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The Effect of Different Doses of Ondansetron in Prevention of Hypotension and Shivering in Patients Undergoing Lower Limb Surgery under Spinal Anesthesia

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Abstract

Background: Spinal anesthesia is a safe and very effective technique for lower limb surgical mannoveurs but it is associated with many side effects as hypotension and shivering which are distressing to the patients. Benefits of spinal anesthesia for lower limb surgery include reduced mortality, deep vein thrombosis (DVT), transfusion requirements and pulmonary complications. Several studies suggested that ondansetron, used for prophylaxis and treatment of nausea and vomiting.

Aim of Study: The aim of this work is to assess the efficacy of administration of different doses of intravenous ondansetron on attenuation of spinal induced hypotension as primary outcome of the present study and shivering as secondary outcome during lower limb surgery.

Patients and Methods: Patients were randomly allocated into three equal groups, Group (C) received normal saline as control group, Group (OL) received 4mg ondansetron i.v, Group (OH) received 8mg ondansetron i.v. slowly. Patients were assessed for haemodynamic changes, motor block, incidence of any complication and the use of pethidine and ephedrine.

Results: In comparison of mean blood pressure of groups OL and OH to the control group. MBP of control group was significantly lower than group OL immediately after induction and also at 5, 10, 15 and 20 minutes intraoperative MBP of control group was significantly lower than group OH immediately after induction and also at 10, 15, 20 and 30 minutes intraoperative. There was significant difference regarding MBP between group OL and group OH at 30 and 60 minutes (MBP of group OH was significantly higher. p-value 0.02 and 0.043 respectively). Dose of administered pethidine and ephedrine was statistically lower in groups OH than group OL than control group.

Conclusion: Administration of two different doses of intravenous ondansetron, 4mg and 8mg, efficiently attenuates spinal induced hypotension and shivering compared to the control saline group. Incidence of hypotension and shivering was less observed in ondansetron 8mg group than ondansetron 4mg group.

Key Words: *Spinal anesthesia – Regional anesthesia – Ondansetron – Hypotension – Shievering – Nausea and vomiting.*

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Introduction

SPINAL anesthesia is a safe and effective technique for multiple surgical procedures but it is frequently associated with many side effects **[1]**.

Cardiovascular side effects are significant during spinal anesthesia, hypotension is the most common side effect which occurs due to reduction in vascular resistance by sympathetic nerve blockade, relative dominance of parasympathetic system, activation of Bezold Jarish reflex and increased baroreceptor activity may lead to bradycardia and some degree of hypotension. The Bezold-Jarisch reflex (BJR) explains the occurrence of hypotension after spinal anesthesia through serotonin receptors together with decreased blood volume, Stimulation of cardiac chemoreceptors in the heart by decreased venous return increases the parasympathetic activity, while it decreases the sympathetic activity resulting in vasodilatation and bradycardia **[2]**.

Several studies suggested that ondansetron,a 5-hydroxytryptamine subtype 3 (5-HT3) receptor antagonist used for prophylaxis and treatment of nausea and vomiting, may also reduce the hemodynamic changes induced by spinal anesthesia **[3]**.

The action of Ondansetron is through inhibition of the Bezold-Jarisch reflex. This reflex is mediated through vagal afferents. When the reflex is activated by decreased venous return and stimulation of cardiac chemoreceptors it causes hypotension and bradycardia **[4]**.

Shivering after spinal anesthesia occurs in more than 56.7% of cases. The main effect of shivering is to increase metabolic heat production, also it increases the oxygen consumption up to 600% of the basal level which increases lactic acid and CO_2 production with consequent increase in the cardiac output and minute ventilation [5].

Beside cardiovascular adverse effects, shivering can cause problems during surgery and increases the risk of postoperative bleeding, It also increases intracranial and intraocular pressures. Moreover, severe shivering increases the risk of incidental trauma, disrupts medical devices and interferes with electrocardiogram and pulse oximetry monitoring so that it is important to provide effective prevention of this clinical dilemma allowing early ambulation [6].

The mechanism of action of ondansetron as anti-shivering is not unknown and it may be due to centrally acting at the level of the pre-optic anterior hypothalamic region by inhibition of serotonin reuptake [7].

Patients and Methods

This randomized controlled study was done after obtaining ethical committee approval No. (Ms/ 17.06.42) and informed written consent from 120 patients, ASA status I or II who undergone lower extremity surgery in Mansoura University Hospitals during October 2017 and April 2018.

