Original Article

Indian Journal of Anaesthesia and Analgesia
2017, 4 (3, Part-I), 682-688
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4317.23

Role of the Effect of Systemic Ondansetron on Intrathecal Spinal Anaesthesia Produced by Bupivacaine

M.K. Giri[1], P.S. Malviya[2], H.C. Chandola[2]

[1]Assistant Professor [2]Professor, Department of Anaesthesiology, MLN Medical College, Allahabad 211002, Uttar Pradesh, India.

Abstract

Background: Subarachnoid block is commonly used technique for anaesthesia in different surgical specialties. Ondansetron is a selective 5-HT_3 antagonist. It is an effective drug for prevention and treatment of nausea and vomiting, so being used generously as antiemetic drug in premedication. Any interaction with regional anaesthesia including the effect on sensory and motor block would be particular interest for anaesthesiologist. This study was done to compare the effect of intravenous ondansetron on sensory and motor blockade induced by intrathecal spinal hyperbaric bupivacaine in patients undergoing orthopaedic surgery. *Methods*: 60 unpremedicated patients of male sex, age 20- 45 years belonging to an ASA physical status I or II is undergoing lower limb orthopaedic procedures being performed under intrathecal spinal anaesthesia were recruited for this study. Group C received i.v saline 2ml and Group O received i.v Ondensetron 4 mg (2ml) 15 min prior to the intrathecal spinal hyperbaric bupivacaine. Sensory and motor block level was assessed in this study. *Results*: We found that in patients group C (control) had the highest block level T4 as compare to group O (ondansetron pretreatment group) in which the highest sensory block level was T6. For maximum sensory block level comparison between group C and group O found significant ($p<0.001$). Duration of the block is also decreased in ondansetron group, i.e. those who had received ondansetron prior to spinal anaesthesia. *Conclusion*: It was observed in our study that the level of maximum sensory block height was significantly lower in ondansetron pretreatment group for hyperbaric bupivacaine. It was also noted that the ondansetron pretreatment group had faster regression of sensory block level. No significant differences were detected between the study groups for motor block.

Keywords: Intravenous Ondansetron; Hyperbaric Bupivacaine; Sensory block; Motor block.

Introduction

Regional anaesthesia is a safe and well accepted technique since it is devoid of the use of multiple anaesthetic drugs and their consequences workload of metabolism and excretion during General Anaesthesia. Minimizing the stress response and using minimal anaesthetic drugs is always beneficial for the patients. Intrathecal spinal anaesthesia is commonly used technique for anaesthesia in different surgical specialties. In those conditions which require longer duration of anaesthesia, the duration can be enhanced by various adjuvant drugs. Analgesics and anaesthetic like opoids [1], neostigmine [2], and clonidine [3,4] enhance the effect of sensory block and may extend analgesia during intra- operative and post-operative period.

Drugs like Nimodipine [5] cause regression of level of sensory block, so any drug which decreases the sensory block height level should better to be avoided. This may cause an unusual situation for anaesthesiologist leading to unwanted over sedation or conversion to general anaesthesia which could have been prevented.

Ondansetron is a selective 5-HT_3 antagonist. It is an effective drug for prevention and treatment of nausea and vomiting, so being used generously as antiemetic drug in premedication. Any interaction

Corresponding Author: Manoj Kumar Giri, PMS Quaters No. 4, SRN Hospital Campus, Allahabad (U.P), India-211002.
E-mail: drmanoj.giri@gmail.com

Received on 13.04.2017, **Accepted on** 24.04.2017

with anaesthetics including the effect on regional anaesthesia would be particular interest for anaesthesiologist.

Methods

After approval from the ethics committee, the study was done at S.R.N. Hospital (Associated to M.L.N. Medical College, Allahabad) over a period of one year. 60 unpremedicated patients of male sex, age 20- 45 years belonging to an ASA physical status I or II is undergoing lower limb orthopaedic procedures being performed under intrathecal spinal anaesthesia were recruited for the study. All patients were visited the day before surgery and the procedure of the intrathecal spinal block was explained to them and written informed consent was obtained. After randomization and double blinding, patients were allocated to one of the following groups:-

Group C

0.5% hyperbaric bupivacaine 2.5 ml in intrathecal anaesthesia + normal saline 2 ml intravenous 15 mins before spinal anaesthesia.

