistical Software: The statistical software namely SPSS 18.0 and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel had been used to generate tables [7].

The two groups were matched with respect to age and weight. There was no significant difference in the demographic data between the two groups.

As shown in table 1, highest dermatomal level achieved in group I patients were T_8 in 15, T_{10} in 7 and T_6 in 5 patients. Highest dermatomal level achieved in group II were T_6 in 20 and T_{10} in 5.

As shown in table 2, Bromage scores at highest dermatomal level in group I patients were 2 in twelve, 3 in nine, 1 in seven and 0 in four patients and those in group II patients were 3 in twenty five, 2 in five and 1 in two patients.

As depicted in table 3, Mean onset of sensory blockade among group I patients was 8.44 ± 2.35 min and in group II was 6.53 ± 1.65 min and it was statistically significant (p<0.001).

Degree of motor blockade among group I patients was 1.81 ± 1.00 and in group II was 2.72 ± 0.58 and it was significant with p value < 0.001.

Mean Two segment regression among group I

Table 1: Highest dermatomal level attained distribution in two groups of patients studied

Highest dermatomal level attained	Group I	Group II	Total
T_{10}	7 (21.9%)	5 (15.6%)	12 (18.8%)
T_9	1 (3.1%)	1 (3.1%)	2 (3.1%)
T_8	15 (46.9%)	4 (12.5%)	19 (29.7%)
T_7	1 (3.1%)	2 (6.3%)	3 (4.7%)
T_6	5 (15.6%)	20 (62.5%)	25 (39.1%)
T_5	3 (9.4%)	0 (0%)	3 (4.7%)
Total	32 (100%)	32 (100%)	64 (100%)

Table 2: Bromage Score at highest dermatomal level distribution in two groups of patients studied

Bromage Score at highest dermatomal level	Group I	Group II	Total
0	4 (12.5%)	0 (0%)	4 (6.3%)
1	7 (21.9%)	2 (6.3%)	9 (14.1%)
2	12 (37.5%)	5 (15.6%)	17 (26.6%)
3	9 (28.1%)	25 (78.1%)	34 (53.1%)
Total	32 (100%)	32 (100%)	64 (100%)

Table 3: Comparison of study variables in two groups of patients studied

Variables	Group I	Group II	Total	P value
Time (min) to achieve highest dermatome	8.44±2.35	6.53±1.65	7.48±2.23	<0.001**
Bromage Score at highest dermatomal level	1.81±1.00	2.72±0.58	2.27±0.93	<0.001**
Two segment regression (Min)	65.38±20.52	86.78±36.88	76.08±31.51	0.006**
Time for rescue analgesia (Min)	312.56±137.42	201.38±96.56	256.97±130.46	<0.001**

patients was 65.38 ± 20.52 min and in group II was 86.78 ± 36.88 min, which was longer in group II compared to that in group I and it was statistically significant (p<0.006).

Time for first request of analgesic dose was shorter in Group II ie., 201.38 ± 96.56 min compared to that in Group I ie., 312.56 ± 137.42 min, and the difference was statistically significant (p<0.001).

Hemodynamic variables

Heart rate was comparable in both the groups throughout the monitoring period. There was no significant difference in changes in oxygen saturation between both the groups.

Variations in mean arterial pressures were comparable in both the groups upto 5 min after the subarachnoid block. There was significant drop in mean arterial pressures after 10 min after subarachnoid block till 90 min in group II compared to that in group I patients.

Visual Analogue Scale (VAS) Scores

Most of the patients in group I showed VAS scores of 1-3 and those in group II showed 3-6 and the difference was statistically significant with p value < 0.001.