Patients were randomly allocated into three equal groups using computer generated random sequence and sealed envelope technique, Group (C) received normal saline as control group, Group (OL) received 4mg ondansetron i.v, Group (OH) received 8mg ondansetron i.v. slowly.

Inclusion criteria:

- ASA physical status I or II patients.
- Age between 20-50 years.
- BMI between (18-30) kg/m^2.
- Patients of either sex.

Exclusion criteria:

- Patients with contraindications to spinal anesthesia.
- Patients known to be allergic or have containdication to ondansetron.
- Patients allergic to local anesthetic drugs.
- Pregnancy.
- History of hypertension, coronary artery disease or other cardiovascular diseases.
- Preoperative use of ondansetron.
- Preoperative fever (>37.5ºc) .
- Hypo- or hyperthyroidism, parkinson's disease, Raynauds syndrome.
- Intraoperative use of vasodilator drugs.

Methods: Preoperative investigations were already done including complete blood picture, INR, Liver function tests (SGPT, SGOT, Albumin, Total and direct bilirubin) kidney function tests (Urea, Creatinine), and ECG. Demographic data (age, weight, height, BMI), ASA and also total surgical time was recorded.

On arrival to the operating room, standard monitoring was taken from all patients including pulse oximeter, noninvasive arterial blood pressure and ECG.

Preoperative hemodynamic data were recorded namely heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), arterial oxygen saturation (SPO_2) and tympanic membrane temperature. An 18-gauge intravenous catheter was placed in the hand and patients received 15ml/kg lactated Ringer solution (warmed to 37ºC over 15 minutes before spinal anesthesia). The temperature of the operating room during the perioperative period was kept at a set average temperature of around 24ºC for all cases.

The patients in (group C) received 1 0mL normal saline intravenous. The intervention groups received 4 mg ondansetron (group OL) and 8mg ondansetron (group OH), diluted in normal saline to 1 0ml also via I.V. route. In all groups, solutions were given over 5 minutes just before induction of spinal anesthesia by doctor not included in study.

In all patients, spinal block was done in the sitting position and a 25 gauge needle was inserted by midline approach into the L3-4 or L4-5 interspaces. After ensuring the correct position of the needle, 20mg of 0.5% hyperbaric bupivacaine was injected. Patients was placed in the supine position with 15 degree head elevation.

Motor blockade degree was assessed according to Modified Bromage scale [8]:

0 = Able to move hip, knee, ankle, and toes.

1 = Unable to move hip, able to move knee, ankle, and toes.

2 = Unable to move hip and knee, able to move ankle and toes.

3 = Unable to move hip, knee and ankle, able to move toes.

4 = Unable to move hip, knee, ankle and toes.

The upper level of sensory blockade was evaluated by application of alcoholic skin prep test from caudal to rostral direction at 5-min intervals up to 20 minutes.

The (SPO_2), (HR), (SBP), (DBP), (MBP) and tympanic membrane temperature were measured and recorded intermittently intra-operatively every 5 minutes in the first half hour then every 30 minutes till the end of surgery and two hours postoperative.

The incidence and severity of shivering was observed intraoperative and two hours postoperative using the scale validated by Tsai and Chu **[8]***:*

0 = No shivering.

1 = Piloerection or peripheral vasoconstriction but no visible shivering.

2 = Muscular activity in only one muscle group (such as extensors of forearm).

3 = Muscular activity in more than one muscle group but not generalized shivering (such as extensors of forearm and extensors of the other forearm).

4 = Shivering involving the whole body.

Grades 3, and 4 shivering for at least 3 minutes were considered positive. Positive shivering or lower grade shivering but described as distressful by the patient treated with IV boluses of pethidine (0.5mg/kg) during the operation and in the recovery room. The total dose of pethidine given was recorded.

Incidence of hypotension at any time intraoperative was recorded. Hypotension is defined as more than 20% drop in mean arterial blood pressure (MAP) compared to basal value, and was treated with repeated IV boluses of ephedrine (10mg), as required. Total dose of ephedrine administered was recorded. Bradycardia (heart rate <50 beat/min) was treated with IV atropine (0.01mg/kg) repeated as required.

Incidence of nausea and vomiting intraoperative and postoperative was recorded.