Group O

0.5% hyperbaric bupivacaine 2.5 ml in intrathecal anaesthesia + Ondansetron (4mg) 2 ml intravenous 15 min before spinal anaesthesia.

After shifting the patient in the operating room, i.v line was started. Standard monitoring of vital sign was instituted that include pulse oximetry, noninvasive blood pressure (NIBP), ECG, respiratory rate, heart rate.

Each patient received 500ml of ringer lactate solution over 15 minutes before intrathecal block and oxygen 3L/min via nasal canula was administered during intra-operative period. Intrathecal injection was given at L_{2-3} interspinous space using quincke 25- gauge needle with patient in sitting position using midline approach. 12.5mg (2.5ml) of 0.5% hyperbaric bupivacaine was injected at a rate of 1ml per 10 seconds with no barbotage. The patients were placed in supine horizontal position after the intrathecal injection. Sensory block was assessed at 10, 15, 20, 25 and 30 minutes and then every 15 minutes in four line voice along posterior, middle, anterior axillary line of left or right abdominal and thoracic wall and a 5 cm medial to the anterior axillary line. A 27G needle was used to check sensory level by Pin prick test. Sensory level was checked along these four lines in cephalad direction. The point of the highest sensory block level was marked and corresponding dermatome was assessed. All measurements were made in supine position and maximum sensory block level was noted. Patients were allowed to go in favoured surgical position thereafter. For Assessing duration of block, i.e. time taken for "maximum sensory block to regress to L_1 level", a towel clip was applied at midpoint of the inguinal ligament, time was noted when the patient complained pain or something pinching on inguinal area. At this time, sensory level was again checked on anterior axillary line to confirm whether the spinal block level had regressed or not, if it had regressed to L_1 level, time was noted.

The obtained results were assessed in the form of-

(1) Maximum sensory block level

(2) Time taken to regress from "maximum sensory block level to L_1 level". Motor block was assessed every 2 mins till maximum motor blockade & then every 15 mins till complete recovery of motor block, using modified bromage scale and scored as follows [6]:

Score-

0. No motor block
1. Being unable to move the hip
2. Being unable to move the knee
3. Being unable to move the ankle
4. Being unable to move the toes.

A Computerized Analysis of data was performed using "MS Excel", and Tests of statistical significance were performed. For Quantitative numerical variable 't' test, 'z' test and 'ANOVA' tests of significance were Applied. For dichotomous data chi square test was applied. A 'p' value of < 0.05 taken as significant.

Observations & Results

The demographic data for the age, height and weight are depicted in Table 1. The patients matched regarding demographic data. There was no significant difference ($p>0.05$) for age, height and weight in both the group C and O.

Sensory block level for each group at 5, 10 ,15 ,20 and 25 mins after intrathecal anaesthesia was assessed, but there was no significant difference between the group C and O. After 30 mins, maximum sensory block level in different groups was assessed. In each group, distribution pattern was studied with

regard to type of treatment and time. In group C, 66.66% of patients achieved a level of maximum T_4 block level as compared to 16.66 % in group O (Ondansetron pretreatment group), whereas 33.33% of patients in group C and 50% of patients in group O achieved maximum T_6 block level (Ondansetron pretreatment group). Thereby showing significant decreases in maximum height of block in group O (Ondansetron pretreatment group) as compared to group C ($p<0.05$) (Table 2 & Graph 1).

Mean time for regression of "maximum sensory level to L_1 level" in group C is 137.63 ± 5.49 minutes, whereas the mean time taken for regression of "maximum sensory level to L_1" in group O (ondansetron pretreatment group) was 96.5 ± 4.30. Since the 'p' value is <0.001 between group C and O, so there was a highly significant difference between group C and O (Graph 2).

