INTRATHECAL TRAMADOL AS AN ADJUVANT IN SUBARACHNOID BLOCK TO PROLONG THE DURATION OF ANALGESIA

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ABSTRACT

Objective: To assess the effect of intrathecal tramadol added to bupivacaine to prolong the duration of analgesia in subarachnoid block for lower limb orthopedic surgeries.

Study Design: Randomized controlled trial.

Place and Duration of Study: Anesthesia department of Combined Military Hospital Sialkot, from Nov 2015 to Apr 2016.

Material and Methods: Patients were selected by non-probability consecutive sampling. One hundred and fifty patients from American Society of Anesthesiologists (ASA) I, II and III category fulfilling inclusion criteria undergoing various lower limb orthopedic surgeries were divided into two groups by lottery system. Group tramadol bupivacaine (TB) received 25mg (1 ml) of tramadol plus 2ml (10mg) of 0.5% bupivacaine while group bupivacaine alone (SB) received 1 ml normal saline plus 2ml (10mg) of 0.5% bupivacaine. Time to first analgesia request was noted as a measure of duration of analgesia. Time of onset of sensory block level and peak sensory block level and time to reach the peak sensory block level were also noted. Quality of anesthesia was compared among two groups. Data were analyzed by using SPSS version 22.

Results: Four patients were excluded from the study. The duration of anesthesia was effectively prolonged in group TB 181.56 ± 12.42 mins as compared to group SB 120.93 ± 15.54 mins. VAS score was significantly lower in group TB. Higher peak sensory block levels (T6) were achieved in group TB as compared to group SB. However time to reach the peak sensory block levels were significantly longer in group TB. (4.5 ± 0.47mins vs 3.09 ± 0.54 mins).

Conclusion: This study showed that intrathecal tramadol (25mg) can safely be used along with bupivacaine in subarachnoid blockade to prolong the duration of analgesia and improve the quality of anesthesia as well.

Keywords: Bupivacaine, Intrathecal administration, Orthopedic procedures, Tramadol, Post operative analgesia.

INTRODUCTION

Pain free surgery and post-operative period is perhaps the most gratifying experience an anesthesiologist can provide to a patient. Uncontrolled postoperative pain may produce a range of detrimental acute and chronic effects[1]. Postoperative pain relief is a growing concern for an anesthesiologist as an uneventful postoperative period makes surgery a comfortable experience for surgical patients. Spinal anesthesia has revolutionized the field of anesthesia in this regard. It is preferred over general anesthesia for most of the lower limb and lower abdominal surgeries. The use of spinal anesthesia has increased dramatically because of its simplicity to perform, cost effectiveness, rapid onset, dense blockade and less failure rates[2].

The use of local anesthesia agents for intrathecal use has always been a matter of great sensitivity. Many different agents have been used in intrathecal injections for surgical and post-surgical pain relief. The most commonly used drug is Bupivacaine with maximum effective time of 75-180 minutes. The routine doses of bupivacaine are associated with prolonged and intense sensory and motor block and significant sympathetic block, which may not be desirable in some patients. Low dose diluted bupivacaine limits the distribution of spinal block and yield a comparably rapid recovery, but may not provide

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Received: 08 Jun 2016; revised received: 01 Aug 2016; accepted: 01 Aug 2016

an adequate level of sensory block or effective surgical anesthesia time[3]. Although major side effects are rare, the use of local anesthetics is not without complications such as hypotension, bradycardia, urinary retention and neurological injuries etc. Most of these complications are found to be dependent on the volume and dose of injected drug and the height of spinal anesthesia[4].

Total effective surgical anesthesia time of these local anesthetic agents on occasions becomes the source of discomfort for the patients. To counter the time limitation factor, different adjuvants have been in clinical practice which can dramatically prolong the effective surgical anesthesia time of local anesthetics. In addition they also increase density of spinal blockade, reduce the total dose of local anesthetics with minimum side effects. But like all drugs these adjuvants have side effects of their own which have always been the basis of debate for use of these agents in such a delicate structure[5].