Statistical analysis:

Sample size calculation was based on the findings of Sahoo and colleagues **[9]** in which MAP of patients who received ondansetron was 87.5 ± 11.3 mmHg compared with 80.4± 10.8 mmHg in patients who received placebo. Sample size calculation using online site (www.openepi.com), 80% test power and an confidence interval 95% indicated 39 patients were required in each group. Our study included 40 patients in each group.

Data collected including history, basic clinical examination, laboratory investigations and outcomes were measured, coded, 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 represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent multiple 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.

Results

Flowchart of the present study shows that the study was conducted on 120 patients randomly allocated into three equal groups. 13 patients were excluded, 9 patients were feverish, 3 patients were hypertensive and one patient was alcholic.

Demodraphic data showed no statistical difference among studied groups as regard age, weight, height and BMI (Table 1).

There was no difference as regarding degree of motor block between groups C, OL and OH (Table 2).

Comparing systolic blood pressure of studied cases, SBP of control group was significantly lower than group OL at times 10, 15 and 20 minutes (*p*-value 0.0001, 0.0001 and 0.05 respectively). SBP of control group was significantly lower than group OH immediately after induction and at times 10, 15, 20 and 30 minutes (*p*-value 0.012, 0.0001, 0.001 and 0.021 respectively).

t-test revealed that there was significant decrease in SBP of control group at 15 minutes compared to basal reading (*p* 0.033). Concerning group OL, there was significant decrease in SBP of OL group at 30 minutes (*p* 0.023) compared to basal reading. Concerning group OH, there was no significant difference regarding SBP between the basal reading and the following readings intraoperative.

There was no significant difference regarding SBP between group OL and group OH at all times during surgery.

In comparison of diastolic blood pressure of groups OL and OH to the control group, showed that DBP of control group was significantly lower than group OL immediately after induction and also at 15 minutes (p-value 0.042 and 0.0001 respectively) intraoperative, DBP of control group was significantly lower than group OH immediately after induction and also at 15, 20 and 30 minutes (p-value 0.001, 0.001, 0.004 and 0.001 respectively) intraoperative.

t-test revealed that there was significant decrease in DBP of control group at times 10, 15, 20, 25 and 30 minutes compared to basal reading. There was significant decrease in DBP of OL group at times 10, 20, 25, 30, 60 and 90 minutes compared to basal reading. Group OH showed significant decrease in DBP at 25 minutes compared to basal reading.

There was significant difference regarding DBP between group OL and group OH at 30 and 60 minutes (p-value 0.014 and 0.046 respectively).

In comparison of mean blood pressure of groups OL and OH to the control group, Table (3) showed that MBP of control group was significantly lower than group OL immediately after induction and also at 5, 10, 15 and 20 minutes intraoperative (p-value 0.004, 0.047, 0.008, 0.001 and 0.048 respectively), MBP of control group was significantly lower than group OH immediately after induction and also at 10, 15, 20 and 30 minutes intraoperative (p-value 0.001, 0.009, 0.001, 0.001 and 0.001 respectively). (Table 3).

t-test revealed that there was significant decrease in MBP of control group at times 10, 15, 20, 25 and 30 minutes compared to basal reading. There was significant decrease in MBP of OL group at times 20, 25, 30 and 60 minutes compared to basal reading. MBP of group OH was significantly decreased compared to basal reading only at 25 minutes after induction. (Table 3).

There was significant difference regarding MBP between group OL and group OH at 30 and 60 minutes (MBP of group OH was significantly higher. p-value 0.02 and 0.043 respectively). (Table 3).

t-test revealed that there was significant decrease in HR of control group at times 30, 60, 90, 120, 150 and 180 minutes compared to basal reading. There was significant decrease in HR of OL group at times 30, 60, 90, 120, 150 and 180 minutes compared to basal reading. HR of group OH was significantly lower than basal reading at times 30, 60, 90, 120, 150 and 180 minutes after induction.

There was significant difference regarding HR between group OL and group OH at 10, 15, 20, 25, 30, 60, 90, 120, 150 and 180 minutes (HR of group OH was significantly higher. p-value 0.019, 0.003, 0.001, 0.015, 0.001, 0.039, 0.046, 0.005, 0.008 and 0.038 respectively).

No significant difference is present among the studied groups regarding the tympanic temperature and oxygen saturation intraoperative or postoperative.

Dose of administered pethidine was statistically lower in groups OL and OH than control group (p-value 0.017 and 0.001 respectively). (Table 4).

Dose of administered pethidine was statistically lower in group OH when compared to group OL (p-value 0.016). (Table 4).