Assessment of Motor Block Level-

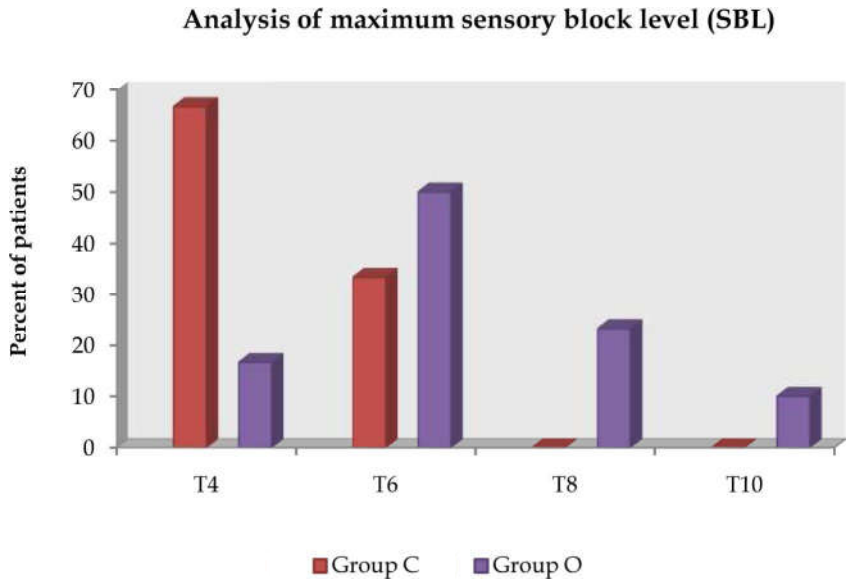
1. Achievement of maximum motor block level between group C (8.7 ± 1.00 min) and group O (9.2 ± 1.38 min) was almost same. Since p= 0.651 there was no statistical significant difference between group C and O (Graph 3).
2. Achievement of one level motor block recovery between group C (107 ± 3.08 min) and O (107.3 ± 2.54 min) was almost same. Since p= 0.823, there was no statistical significant difference between group C and O (Graph 4).
3. Achievement of complete motor block recovery between group C (156.86 ± 2.84 min) and O (156.16 ± 2.66 min) was almost same. Since p = 0.295, so there has been no statistical significant difference between group C and O (Graph 5).

Table 1: Comparision for Age, Weight and Height

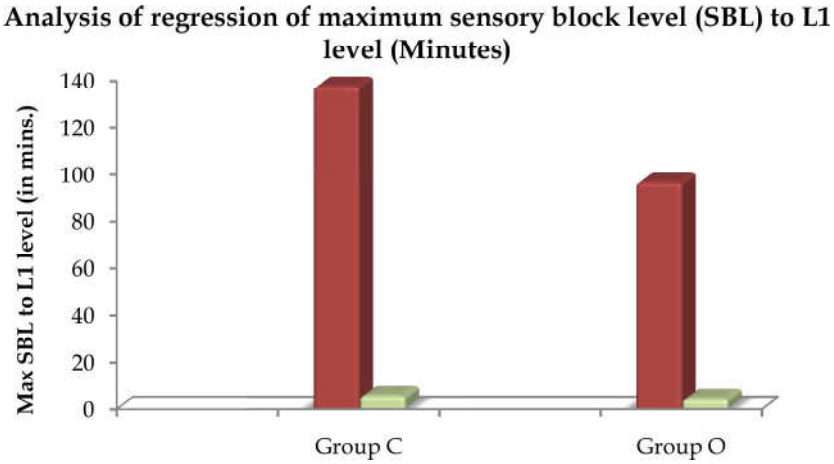
Demographic Profile	Group C	Group O	P value
Age (yrs) (Mean ± SD) Range (yrs)	32.66 ± 8.73	32.06 ± 7.82	0.815
Wt. (kg) (Mean ± SD) Range (kg)	58.2 ± 5.31	59.06 ± 6.00	0.428
Ht. (cm) (Mean ± SD) Range (cm)	156.46 ± 4.81	155.93 ± 4.76	0.849

Table 2: Analysis of Maximum Sensory Block level (SBL)