Side Effects

Table 4: Side Effects distribution in two groups of patients studied

Side Effects	Group I (n=32)	Group II (n=32)	Total (n=64)
No	28 (87.5%)	28 (87.5%)	56 (87.5%)
Yes	4 (12.5%)	4 (12.5%)	8 (12.5%)
Hypotension	1 (3.1%)	4 (12.5%)	5 (7.8%)
Bradycardia	1 (3.1%)	0 (0%)	1 (1.6%)
Nausea	1 (3.1%)	0 (0%)	1 (1.6%)
Vomiting	1 (3.1%)	0 (0%)	1 (1.6%)

P=1.000, Not Significant, Fisher Exact Test

As shown in table 4, hypotension was seen 1 patient in group I and 4 patients in group II. Bradycardia was seen in only 1 patient in group I. Nausea was complained by 1 patient in group I and vomiting by 1 patient in group I.

All these side effects did not show any statistical significance.

Discussion

Spinal anaesthesia is the technique of choice for infraumbilical surgeries especially TURP procedures due to its reliability, speed, simplicity, and added advantage of avoiding polypharmacy. Complications like TURP syndrome, bladder perforations can easily be diagnosed under spinal anaesthesia with dermatomal blockade of upto T_{10} [8].

The prostate gland receives its nerve supply from the inferior hypogastric plexus and carries both parasympathetic fibres from S_2–S_4 and sympathetic fibres from T_{11}-L_2. These S_2–S_4 sacral nerves carry the pain fibres from the prostate gland, prostatic urethra and bladder mucosa. The pain that occurs due to the distension of the bladder travels along the sympathetic nerve fibres of T_{11}-L_2. Parasympathetic fibres of S_2–S_4 carry the stretch sensation of bladder. Taking this innervations into consideration, height of subarachnoid blockade upto T_{10} may be considered sufficient for TURP procedures. The pain on perforation of the prostatic capsule or the bladder might get masked if the level of block achieved is higher.

The main aim is to produce a prolonged and effective analgesia with minimum side effects and stable hemodynamics as the TURP procedures are usually performed in elderly patients with compromised cardiopulmonary functions. Lignocaine and Bupivacaine are the commonly used local anaesthetics for spinal anaesthesia in India. Bupivacaine is not associated with transient neurological syndrome seen with earlier drugs like lidocaine [9]. Bupivacaine 0.5% heavy when given intrathecally provides analgesia for about 2-4 hrs, but the post-operative analgesic duration is limited [10]. Hence, by adding an adjuvant to local anaesthetic agent, the dose of local anaesthetic can be reduced, duration of anaesthesia and post-operative analgesia can be prolonged without much changes in hemodynamics.

Among the additives, opioids are preferable in increasing the analgesic effect. Few authors have used lower dose bupivacaine in doses of 4 mg and 5 mg in combination with opioids as spinal anaesthesia drug for TURP procedures [3]. There were no studies with low dose injection bupivacaine 2.5 mg in combination with tramadol 50 mg being used in spinal anaesthesia for TURP procedures. In this study, we had taken tramadol as the intrathecal adjuvant as it provides good analgesia with minimal side effects compared to other opioids.

Tramadol exists as the racemic (1:1) mixture of the (+) and (−) enantiomer. It has dual mechanism of action. The (+) enantiomer of tramadol contributes to analgesia by inhibiting the reuptake of serotonin, the (−) enantiomer by inhibiting the reuptake of noradrenaline, and the O-desmethyl metabolite by binding with relative high affinity (compared to tramadol) to the μ-opioid receptor. The monoaminergic activity of tramadol increases the inhibitory activity of the descending pain pathways that results in the suppression of nociceptive transmission at the spinal level [11,12].

Several studies have demonstrated the advantage of combining tramadol with bupivacaine in spinal anaesthesia to prolong the duration of anaesthesia and analgesia. Hussain A demonstrated that intrathecal tramadol in orthopaedic patients prolonged duration of analgesia with minimum side effects [13]. In a study done by Afolayan JM, it was shown that intrathecal tramadol 25 mg was a safe alternative to intrathecal fentanyl 25 mg in the management of visceral pain in open appendicectomy patients, without any adverse outcomes except postoperative vomiting [14]. Pharmacodynamic studies conducted in animals with intrathecal tramadol doses upto 100mg provided demonstrable analgesia without reported toxicity [15,16].