Dose of administered ephedrine was statistically lower in groups OL and OH than control group (p-value 0.02 and 0.001 respectively). (Table 4).

Dose of administered ephedrine was statistically lower in group OH when compared to group OL (p-value 0.041). (Table 4).

Number of patients treated with pethidine in the control group was significantly higher than both groups OL and OH (21 patients in control group versus 15 patients in group OL and 14 patients in group OH). There was no difference between group OL and group OH as regard number of patients treated with pethidine. (Table 5).

Number of patients treated with ephedrine in the control group was significantly higher than both groups OL and OH (29 patients in control group versus 15 patients in group OL and 10 patients in group OH). There was a significant difference between group OL and group OH as regard number of patients treated with ephedrine. (Table 5).

No statistical difference between the three groups as regard treatment with atropine. (Table 5).

As regards shivering, number of patients complained of intraoperative shivering in the control group was significantly higher than both groups OL and OH (21 patients in control group versus 15 patients in group OL and 14 patients in group OH). There was no significant difference between group OL and group OH as regard number of patients complained of intraoperative shivering. (Table 6).

In the postoperative period, number of patients complained of shivering in the control group was significantly higher than both groups OL and OH (8 patients in control group versus 2 patients in group OL and 1 patient in group OH). There was no significant difference between group OL and group OH as regard number of patients complained of postoperative shivering. (Table 6).

No statistical difference is found between the three groups as regard the number of patients complaining of intraoperative nausea. (Table 6).

In the postoperative period, number of patients complained of nausea in the control group was significantly higher than both groups OL and OH (19 patients in control group versus 13 patients in group OL and none of patients in group OH). Ofcourse, there was no significant difference between group OL and group OH as regard number of patients complaining of postoperative nausea. (Table 6).

As regards vomiting, number of patients complained of vomiting in the control group was significantly higher than both groups OL and OH (6 patients in control group versus 2 patients in group OL and none of patients in group OH). There was no significant difference between group OL and group OH as regard number of patients complained of vomiting. (Table 6).

Table (1): Demographic data of studied group. Values are in (mean ± SD).

Demographic data	Group C (n=40)	Group OL (n=40)	Group OH (n=40)	*p*-value
Age/years	35.6±9.28	31.6±8.08	34.5±8.77	0.105
Weight/kg	79.2±12.48	80.3±11.79	79.1±10.96	0.875
Height/cm	171.2±8.06	173.8±6.03	172.4±7.09	0.203
BMI (kg/m^2)	26.9±3.26	26.4±3.16	26.5±1.92	0.651

Group C = Control group.
Group OL = Ondansetron low dose group.
Group OH = Ondansetron high dose group.
p-value is significant when it is ≤0.05.

Table (2): Degree of motor block of the studied groups. Values are in (mean ± SD).

Degree of motor block	Group C (n=40)	Group OL (n=40)	Group OH (n=40)	*p*-value
	3.6±0.5	3.6±0.5	3.7±0.5	0.868

Group C = Control group.
Group OL = Ondansetron low dose group.
Group OH = Ondansetron high dose group.

Table (3): Mean blood pressure measurements (mmHg) among studied groups. Values are in (mean ± SD).

Mean blood pressure (mmHg)	Group C (n=40)	Group OL (n=40)	Group OH (n=40)	*p*-value
Before induction	80±10.82	83±8.42	82±5.77	0.289
Immediately after induction	86±7.77	92±8.73*	93±9.70*	0.001
At 5 minutes	81±8.01	85±9.40*	84±12.23	0.129
At 10 minutes	74±8.55†	80±8.88*	80±12.82*	0.010
At 15 minutes	70±8.97†	81±11.68*	81±9.36*	0.001
At 20 minutes	72±8.71†	76±11.14*†	80±11.97*	0.002
At 25 minutes	73±10.19†	75±9.36†	77±13.98†	0.330
At 30 minutes	71±9.01†	74±9.68†#	80±12.57*	0.002
At 60 minutes	79±8.24	76±6.63†#	80±12.58	0.125
At 90 minutes	81±10.73	80±9.23	82±12.49	0.702
At 120 minutes	84±9.91	81±9.58	81±12.56	0.532
At 150 minutes	82±9.19	82±9.24	82±11.64	0.982
At 180 minutes	83±9.25	82±9.46	83±10.96	0.962
1 Hour post-operative	84±9.14	81±6.03	82±5.78	0.141
2 Hours post-operative	84±5.33	81±5.90	81±4.91	0.086

* Significant compared to control group.
† Significant compared to basal reading of each group.
# Specific significance between two ondansetron groups.

