ASSSESSMENT OF POSTSPINAL SHIVERING AND POSTOPERATIVE SYMPTOMS WHEN USING PROPHYLACTIC INTRAVENOUS ONDANSETRON IN ORTHOPEDIC SURGERIES WHO UNDERWENT SPINAL ANESTHESIA

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ABSTRACT

Background: Post-spinal shivering, postoperative nausea and vomiting may cause discomfort to patients and. This may be deleterious in patients with impaired cardiovascular reserve.

Aim of the study: This work was done to compare between the effects of prophylactic intravenous of two different doses of ondansetron (4 mg) and (8 mg) in attenuating hypotension, shivering, nausea, and vomiting in patients undergoing orthopedic surgeries under spinal anesthesia.

Patients and methods: This study was a prospective comparative randomized controlled clinical trial that have been carried out in Zagazig University Hospitals and included 66 patients, their ages ranged from 21 to 60 years old patients for only unilateral orthopedic surgeries under spinal anesthesia, duration of surgery less than 2 hours in the study. Patients were randomly divided into three equal groups, 22 patients for each group, Group "O1" received IV ondansetron (4mg) diluted in 10 ml saline, group "O2" received IV ondansetron (8mg) diluted in 10 ml saline, and group C (control) received only 10 ml IV saline alone. Medications were administrated 5 min before starting the subarachnoid block by an anesthesiologist blinded to them, they were assessed for their cardiovascular effects throughout and after operation. We assessed the incidence of shivering, nausea, and vomiting

Results: Each of the two different doses 4mg or 8mg ondansetron have the ability to reducing the incidence and severity of shivering, during spinal anesthesia with n significant differences between them. Also, there were significant increase in the number of patients developing, Shivering in the control group compared to (O1) and (O2) groups with no significant difference between (O1) & (O2) group.

Conclusion: Ondansetron 4mg and ondansetron 8mg can reduce the incidence of shivering and vomiting. Moreover, ondansetron significantly decreased the incidence of vomiting , and shivering among our patients, which may open the door to find more other drugs to face the complication of spinal anesthesia , and who knows we may use drugs neuraxial to overcome such drawbacks.

Key words: Spinal Anesthesia, Orthopedic Surgeries, ondansetron.

I. INTRODUCTION:
Spinal anesthesia or sub-arachnoid block (SAB), is a form of regional anesthesia involving injection of a local anesthetic into the subarachnoid space, When performing spinal anesthesia using the midline approach, the layers of anatomy that are traversed (from posterior to anterior) are skin, subcutaneous fat, supraspinous ligament, interspinous ligament, ligamentum flavum, dura matter, subdural space, arachnoid mater, and finally the subarachnoid space,on the other hand When the paramedian technique is applied, the spinal needle should traverse
the skin, subcutaneous fat, ligamentum flavum, dura mater, subdural space, arachnoid mater, and then pass into the subarachnoid space (Morgan et al., 2018) The causes of bradycardia can be attributed to increased parasympathetic tone blocking of the cardio stimulatory nerve fibers and diminishing baroreceptor activity. Moreover, Bezold-Jarisch reflex (BJR) has been considered the eminent cause of bradycardia after spinal anesthesia; it is a cardio inhibitory reflex that causes bradycardia hypotension, and cardiovascular collapse via the non-myelinated type C fibers while turning on peripheral serotonin receptors 5-hydroxytryptamine (5-HT3) and initiation of BJR (1).

Sympathetic blockade results in cardiovascular changes of hemodynamic consequences in proportion to the degree of sympathectomy. The sympathetic chain originates from the thoraco-lumbar fibers. The fibers involved in smooth muscle tone of the arterial and venous circulation arise from T4 and L1. Arteries retain most of their tone despite sympathectomy because of local mediators thus there is no arteriolar vasoplegia, but the venous circulation does not contain such local mediators. The consequence of total sympathectomy is an increase in the volume of the capacitance vessels, especially in the splanchnic circulation, decreasing the venous return to the heart and hypotension occurs (2).

Nausea and vomiting occur due to decrease in blood pressure causing hypoperfusion of the medulla or cephalad spread of opioids to the chemoreceptor trigger zone. The incidence of nausea and vomiting after neuraxial opioid is much greater with the relatively poorly lipid soluble morphine compared to more lipid soluble agents, such as sufentanil, because morphine tends to travel cephalad within the CSF (3).