Parthasarathy S evaluated postoperative pain scores in appendicectomy patients who received intrathecal tramadol 10 mg with hyperbaric lignocaine 5% and concluded that analgesic requirements were less in patients who received intrathecal tramadol with hyperbaric lignocaine 5% compared to those who received plain hyperbaric lignocaine 5% [17]. In a study conducted by Mostafa GM in patients posted for transurethral resection of bladder tumour, intrathecal tramadol 50 mg versus intrathecal nalbuphine 2 mg when administered along with 0.5% bupivacaine showed a similar effect in providing postoperative analgesia, with minimal side effects [18].

Tramadol is being used widely as an oral and intravenous analgesic agent. It was approved by the United States FDA in 1995. There are several studies demonstrating the effects of intrathecal administration of tramadol in prolonging postoperative analgesia with minimal side effects in different surgeries. Various studies done in regional anaesthesia using tramadol as an adjuvant in spinal, epidural or caudal anaesthesia by Tandon R et al., Frikha N et al., Brijesh J et al., Gupta H et al., Ozcengiz D et al., showed its efficacy in providing adequate analgesia when compared to other opioid agents [19-23]. Hence we had undertaken this study with preservative free intrathecal tramadol 50 mg (1 ml) combined with 0.5% hyperbaric bupivacaine 2.5 mg (0.5 ml) and normal saline 0.5 ml as an alternative to conventional dose of bupivacaine 10 mg (2 ml) in spinal anaesthesia for TURP procedures and analyzed the results.

Analysis of data between the two groups

Demographic data

The two groups were matched with respect to age and weight. The mean age in Group I is 67.56±6.98 years and in Group II 65.16±6.87 years. There was no significant difference in weight between the two groups. Demographic data comparing age, and weight showed no significant difference statistically, among both the groups.

Sensory and motor blockade:

In our study, Highest dermatomal level achieved in group I patients were T8 in 15, T10 in 7 and T6 in 5 patients. Highest dermatomal level achieved in group II were T6 in 20 and T10 in 5. Mean onset of sensory blockade ie., time to achieve highest dermatomal level among group I patients was 8.44±2.35 min and in group II was 6.53±1.65 min and it was statistically significant ($p<0.001$).

In a study done by Kim NY et al., it was observed that, for short procedures like TURP in elderly patients, Selective spinal anaesthesia given using low dose bupivacaine ie., 1 mg along with adjuncts like fentanyl not only provided adequate anaesthesia, but also reduced the incidence of hypotension [24]. They concluded that addition of fentanyl improves the quality of block, increases duration of sensory block and makes the blockade hemodynamically more stable than conventional dose bupivacaine. Hence in our study, we had taken 0.5% low dose bupivacaine heavy 2.5 mg along with opioid tramadol 50 mg comparing it with conventional dose of bupivacaine heavy 10 mg and evaluated the blockade.

In our study, Mean Two segment regression among group I patients was 65.38 ± 20.52 min and in group II was 86.78±36.88 min, which was longer in group II compared to that in group I and it was statistically significant ($p<0.006$). But, the analgesic effect was prolonged in group I compared to group II. Time for first request of analgesia was shorter in Group II ie., 201.38±96.56 min compared to that in Group I ie., 312.56±137.42 min, and the difference was statistically significant ($p<0.001$).

A study conducted by Chakraborty S et al., demonstrated favorable results of tramadol use with bupivacaine in major gynaecological surgeries when duration of anaesthesia and VAS scores were compared between two groups. In this study 20 mg of tramadol added to 15 mg of bupivacaine effectively prolonged the duration of analgesia from 210 ± 10.12 min in bupivacaine saline group to 380 ± 11.82 min in bupivacaine-tramadol group [25].