Group C = Control group.
Group OL = Ondansetron low dose group.
Group OH = Ondansetron high dose group.

Table (4): Pethidine and ephedrine dose (mg) distribution among the studied groups. Values are in (mean ± SD).

	Group C (n=40)	Group OL (n=40)	Group OH (n=40)	*p*-value
Dose of pethidine (mg)	31±3.16	28±3.84*#	24±4.59*	0.001
Dose of ephedrine (mg)	20±7.01	12±8.84*#	9±6.95*	0.026

* Significant compared to control group.
# Specific significance between two ondansetron groups.

Group C = Control group.
Group OL = Ondansetron low dose group.
Group OH = Ondansetron high dose group.

Table (5): Patients treated with ephedrine, atropine and pethidine. Values are in number of cases and percentage.

	Group C (n=40) %	Group OL (n=40) %	Group OH (n=40) %	*p*-value
TTT with pethidine	21 52.5%	15* 37.5%	14* 35.0%	0.026
TTT with ephedrine	29 72.5%	15*# 37.5%	10* 25.0%	0.001
TTT with atropine	5 12.5%	4 10.0%	3 7.5%	0.75

* Significant compared to control group.
# Specific significance between two ondansetron groups.

Group C = Control group.
Group OL = Ondansetron low dose group.
Group OH = Ondansetron high dose group.

Table (6): Incidience of perioperative shivering, nausea and vomiting. Values are in number of cases and percentage.

	Group C (n=40) %	Group OL (n=40) %	Group OH (n=40) %	*p*-value
Intraoperative shivering	21 52.5%	15* 37.5%	14* 35.0%	0.026
Postoperative shivering	8 20.0%	2* 5.0%	1* 2.5%	0.012
Intraopeative nausea	4 5.0%	3 10.0%	2 7.5%	0.69
Postoperative nausea	19 47.5%	13*# 32.5%	0* 0.0%	0.001
Perioperative vomiting	6 15.0%	2* 5.0%	0* 0.0%	0.02

* Significant compared to control group.
# Specific significance between two ondansetron groups.
Group C = Control group.
Group OL = Ondansetron low dose group.
Group OH = Ondansetron high dose group.

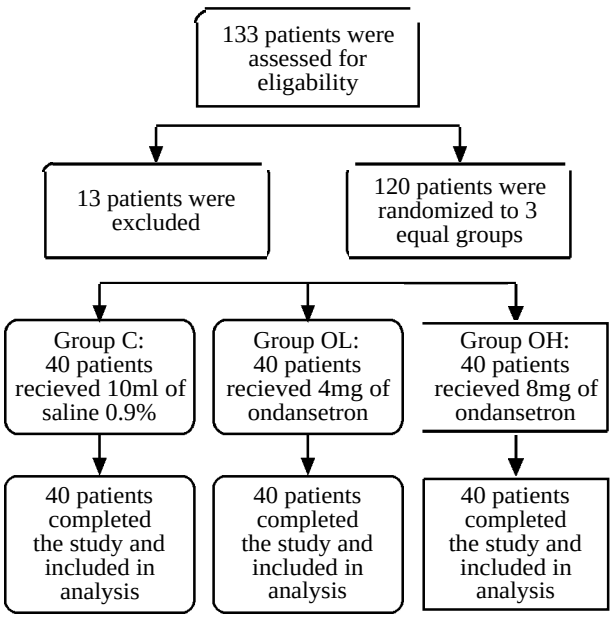

Fig. (1): Flow chart of the study.

Discussion

Spinal anesthesia is a safe and good technique for lower limb surgical mannoveurs but it is associated with many side effects such as hypotension and shivering which are distressing to the patients **[10]**.

In our study results, ondansetron given i.v. immediately before induction of spinal anesthesia has been proved to be an effective drug to attenuate spinal-induced hypotension. Patients in groups OL and OH have shown more haemodynamic stability when compared to patients in the control group. Morever, patients who were administered 8mg ondansetron in group OH were more stable concerning blood pressure than patients who were administered just 4mg ondansetron in group OL.