"Cocainization of the spinal cord" is the term used for using cocaine in intrathecal route and was first described by the August Bier in 1899[6]. Since then this technique has been refined and many different opioids have been used for this purpose with different degree of success. Morphine, fentanyl, sufentanyl, midazolam, magnesium sulphate, clonidine and many other drugs have been used in this regard[5-7]. Many studies have compared and proved the benefits of such adjuncts in different doses but also documented some adverse effects that have caused debate over routine use of such agents[7].

Tramadol is a synthetic 4-phenyl-piperidine analogue of codeine with a dual mechanism of action. It stimulates the μ-receptor and to a lesser extent δ- and κ-opioid receptors. Similar to tricyclic antidepressants, it activates spinal inhibition of pain by decreasing the reuptake of norepinephrine and serotonin. This produces a non-opioid basis of analgesia[8]. Apart from the works of Parthasarathy and Ravishkar[9], Chakraborty et al[10]. Alhashemi and Kaki[11] and Frikha et al[12] not many researches have been carried out on intrathecal administration of tramadol.

There have been no studies done in Pakistan using tramadol in subarachnoid space. Although it is being widely used as an IV analgesia agent with appreciable results and very few side effects. The aim of our study is to introduce tramadol as a safe adjuvant for routine use in spinal anesthesia to improve the quality of spinal anesthesia.

The primary aim of the study was to assess which group produced a longer duration of analgesia measured in terms of the first request for analgesia post-operatively. The secondary aim was to compare the two groups in terms of time of onset of analgesia (T10 block level assessed by pin prick), peak sensory block level, and time to reach peak sensory block level and quality of anesthesia.

MATERIAL AND METHODS

After approval from Ethics committee of Combined Military Hospital Sialkot this randomized controlled trial study was undertaken from July 2015 to December 2015. We recruited 150 ASA I, II and III patients of both genders between the ages of 30 to 70 years scheduled for lower limb orthopedic surgery under spinal anesthesia by non-probability consecutive sampling. Sample size was calculated using WHO calculator from a previous study as a reference[11]. Informed consent was taken from all patients. Any case that was converted to general anesthesia for any reason, contraindicated for spinal anesthesia or having cerebrovascular disease was excluded from the study.

All eligible patients were randomly assigned into two groups. Group SB (Bupivacaine alone) and Group TB (Tramadol-Bupivacaine) containing 75 patients each by opening unmarked envelop indicating the type of coded spinal solution package to be used. A second anesthetist who was not involved in the study prepared the spinal solutions and labelled them appropriately.

The anesthetist performing the block was blind to the spinal solution administered.

In the operating room, baseline pulse rate, non-invasive blood pressure, oxygen saturation were recorded before induction of spinal anesthesia and subsequently during the procedure for each patient. A venous access was secured using 18 gauge intravenous cannula and the patient was preloaded with Ringer Lactate (10 ml/kg) before the induction of spinal anesthesia. Aseptically, spinal anesthesia was carried out in a sitting position, using 25G Quincke spinal needle at L3-4 vertebral level. After confirming free flow of cerebrospinal fluid, each patient received one of the coded spinal solutions. Patients in Group SB (n=75) received intrathecal 0.5% hyperbaric bupivacaine 2ml (10mg) and 1ml normal saline, patients in Group TB (n=75) received intrathecal tramadol 1ml (25mg) plus 2 ml (10mg) of 0.5% hyperbaric bupivacaine.

Sensory block height was assessed at 1 minute interval using pin prick test in mid clavicular line until it reached T10 level and then every 2 minutes until it reached peak sensory block level (PSBL). Peak sensory block level is defined as the level that remained same during four consecutive tests. The quality of anesthesia was assessed as excellent (no discomfort or pain), good (mild pain or discomfort and no need for additional analgesics), fair (pain that required single dose of analgesia), poor (severe pain that required multiple doses of analgesia) determined by the patient at the end of surgery. Rescue analgesia in the form of IV fentanyl 50-100 mcg was provided appropriately on request of patient.