In a study conducted by Zahid F et al., in patients undergoing lower limb orthopaedic surgeries, Group tramadol bupivacaine (TB) received 25 mg (1 ml) of tramadol plus 2 ml (10 mg) of 0.5% bupivacaine while group bupivacaine alone (SB) received 1 ml normal saline plus 2 ml (10 mg) of 0.5% bupivacaine [26]. The duration of anaesthesia was effectively prolonged in group TB 181.56 ± 12.42 mins as compared to group SB 120.93 ± 15.54 mins and VAS score was significantly lower in group TB.

Bromage scores at highest dermatomal level in group I patients were 2 in twelve, 3 in nine, 1 in seven and 0 in four patients and those in group II patients were 3 in twenty five, 2 in five and 1 in two patients. This concluded that degree of motor blockade was 1-2 in group I whereas it was 2-3 in group II.

In a study conducted by Abdelmonem AMR, he concluded that hyperbaric bupivacaine 7.5 mg injected at T_{12}–L_1 is enough to provide adequate sensory block, along with hemodynamic stability in the TURP surgeries [27]. It also provides added advantage of decreased duration of motor block in these patients ie., more rapid motor recovery early ambulation and discharge from the PACU, but care should be taken while doing the procedure at the level of T_{12}-L_1, as there is risk of injuring conus medullaris.

Prajapati. J and Parmar. H**,** compared the effects of low dose bupivacaine 0.5% 5 mg in combination with fentanyl 25 µg with regular dose of bupivacaine 0.5% 7.5 mg in elderly patients undergoing TURP. In group B, onset of motor blockade was delayed when compared to group A and was statistically significant [28].

Kararmaz. A et al., evaluated the effect of low-dose bupivacaine plus fentanyl administered intrathecally in elderly patients undergoing transurethral prostatectomy [3]. Patients in Group F received plain bupivacaine 4 mg with 25 micrograms of fentanyl and sterile water to a total of 1.5 ml, and those in Group B received only 0.5% plain bupivacaine 7.5 mg for spinal anaesthesia. Sensory block was adequate for surgery in all patients. In Group B, the mean level of motor block was higher ie., 2-3 whereas in group F, it was 1-2 and the duration of motor block was longer in group B compared to that of group F. Hence, in our study, we evaluated the bromage scores in both the groups and the results were comparable to the above study.

Time for rescue analgesia and VAS scores

In our study, time for first request of analgesic dose was shorter in Group II ie., 201.38 ± 96.56 min compared to that in Group I ie., 312.56 ± 137.42 min, and the difference is statistically significant ($p<0.001$). Most of the patients in group I showed VAS scores of 1-3 and those in group II showed 3-6 and the difference was statistically significant with p value < 0.001. Studies done by Zahid et al. and Chakraborty S et al., demonstrated favourable results towards the use of tramadol with bupivacaine [25,26]. They showed that significantly lower VAS scores were obtained when used with tramadol compared to the conventional group and the time for rescue analgesia was also prolonged with the use of tramadol. However, in a study done by Verma D et al., the authors compared the effects of intrathecal nalbuphine 2 mg added to hyperbaric bupivacaine, intrathecal tramadol 50 mg added to hyperbaric bupivacaine and plain hyperbaric bupivacaine in patients posted for lower limb orthopaedic surgeries and concluded that intrathecal nalbuphine group showed significant effect in enhancing postoperative analgesia compared to that of other two groups [29].

Hemodynamic effects

Variations in mean arterial pressures were comparable in both the groups upto 5 min after the subarachnoid block. There was significant drop in mean arterial pressures after 10 min after subarachnoid block till 90 min in group II compared to that in group I patients.

Heart rate was comparable in both the groups throughout the monitoring period. In this study, there was no incidence of hypoxia in both the groups during the follow up. There was no significant difference in changes in oxygen saturation between the groups.