In agreement to our results, Tubog and his colleagues (2017) performed a meta-analysis which included Thirteen RCTs, totaling 1,225 subjects and founded that i.v. ondansetron may mitigate the risks of SIH and bradycardia following spinal anesthesia. Intravenous ondansetron reduced the incidence of hypotension in both the all-procedure analysis group and cesarean delivery group **[11]**.

Also in agreement to our results, Marashi and his colleagues (2014) performed a study on two hundred and ten patients aged 20-50 years old scheduled for spinal anesthesia and divided randomly into three equal groups. The control group received normal saline and intervention groups received 6mg or 12mg of intravenous ondansetron. The study found that the two experimental ondansetron groups were less hypotensive than the control group. However, the study could not find statistical difference between the ondansetron groups as regard blood pressure **[12]**.

Palai and his colleagues (2018) compared the effect of 4mg ondansetron to 75 microgram of palonsetron to control group on patients undergoing elective abdominal hystrectomy (50 patients in each group) and found that fall in mean arterial pressure was least in ondansetron group followed by palonsetron group and control group which came in agreement to our results **[13]**.

In accordance to our results, Shah and colleagues (2019) compared the effect of 8mg ondansetron to placebo in elderly patients and concluded that intravenous administration of 8mg of ondansetron, 5 minutes prior to subarachnoid block, is effective in decreasing frequency of hypotension in elderly patients **[14]**.

In agreement to our results, Nada and colleagues (2018) concluded that prophylactic ondansetron 6mg 5min before spinal anesthesia for percutaneous nephrolithotomy operation is comparable to prophylactic 15mg ephedrine immediately after block in attenuating the incidence of hypotension **[15]**.

Mohamed and colleagues (2018) concluded that prophylactic bolus intravenous ondansetron 4mg and to less extent 2mg could decrease the fall in mean blood pressure of parturients following spinal anesthesia as well as intravenous ephedrine 1 0mg. Their study results were similar to our results

however different doses of ondansetron were used **[16]**.

Owczuk and colleagues (2008) also found that Ondansetron 8mg given intravenously help the decrease of systolic and mean blood pressure compared to the control group which came in agreement with our study results **[3]**.

In accordance to our results, Nivatpumin and colleagues (2017) found that There was no significant difference in maternal blood pressure in women administered prophylactic ephedrine (10mg) or ondansetron (8mg) after spinal anesthesia compared with placebo **[17]**.

In agreement to our results, Gao and colleagues (2015) in their meta-analysis founded that prophylactic ondansetron decreases the incidence of spinal anesthesia-induced hypotension and vasopressor consumption in both obstetric and non-obstetric patients **[1]**.

In contrast to our results, Ranjbar and his colleagues (2018) found that i.m. injection of ephedrine 25 minutes prior to the spinal anaesthesia leads to better prevention of systolic blood pressure changes compared with intravenous 4 mg ondansetron and ringer, while administration of ondansetron and ringer had the same effects on reducing maternal hemodynamic changes **[18]**.

In contrast to the present study, the study by Ortiz-Gómez and colleagues (2014) showed that prophylactic ondansetron at 2, 4, or 8mg i.v. had little effect on the incidence of hypotension in healthy parturients undergoing spinal anesthesia with bupivacaine and fentanyl for elective cesarean section **[19]**.

In contrast to our results, Zhou and colleagues (2018) concluded that ondansetron had no capabilities to decrease the incidence of hypotension and shivering during cesarean delivery after spinal anesthesia **[20]**.

Although heart rate of group OH (8mg ondansetron) was statistically higher than group OL and group C, Incidence of bradycardia and need for atropine were similar between all groups.

Palai and his colleagues (2018) observed no significant difference regarding heart rate **[13]**.

Shah and colleagues (2019) concluded that intravenous administration of 8mg of ondansetron, 5 minutes prior to subarachnoid block, is effective in decreasing frequency of bradycardia in elderly patients **[14]**.

Nada and colleagues (2018) concluded that prophylactic ondansetron 6mg 5min before spinal anesthesia for percutaneous nephrolithotomy operation is comparable to prophylactic 15mg ephedrine immediately after block in attenuating the incidence of bradycardia **[15]**.

Owczuk and colleagues (2008) found no changes in heart rate compared to placebo group **[3]**.

In meta-analysis done by Gao and his colleagues (2015), they observed that ondansetron can decrease adverse outcomes such as bradycardia **[1]**.

Zhou and colleagues (2018) concluded that ondansetron could efficiently decrease the incidence of bradycardia **[20]**.