In the post op period the time for the first request of analgesic dose was considered as the time limit for that group and rescue analgesia was provided accordingly. Quality of anesthesia was assessed at this time by asking the patient. All the necessary data were endorsed in the appropriate data entry form.

Data were collected and were analyzed using SPSS version 22 for windows before interpretation of results were made. Quantitative variables were expressed as mean ± SD while qualitative data were expressed as percentages. Student's unpaired t-test was used for parametric data and chi-square tests were used for non-parametric data. A *p*-value <0.05 was considered significant.

Table-I: Demographic profile of the two groups data presented as mean ± (SD).

Variables	Group SB (n=73)	Group TB (n=73)	*p*-value
Age (years)	54.64 ± 8.42	54.24 ± 9.37	0.867
Sex Distribution			
Male	40 (54.8%)	41 (56.2%)	0.862
Female	33 (45.2%)	32 (43.8%)	
ASA Status			
I	13 (17.8%)	17 (23.3%)	0.714
II	32 (43.8%)	29 (39.7%)	
III	28 (38.4%)	28 (37%)	
Operative Time (Minutes)	99.28 ± 25.14	101.31 ± 23.33	0.471

RESULTS

Two out of 75 patients were excluded from tramadol group due to administration of general anesthesia and 2 out of 75 were excluded from bupivacaine group because of administration of general anesthesia in first one and inadequate documentation in second one. There was no statistical significant difference among the two groups regarding demographic profile like age, sex, height, weight and duration of surgery (table-I).

The duration of analgesia was significantly prolonged in tramadol group as compared to bupivacaine group. The mean duration of

analgesia in tramadol group was 181.56 ± 12.42 mins whereas in bupivacaine group it was 120.93 ± 15.54 mins as shown in table-II (p<0001).

Peak sensory block level achieved was also much higher in tramadol group. Almost more than 50% of the patients achieved sensory block level higher than T8 in tramadol group. Table-II shows the percentage of patients achieving different block levels.

Table-II: Characteristics of spinal block among study groups.

Variables	Group SB (n=73)	Group TB (n=73)	*p*-value
Time to request first analgesia (minutes)	120.93 ± 15.54	181.56 ± 12.42	<0.001
Peak sensory Block level (% of n)			
T10	21 (28.8 %)	NIL	
T9	38 (52.1 %)	2 (2.7 %)	<0.001
T8	12 (16.4 %)	16 (21.9 %)	
T7	2 (2.7 %)	34 (46.6 %)	
T6	NiL	21 (28.8 %)	
Time to reach peak sensory block level (minutes)	3.09 ± 0.54	4.5 ± 0.47	<0.001
Quality of Anesthesia (% of n)			
Excellent	11(15.1 %)	41 (56.2 %)	
Good	33 (45.2 %)	29 (39.7 %)	<0.001
Fair	25 (34.2 %)	3 (4.1 %)	
Poor	4 (5.5%)	Nil	

Table-II also shows time to reach the peak sensory block levels in both groups. Patients in tramadol group took long time to reach the peak sensory block level. The average time to reach the peak sensory block level was 4.5 ± 0.47mins in Group TB as compared to 3.09 ± 0.54 mins in Group SB.

Quality of anesthesia was also compared among both groups. Group TB shows more patients having excellent quality of anesthesia as compared to more percentage of patients experiencing fair quality of anesthesia in group SB.

DISCUSSION

Opioids have been the cornerstone of analgesia ever since their discovery. Intravenous, Intrathecal or Epidural routes have all been used for pain relief in surgical patients. Opioids have also been used along with local anesthetics to enhance the efficacy. Many studies have shown morphine, fentanyl and sufentanil to be the most commonly used agents with satisfactory results[13-16].