Post-spinal shivering is spontaneous, involuntary, rhythmic, oscillating, tremor-like muscle hyperactivity that increases metabolic heat production up to 600% after general or regional anesthesia (3).

Several studies have been found that ondansetron attenuates the incidence of SIH and bradycardia during spinal anesthesia. It is also Ondansetron a 5-HT3 antagonist is used for prophylaxis and treatment of postoperative nausea and vomiting. Considering this antagonistic effect on the 5-HT3 receptor it may be an alternative agent in diminishing SIH and bradycardia (1; 4 and 5).

We aimed at this work to compare between the effects of prophylactic intravenous of two different doses of ondansetron (4 mg) and (8 mg) in attenuating hypotension, shivering, nausea, and vomiting in patients undergoing orthopedic surgeries under spinal anesthesia

II. PATIENTS AND METHODS:

This study was a prospective comparative randomized controlled clinical trial that have been carried out in Zagazig University Hospitals and included 66 patients, their ages ranged from 21 to 60 years old patients for only unilateral orthopedic surgeries under spinal anesthesia, duration of surgery less than 2 hours in the study.

Patients with history of allergic reaction to local anesthetic, bleeding disorders, aspirin ingestion in the preceding week, mental diseases, preexisting neurological or spinal diseases, infection at the site of injection, hypotensive patients, allergy to any of the used drugs, patients autonomic neuropathy, patients with advanced cardiac or liver or renal diseases, patients taken selective serotonin reuptake inhibitor, and history of nausea and/or vomiting during the 24 h before induction of anesthesia have been excluded from the study.

Ethical approval: Approval have been obtained from the Institutional Review Board (IRB) Zagazig University. Written informed consents were obtained from all patients participating in the study.

- Patients were divided randomly using closed envelops into three groups:
  - **Group (O1)** (ondansetron (4 mg) n=22). patients received 4 mg ondansetron intravenous in to 10 ml of normal saline five minutes before the spinal block.
  - **Group (O2)** (ondansetron (8 mg) n=22). patients received 8 mg ondansetron intravenous in to 10 ml of normal saline five minutes before the spinal block.
  - **Group (C)** (control group n=22). patients received 10 ml of normal saline five minutes before the spinal block.

For each patient an 18-G peripheral venous catheter have been be inserted and 500 ml of Ringer’s lactate have been infused before and during the blockade at a rate of 10 ml/kg/h. After preoperative fluid infusion standard monitoring (ECG, sphygmomanometer cuff for blood pressure measurement and pulse oximeter) were applied with basal
reading obtained for (HR, MBAP and SPO2) Patients in group O1 & O2 had been respectively received 4 & 8 mg ondansetron (Zofran) intravenously before the intra thecal block.

The block was performed in the sitting position at the L3-L4 level, midline approach using 25-G Quincke needle. A volume of 3-ml hyperbaric bupivacaine 0.5% with 25-μg fentanyl (total 3.5 ml) will be injected intrathecally. Patients were positioned supine. An oxygen mask was placed with a flow rate of 5 l/min

The Sensory level had been determined by pinprick after the block and every minute until the level will be fixed for five consecutive minutes.

The motor blockade was evaluated using modified Bromage’s criteria.

Scale 0=full flexion of foot, knee and hip, i.e no motor block. Scale 1= full flexion of the foot and knee, unable to hip flexion. Scale 2= full flexion of foot, unable to flex the knee or hip the flexion.

Scale 3=total motor block, unable to flex the foot, knee or hip the flexion.

If the patient complains of inadequate analgesia after 20 minute of spinal anesthesia general anesthesia was given and the patient have been excluded.

The study Mean arterial blood pressure and heart rate were measured and recorded preoperatively (base line), after block then every 5 min till the end of surgery, The highest sensory level, duration of surgery. Hypotension (mean arterial blood pressure decrease >20% of basal readings) have been managed by intermittent doses of ephedrine 0.1 mg/kg intravenously with increments and the total amount of ephedrine given will be recored Bradycardia (heart rate <20 of basal reading) was treated by intravenous atropine 0.01 mg/kg (number of patients take atropine was recorded and amount of atropine given was recorded). Any other complications also have been recorded.