Side effects

Hypotension was seen in 1 patient in group I and 4 patients in group II. It was corrected by inj. Mephentermine 6 mg iv in bolus doses. Bradycardia was seen in only 1 patient in group I, corrected

with inj. Atropine 0.6 mg iv bolus. Nausea was complained by 1 patient in group I and vomiting by 1 patient in group I, which were managed by inj. Ondansetron 4 mg iv. All these side effects did not show statistical significance.

In a study done by Gupta P, the authors concluded that intrathecal tramadol when combined with hyperbaric bupivacaine attenuates the postanaesthesia shivering along with prolongation of duration of sensory and motor blockade and analgesia [30]. In our study no patient from either groups complained of shivering or pruritus.

Case report done by Orliaguet G et al. showed respiratory depression in pediatric patient who received tramadol orally at 1 mg/kg body weight and another case report by Stamer UM et al. showed respiratory depression in patient with renal impairment on patient controlled analgesia who received tramadol intravenously [31,32]. Both these patients were found to be rapid metabolisers and the metabolite of tramadol showed high affinity to μ receptors. Renal impairment in the second patient resulted in the accumulation of the metabolite. These opioid overdose effects were reversed by naloxone in both the cases. After these incidents, FDA announced that tramadol should be cautiously used in patients at risk for respiratory depression.

Respiratory depression was seen in none of the patients in our study. Alam W et al. reported respiratory depression in a patient who received intrathecal tramadol for knee arthroscopy and anterior cruciate ligament repair which was reversed by naloxone [33]. Apart from this report, none of the studies mentioned above showed respiratory depression with intrathecal tramadol administration. Yet, we suggest that vigilant monitoring is mandatory and it helps in early detection of any adverse events.

In a case report done by Barrett NA, intrathecal tramadol 25 mg was given to a patient who was on palliative management for widely metastatic squamous cell carcinoma of unknown primary [34]. The patient was on treatment with intrathecal morphine, fentanyl patch, oral tramadol and paracetamol for chronic pain. She developed myoclonic jerks and hypotension after 10 min of intrathecal tramadol injection. The reason for these adverse effects might be multifactorial as the patient was on multiple opioids. Hence, we conducted our study in patients with ASA Physical Status I and II without any neurological and respiratory diseases, to avoid the risk of these adverse events with intrathecal tramadol administration. None of our patients showed neurotoxicity or respiratory depression.

Few literature suggested that there is no benefit of adding tramadol to intrathecal space in postoperative analgesia. Studies done by Alhashemi JA et al., and Salhotra. R et al. have not shown any clinical benefit with intrathecal tramadol in prolongation of post-operative analgesia for TURP patients [35,36]. Proper post operative follow up and increase in sample size may help in getting better results. This study can be further evaluated in ASA-PS III and IV patients as it has shown better hemodynamic stability in elderly patients who had undergone TURP procedures. Hence further studies were advised to evaluate the efficacy of intrathecal tramadol and also to determine the exact underlying mechanism.

Conclusion

We conclude from our study that intrathecal low dose bupivacaine when combined with tramadol provides adequate subarachnoid block and postoperative analgesia for TURP surgeries. Both the groups were effective in providing adequate surgical anaesthesia, but bupivacaine when combined with tramadol provided good quality of intraoperative analgesia, hemodynamically stable conditions, early ambulation and excellent quality of postoperative analgesia. Intrathecal tramadol shows less side effects and not associated with respiratory depression or neurological sequelae in routine clinical use.

Acknowledgement

We acknowledge the support given by Dr Dinesh K, Professor and Head, Sri Devaraj Urs Medical College, Kolar, Karnataka to do this study.

Key Messages

TURP procedure is usually done in geriatric patients who will be having limited cardiopulmonary reserve. Though spinal anaesthesia offers added advantage of an awake patient with easy identification of complications associated with TURP procedure, it is associated with few hemodynamic changes like hypotension and bradycardia in elderly. Addition of tramadol to intrathecal low dose bupivacaine improves the duration of post operative analgesia, maintains intraoperative stable hemodynamics with less chances of adverse effects.