Tramadol is a centrally acting partial opioid analgesic agent with terminal half-life of 5.5 hours and analgesic activity for 10 hours after epidural analgesia. The analgesic activity of tramadol is quite different than that of the μ opioid agonists. Tramadol acts as weak μ-receptor agonist and to a lesser extent δ-and κ-opioid receptors agonist. Serotonin reuptake inhibition and norepinephrine reuptake inhibition also contributes to its analgesic properties[17]. Some studies show that tramadol may have local anesthetic effect on peripheral nerves as well[18].

Results of our study show a distinct advantage of adding tramadol to intrathecal bupivacaine as it effectively prolonged the duration of analgesia, and also achieved higher block levels. Although it took more time to reach

peak sensory block levels than bupivacaine alone. Addition of tramadol did not produce any adverse effects on hemodynamic profile or any other typical side effects of pure opioid agonists such as nausea, vomiting, pruritus and respiratory depression.

Several studies have demonstrated the benefit of using tramadol in spinal anesthesia along with the bupivacaine to prolong the duration of anesthesia as well as analgesia. A study done by Hussain A[19] on intrathecal tramadol in orthopedic patients significantly prolonged duration of analgesia and also produced minimum side effects. Another study done by Afolayan J showed that intrathecal tramadol 25 mg was a safe replacement for intrathecal fentanyl 25 mcg in open appendectomy patients. They reported postoperative vomiting to be the most common complication in tramadol but no adverse outcome was mentioned[8].

Chakarbarty S also demonstrated favorable results of tramadol use with bupivacaine in major gynecological surgeries when duration of anesthesia and VAS scores were compared between two groups. In his study 20 mg of tramadol added to 15mg 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[10] A comparative study of 50 mg tramadol and 2 mg nalbuphine used in subarachnoid block done by Mostafa MG[20] demonstrated equally effective prolongation of duration of analgesia and Lower VAS scores along with minimal side effects related to these agents although sedation score was found to be higher in tramadol group.

Parthasarathy S exhibited significantly prolonged duration of analgesia and lower VAS scores with intrathecal tramadol in the management of post appendectomy patients along with lignocaine in spinal anesthesia. 10mg of tramadol added to 1.8ml of 5% lignocaine almost doubled the mean time for analgesia in postoperative period[9]. Other studies done with tramadol in Regional anesthesia by Kumari P[21], Farikha N[12], Brijesh J[22], Ozcengiz D[23] have demonstrated its efficacy as an adjuvant in spinal epidural or caudal anesthesia in place of pure opioid agonists.

However some studies suggested no benefit of adding tramadol to subarachnoid space as demonstrated by Alhashimi JA[11]. His work did not produce any benefit in post-op analgesia for TURP patients when intrathecal tramadol was used. Grace D[24] and Wilder-smith CH[25] have also failed to mention any benefit of intrathecal tramadol over bupivacaine alone. There were many possible assumptions for this failure but exact mechanism still eluded them and further studies were advised to determine the exact underlying mechanism.

Addition of 25 milligram of tramadol in subarachnoid block with 10 milligram of 0.5% bupivacaine effectively improve quality of blockade and most importantly prolonged the duration of blockade for surgery 0.25 mg dose of tramadol was added after reviewing many authors and considering it to be a adequately safe dose as this was a first study of adding intrathecal adjuvant for surgery and it did not produce any anticipated adverse effects but it did produce admirable result. However follow up to the post op care unit was a limitation of our study due to shortage of staff and exhausting workload. Further studies with multiple doses and long follow up should be carried out in order to determine the optimal dose and safety profile of tramadol for intrathecal use.

CONCLUSION

We conclude that tramadol seems to be a splendid choice for intrathecal administration for intraoperative anesthesia and post-operative analgesia. Twenty five mg of tramadol is a safe dose with minimum side effects and it should be utilized as a starting point for more studies to improve the quality of anesthesia and patient care and most importantly the pain free experience for the patients.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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