**Statistical analysis**

Data collected, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative have been represented as number and percentage, quantitative continues group well be represented by mean ± SD, the following tests were used to test differences for significance. Difference and association of qualitative variable by Chi square test (X2). Multiple quantitative by ANOVA. P value was set at <0.05 for significant results & <0.001 for high significant result.

Data were collected and submitted to statistical analysis. The following statistical tests and parameters were used.

**III. RESULTS**

There was no significant difference among groups regarding the patient characteristics (**Figure 1, 2**).

MBP was significantly lower among the control group from (10 min tell the 20 minutes) compared to (O1) and (O2) groups with no significant difference between (O1) or(O2) groups and finally also no significant difference among the three groups regarding other times (**Figure 3**).

Incidence of postoperative nausea was significantly lower in the group (O2) followed by Group (O1) compared to group C. Control group was significantly associated with vomiting, Group (O2) was the lowest regard vomiting rate followed by Group (O1) (**Table 1**).

Control group was significantly associated with Shivering, Group O2 had the lowest incidence of Shivering rate followed by Group O1 (**Table 2**).
Table 1: Nausea and Vomiting distribution among studied groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Total</th>
<th>X²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>Group O1</td>
<td>19</td>
<td>86.4%</td>
</tr>
<tr>
<td></td>
<td>Group O2</td>
<td>21</td>
<td>95.5%</td>
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<tr>
<td></td>
<td>Group C</td>
<td>10</td>
<td>45.5%</td>
</tr>
<tr>
<td>Yes</td>
<td>N</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group O1</td>
<td>3</td>
<td>13.6%</td>
</tr>
<tr>
<td></td>
<td>Group O2</td>
<td>1</td>
<td>4.5%</td>
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<tr>
<td></td>
<td>Group C</td>
<td>12</td>
<td>54.5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>No</td>
<td>N</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>N</td>
<td>3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>No</td>
<td>N</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>N</td>
<td>1</td>
</tr>
</tbody>
</table>
| Total  | N     | %  |     |%
|        | Group O1 | 22 | 100.0% | 19.85 0.00** |
|        | Group O2 | 22 | 100.0% | 19.85 0.00** |
|        | Group C  | 22 | 100.0% | 19.85 0.00** |

Table 2: Shivering and Pain distribution among studied groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Total</th>
<th>X²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Shivering</td>
<td>No</td>
<td>N</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>N</td>
<td>2</td>
</tr>
<tr>
<td>Pain</td>
<td>No</td>
<td>N</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>N</td>
<td>5</td>
</tr>
</tbody>
</table>
| Total  | N     | %  |     |%
|        | Group O1 | 22 | 100.0% | 0.15 0.92 |
|        | Group O2 | 22 | 100.0% | 0.15 0.92 |
|        | Group C  | 22 | 100.0% | 0.15 0.92 |

Figures 1: Demographic mean age among groups

Figure 2: Demographic mean BMI among groups.
IV. DISCUSSION:

Spinal anesthesia is a safe anesthetic technique practiced commonly worldwide. Hemodynamic changes such as hypotension and bradycardia occur after spinal anesthesia and usually benign and respond by fluid therapy and vasopressors. However, rarely, it may cause severe bradycardia and cardiac arrest (6).

Shivering is an involuntary, oscillatory muscular activity, it is a physiological thermoregulatory response to cold, under spinal anesthesia, shivering occurs as a response to lowering of core body temperature and decrease in blood supply to the upper body (7).

Factors leading to hypothermia and Shivering are age, duration of surgery, the operating room temperature, type of regional anesthesia (spinal or epidural), and the infusion solution (8).

Volume preload may cause fluid overload and cardiovascular collapse in labile patients, prophylactic use of vasopressors has no role in preventing hypotension in turn which may cause HTN and increase cardiac workload (9).

A study was done by (10) as they tested the effect of Ondansetron on the hypotension following, spinal anesthesia in pregnant candidate women for elective cesarean section. They concluded that the use of ondansetron leads to a less reduction in MBP which goes side by side with the results of the present study.

Our primary aim was to assess the mean blood pressure (MBP) and the incidence of postspinal shivering, postoperative nausea and vomiting in ondansetron4mg group (group O1), ondasteron 8mg group (O2) and control group (group C) in different time intervals. As well as, any complications during or after surgery.