Conflict of Interest: Nill

References

1. Millar JM, Jago RH, Fawcett DP. Spinal analgesia for transurethral prostatectomy. Br J Anaesth. 1986;58:862-7.
2. Bhattacharyya S, Bisai S, Biswas H, Tiwary MK, Mallik S, Saha SM. Regional anaesthesia in TURP surgery: A comparative study between saddle block and subarachnoid block. Saudi J Anaesth. 2015;9:268-71.
3. Kararmaz A, Kaya S, Turhanoglu S, Ozyilmaz MA. Low-dose bupivacaine-fentanyl spinal anaesthesia for transurethral prostatectomy. Anaesthesia. 2003;58:526-30.
4. Ackaboy ZN, Ackaboy EY, Mutlu NM, Serger N, Aksu C, Gogus N. Spinal Anaesthesia with Low-Dose Bupivacaine-Fentanyl Combination: a Good Alternative for Day Case Transurethral Resection of Prostate Surgery in Geriatric Patients. Rev Bras Anestesiol. 2012;62:753-61.
5. Bromage PR. A comparison of hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand. 1965;16:55-69.
6. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstat L, Hals B et al. Assessment of pain. Br J Anaesth. 2008;101:17-24.
7. Suresh KP, Chandrasekhar S. Sample Size estimation and Power Analysis for Clinical research studies. Journal Human Reproduction Science. 2012;5:7-13.
8. Smyth SM, Vasdev N, Mohan SG. Spinal Anesthesia Facilitates the Early Recognition of TUR Syndrome. Curr Urol. 2015;9:57-61.
9. Chohedri A, Estabragh RR, Eghbal MH, Sahmeddini MA, Eftekharian H, Shahabifar R. Comparing the duration of spinal anesthesia induced with bupivacaine and a bupivacaine-lidocaine combination in trans-urethral resection of the prostate (TURP). Anesth pain med. 2015;5:e25675.
10. Prabhavathi R, Kumar GC, Reddy PN, Pradeep P, Chaitanya KK, Sujith T, Prakash S, et al. Low vs high dose spinal hyperbaric bupivacaine on hemodynamic variables in patients undergoing transurethral resection of the prostate: A prospective two arm open label randomized comparative study. J Evol Med Dental Sci. 2014;3:8072-80.
11. Dubey K, Paddalwar S, Chandak A. A comparative double blind study of tramadol and fentanyl as adjuvants to lignocaine for intravenous regional anesthesia for forearm orthopedic surgeries. Indian J Pain. 2014;28:29-35.
12. Tripathi KD. Opioid Analgesics and Antagonists. 7th ed. Chapter 34. In:Essentials of Medical Pharmacology. 2013.pp.469-85.
13. Hussain A, Siddiqui SA, Sharma M, Madhesiya G. 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;6:4-6.
14. Afolayan JM, Olajumoke TO, Amadasun FE, Edomwonyi NP. Intrathecal tramadol versus intrathecal fentanyl for visceral pain control during bupivacaine subarachnoid block for open appendicectomy. Niger J Clin Pract. 2014;17:324-30.
15. Dhasmana K, Banerjee A, Rating W, Erdmann W. Analgesic effect of tramadol in the rat. Acta Pharmacol Sin. 1989;10:289-94.
16. Lubenow T. Analgesic, hemodynamic and respiratory responses to intrathecal tramadol in dogs. Anaesthesiology. 1995;83:a822.
17. Parthasarathy S, Ravishankar M. Single dose intrathecal tramadol in the management of post appendicectomy-pain. J Anaesthesiol Clin Pharmacol. 2002;18:419-22.
18. Mostafa MG, Mohamad MF, Farrag WS. Which has greater analgesic effect: intrathecal nalbuphine or intrathecal tramadol. J Am Sci. 2011;7:480-4.
19. Tandon R, Waikar C, Agrawal SN. A comparative clinical study of intrathecal hyperbaric bupivacaine 0.5% with 25 mg pethidine versus 25 mg tramadol for infraumbilical surgeries. IJCMR. 2017;4:1856-60.
20. Frikha N, Massoudi K, Ouergh S. Spinal tramadol for caesarean section. Obstet Anaesth. 2008;8:72.
21. Brijesh J, Saraswat VK. Efficacy of intrathecal tramadol for post operative pain relief in cases of L.S.C.S and major gynecological surgeries- A clinical evaluation. Indian J Anaesth. 2001;45:282.
22. Gupta H, Wani Z, Sharma M. Using intrathecal tramadol as an adjuvant in subarachnoid block for prolonging the duration of analgesia. IJSR. 2017;6:12.
23. Ozcengiz D, Gunduz M, Ozbek H, Isik G. Comparison of caudal morphine and tramadol for postoperative pain control in children undergoing inguinal herniorrhaphy. Pediatric Anesthesia. 2001;11:459-64.
24. Kim NY, Kim SY, Ju HM, Kil HK. Selective spinal anesthesia using 1mg of bupivacaine with opioid in elderly patients for transurethral resection of prostate. Yonsei Med J. 2015;56:535-42.
25. Chakraborty S, Chakrabarti J, and Bhattacharya D. Intrathecal tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after major gynecological surgeries. Indian J Pharmacol. 2008;40:180–2.
26. Zahid F, Tarar HM, Tariq M, Nazir H, Zafar I, Munir S. Intrathecal tramadol as an adjuvant in subarachnoid block to prolong the duration of analgesia. Pak Armed Forces Med J. 2017;67:534-9.
27. Abdelmonem A. Low dose hyperbaric bupivacaine injected at T12-L1 provides adequate anaesthesia