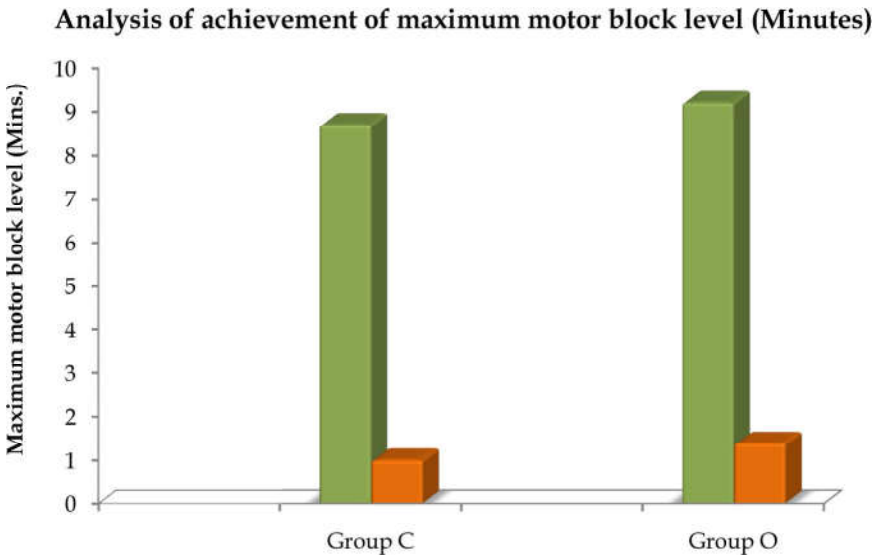
Sensory block level	Group C		Group O	
	No.	%	No.	%
T_4	20	66.66	5	16.66
T_6	10	33.33.	15	50.00
T_8	-	-	7	23.33
T_{10}	-	-	3	10
Total	30	100	30	100



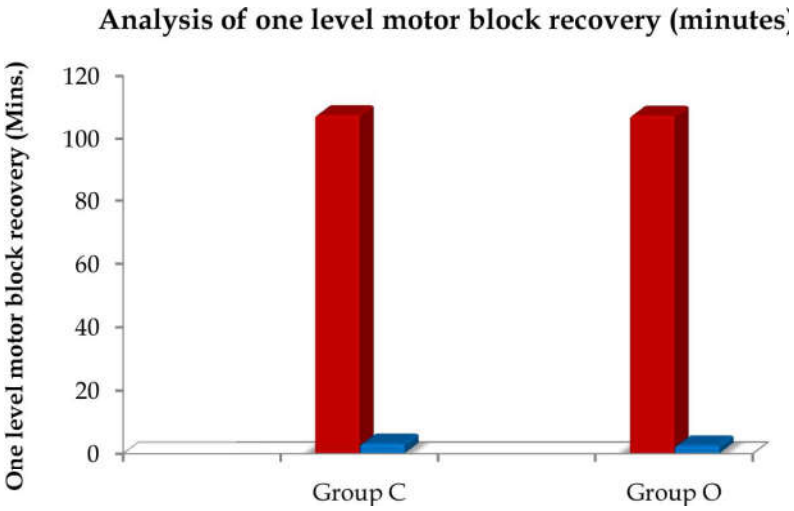
Graph 1: Analysis of maximum sensory block level (SBL)



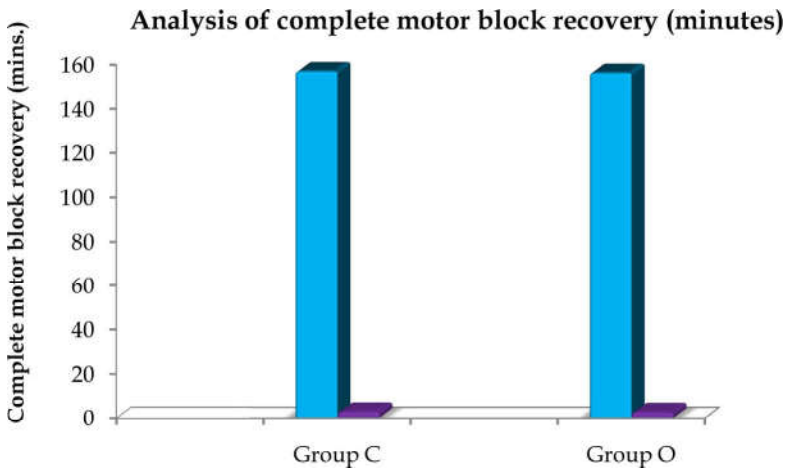
Graph 2: Analysis of regression of maximum sensory block level (SBL) to L_1 level (Minutes)



Graph 3: Analysis of achievement of maximum motor block level (Minutes)



Graph 4: Analysis of one level motor block recovery (minutes)



Graph 5: Analysis of complete motor block recovery (minutes)

Discussion

The results of advances in newer drugs, monitoring equipment, and a greater understanding of the relationship between the dose's, concentration and their subsequent effect, subarachnoid blockade with local anaesthetics in surgeries below the umbilicus and lower limb are a common practice.