Our study showed that, there was no significant difference between the groups O1 (n=22) group O2 (n22) and group C (n=22) as regards to the demographic data including mean age (50years), BMI and parity in all groups.

These results are in agreement with that of Trabelsi et al., (11) who compared ondansetron 5 mg (n=40) with placebo (n=40), Owczuk et al., (12) who compared ondansetron 8mg in their patients (n=35) with placebo (n=36), and Sahoo et al., (1) who compared ondansetron 4 mg (n=24) with placebo (n=24).

MBP was significantly lower among control group from 10 min tell the 20 minutes compared to(O1) and(O2) groups with no significant difference between (O1) & (O2) groups and also no significant difference among three groups regarding other times.

Our finding is in agreement with the results obtained by Sahoo et al., (1) who used 4 mg ondansetron given 5 minutes before spinal block for caesarean section and (11) who used 5 mg ondansetron, they found that SBP, DBP, and the MBP were higher in patients who were given ondansetron compared to their control group.
Also, in agreement to our findings Ahmed and Haidy (13) studied 120 parturient scheduled for elective cesarean delivery under spinal anesthesia and found that the prophylactic bolus intravenous ondansetron 4 mg could decrease the fall in MAP of parturient women following spinal anesthesia.

In contrast to our result, Tatikonda et al., (5) In their comparative randomized controlled double-blinded study done on patients who were posted for elective orthopedic, gynecological and general surgical procedures under spinal anesthesia, found that there was no statistically significant difference in the systolic blood pressure, diastolic blood pressure and MAP.

The current study revealed that, the incidence of postoperative nausea and vomiting was lower significantly in group O1andO2 compared to group C. these finding are in agreement with the results reported by (14) on 63 parturient women in their study undergoing cesarean section under spinal anesthesia as they found that intravenous ondansetron 4 mg before giving spinal anesthesia is more effective to the prevent incidence of nausea and vomiting in cesarean section.

On the contrary, in disagreement with our study, the study done by (15) who reported that ondansetron premedication does not reduce the incidence of nausea and vomiting. This contrary may be due to difference in anesthetic regimen as all patients in that study received 500 mL of hetastarch (Voluven) also 20μg of fentanyl and 100μg of preservative-free morphine administered in subarachnoid block.

The results of our present study showed that the Control group was significantly associated with Shivering and that Group O2 had the lowest regard Shivering rate followed by Group O1. Our Results which are also similar to the theme of (16) who suggested that the prophylactic administration of low dose ketamine 0.25 mg/kg and ondansetron 4mg produces a significant antishivering effect in comparison with placebo of their patients undergoing spinal anesthesia, and that ketamine 0.25 mg/kg is significantly more effective than ondansetron (4 mg).  

In a prospective double-blinded study by (17) on 90 American Society of Anesthesiologists I-II patients undergoing elective cesarean section which randomly assigned to one of three equal groups. Group T received tramadol; Group G received granisetron, Group M received meperidine, and Group P received only saline 0.9% as placebo. They found that prophylactic use of granisetron is as effective as meperidine and tramadol in preventing postanesthetic shivering.

Also, our results matched that of (7) who obtained 5-HT3 receptor antagonists appear to prevent postoperative shivering, with a broadly comparable efficacy to meperidine.

Moreover, (18) in a study done on the efficacy of IV ondansetron for prevention of shivering in spinal anesthesia administered in elderly patients concluded that Intravenous administration of 8 mg of Ondansetron prior to a subarachnoid block, is effective in decreasing the frequency of shivering.

In contrast with our study results (19) concluded that intravenous ondansetron 8mg prior to performing combined spinal epidural anesthesia in women undergoing elective cesarean delivery did not decrease the incidence or severity of shivering. The variability in the findings of our present study with that of Browning might be explained as they used spinal epidural combined technique instead of only spinal given in our present study.

V. CONCLUSION

From the previous results, we demonstrated that ondansetron 4mg and ondansetron 8mg can reduce the incidence of shivering and vomiting. Moreover, ondansetron significantly decreased the incidence of vomiting, and shivering among our patients, which may open the door to find more other drugs to face the complication of spinal anesthesia, and who knows we may use drugs neuraxial to overcome such drawbacks.

REFERENCES