with stable hemodynamics for elderly patients undergoing TURP. Eg J Anaesth. 2011;27:95-100.

28. Prajapati J, Parmar H. Low dose bupivacaine and bupivacaine with fentanyl for spinal anesthesia for transurethral resection of prostate. IAIM. 2015;2:11-9.
29. Verma D, Naithani U, Jain DC, Singh A. Postoperative analgesic efficacy of intrathecal tramadol versus nalbuphine added to bupivacaine in spinal anaesthesia for lower limb orthopaedic surgery. JEMDS. 2013;2:6196-206.
30. Gupta P, Gupta M. Intrathecal tramadol for prevention of postanesthesia shivering after subarachnoid block: A prospective randomized placebo-controlled comparison of two different doses (10 and 20 mg). Anesth Essays Res. 2018;12:495-500.
31. Orliaguet G, Hamza J, Couloigner V, Denoyelle F, Loriot MA, Broly F et al. A case of respiratory depression in a child with ultrarapid CYP2D6 metabolism after tramadol. Pediatrics. 2015;135:e753-5.
32. Stamer UM, Stuber F, Muders T, Musshoff F. Respiratory depression with tramadol in a patient with renal impairment and CYP2D6 gene duplication. Anesth Analg. 2008;107:926-9.
33. Alam W, Saeed MA, Yakub KM. Intrathecal tramadol may cause respiratory depression. Anaesth Pain & Intensive Care. 2017;21:87-9.
34. Barrett NA, Sundaraj SR. Inadvertent intrathecal injection of tramadol. Br J Anaesth; 2003;91:918-20.
35. Alhashemi JA, Kaki AM. Effect of intrathecal tramadol administration on postoperative pain after transurethral resection of prostate. Br J Anaesth2003;91:536-40.
36. Salhotra R, Mohta M, Agarwal D, Sethi AK. Intrathecal ropivacaine with or without tramadol for lower limb orthopedic surgeries. J Anaesthesiol Clin Pharmacol. 2016;32:483-6.