We commonly use 5-HT_3 antagonist (Ondansetron and Granisetron) as prophylactic to prevent nausea & vomiting in these settings. But there is a problem with using ondensetron, that it will affect the sensory block level and/or depth of spinal anaesthesia.

The mechanism of action of ondansetron in decreasing the level of block in still not well understood. 5-HT3 receptors at the spinal cord level are antinociceptive effect, which can be antagonized by selective 5-HT3 receptor antagonist [7,8]. Animal studies clarified that serotonin has an antinociceptive effect at the spinal cord level by inhibiting the excitatory transmitters and increasing the inhibitory transmitters [9,10,11].

Administering ondansetron in addition to tramadol resulted in decreased efficacy of analgesic effect of tramadol. One study shows Co administration of ondansetron with tramadol lead to early postoperative pain score increased by 25% [12]. Increase in tramadol consumption seen in patients with patient controlled analgesia, who were receiving continuous ondansetron infusion as an anti emetic after head & neck surgery [13]. So they concluded that ondansetron reduced the overall analgesic effect of tramadol probably by blocking spinal 5-HT_3 receptors.

In previous studies of intravenous ondansetron on the level of sensory block in lidocaine intrathecally for patients undergoing various transuretheral procedures [14]. Subarachnoid lidocaine anaesthesia in patients receiving ondansetron will be associated with a more rapid regression of sensory block. They did not work on the ondansetron group for a total duration of anaesthesia and maximum sensory block level. In our study, we found significant difference for maximum sensory block level as well as for duration of anaesthesia.

Mowafi et al [15] did the study of intravenous granisetron on sensory and motor component of spinal anaesthesia produced by intrathecal bupivacaine. They found no significant difference between the two groups in the maximum cephalad spread of sensory block or the time to maximum sensory level compared with control groups, whereas we found significant difference for maximum sensory block level. Patients who received granisetron had significantly faster sensory regression, time by two segments, in contrast motor block did not differ between the two groups at any study time, this finding comparable to our study.

Omyma Sh. M. Khalifa [16] who did their study on elective caesarean section under spinal anaesthesia. Patients were divided randomly into four equal groups (G, O, E, and C). 'Group G' received 1 mg i.v. granisetron, 'group O' received 4 mg i.v. ondansetron, 'group E' received 10 mg i.v. Ephedrine, and 'group C' received 10 ml normal saline. There was a Significant faster recovery of sensory block was detected in the Granisetron group, but no significant effect seen in motor block among the groups.Whereas, in our study we found a Significant faster recovery of sensory block for ondansetron group.

Anteia Paraskeva et al [17] did their study on transurethral surgery who received 8 mg oral ondansetron in the evening before surgery plus IV 8 mg ondansetron 15 min before subarachnoid anaesthesia or placebo. All patients received 2.2 ml of 0.75% plain ropivacaine intrathecally. They found that Ondansetron had no effect on the subarachnoid sensory or motor block produced by ropivacaine. These discrepancies with our study may be due to ropivacaine is different from bupivacaine for onset as well for the duration of anaesthesia. We used the hyperbaric drug for study and they used isobaric ropivacaine. Different time intervals between block assessments may also a factor, that's why the results obtained with hyperbaric bupivacaine do not appear to support to spinal plain ropivacaine. On the other hand, the pharmacokinetics of the 5-HT3 antagonist and the pharmacokinetics of the local anaesthetic drug administered in the intrathecal space may account for a clinically evident interaction of the 5-HT3 receptor antagonist and sensory block of intrathecal anaesthesia.

Conclusion

On the basis of study following conclusions were drawn:-

1. Pretreatment of Ondansetron caused lowering of level of maximum sensory block height in patients given intrathecal spinal anaesthesia by hyperbaric bupivacaine.
2. The time taken for sensory block regression from its "maximum sensory block level to L_1" level was significantly less in Ondansetron pretreatment groups (group O).
3. There were no significant differences found for motor block between the two groups. So, we concluded that Ondansetron had no any effect on the motor block produced by intrathecal hyperbaric bupivacaine.

There for it can be stated that preoperative systemic Ondansetron antagonizes both the duration and level of sensory block produced by intrathecal bupivacaine. So any surgery which is expected to be of long duration or where higher levels of sensory block is required for surgical procedures, Ondansetron should not be used on a regular basis for prevention or treatment of nausea and vomiting.

Source of Support : Nil

Conflict of Interest: None declared

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