Our results demonstrated that the administered dose of ephedrine and munber of patients treated with ephedrine was lowest in group OH followed by group OL and the highest dose and number of patients treated with ephedrine was in the control group.

In accordance to our results, Nada and colleagues (2018) concluded that the need for rescue vasopressor is markedly decreased after administration of prophylactic ondansetron 6mg 5min before spinal anesthesia for percutaneous nephrolithotomy operation which is comparable to prophylactic 15mg ephedrine **[15]**.

Palai and colleagues (2018) observed that ondansetron (4mg) and palonsetron (75mic) had significantly lower requirement of vasopressor compared to placebo group **[13]**.

The cause of hypotension and bradycardia following induction of spinal anesthesia is multifactorial. Studies proposed that the basis of SIH is reduction in systemic vascular resistance with concomitant inadequate increase in CO. During spinal anesthesia, neuraxial blockade reduces venous return. The reduction in preload triggers the BJR, which is mediated by the peripheral 5-HT3 type receptors. The BJR is an inhibitory cardiovascular response to noxious chemical substances and ventricular stretch sensed by the chemoreceptors and mechanoreceptors, which are primarily located in the wall of the left ventricle. The stimulation of the 5-HT3 type receptors increases parasympathetic activity and decreases sympathetic activity, resulting in the triad responses of bradycardia, vasodilation, and hypotension **[1]**.

Ondansetron also seems to attenuate spinal induced hypotension through inhibition of chem-

oreceptors located in vagal nerve ending. These receptors are 5-HT3 in nature and structurally G protein coupled, ligand-gated fast-ion channels and stimulation results in increased efferent vagal nerve activity, frequently producing bradycardia and hypotension [7].

Positive shivering (grades 3 and 4) was lower in both groups OL and OH than the control group.

In agreement to our results, Gupta and colleagues (2018) found no significant difference in incidence of postoperative shivering in ondansetron (4mg) and pethidine (25mg) groups Therefore, ondansetron is as much effective as pethidine in preventing postoperative shivering [21].

In agreement to our results, Hussain and colleagues (2017) found that the prophylactic administration of low dose ketamine (0.25mg/kg) and ondansetron (4mg) produces anti-shivering effect in patients undergoing spinal anaesthesia [22].

In agreement to our results, Botros and colleagues (2018) concluded that prophylactic administrations of dexmedetomidine 1 µg/kg or ondansetron 8mg efficiently reduce the incidence and severity of shivering after spinal anesthesia as compared to placebo without significant difference between their efficacies when compared to each other [23].

Nada and colleagues (2018) observed that incidence of shivering was lower in ondansetron 6mg compared to placebo [15].

In accordance to our results, Safavi and colleagues (2014) found that intrathecal 0.2mg/kg meperidine and IV 8mg ondansetron comparably can decrease intensity and incidence of shivering compared to control group as well as decreasing the requirement to additional doses of meperidine for shivering the control without any hemodynamic side effect [24].

Our results showed that number of patients in groups OL and OH treated with pethidine was significantly higher than control group with slight difference between group OL and group OH. The mean dose of pethidine (needed as a rescue drug to treat shivering) was least in group OH followd by group OL and the highest dose was in the control group.

In agreement to our results, Safavi and colleagues (2014) found that intrathecal 0.2mg/kg meperidine and IV 8mg ondansetron comparably can decrease intensity and incidence of shivering compared to control group as well as decreasing the requirement to additional doses of meperidine for shivering the control without any hemodynamic side effect [24].

Ondansetron, which is a specific 5-HT3 receptor antagonist, influence both heat production and heat loss pathways.The mechanism for 5-HT3-receptor antagonists to treat shivering is still unclear but is thought to be related to inhibition of serotonin reuptake on the preoptic anterior hypothalamic region [24].

In this study, it was observed that the incidence of nausea and vomiting was least in group OH and was highest in the control group.

This observation came in agreement with other studies but with different dose of ondansetron. Botros and colleagues (2018) observed that the incidence of nausea and vomiting was lower in ondansetron 6mg [23].

Meta-analysis by Gao and colleagues (2015) found that ondansetron can reduce related adverse outcomes such as nausea and vomiting [1].

Zhou and colleagues concluded that ondansetron could efficiently decrease the incidence of nausea and vomiting [20].

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تأثير جرعات مختلفة من عقار اونداستيرو فى الوقاية من إنخفاض ضغط الدم والرعشة عند المرضى الذين يخضعون لجراحة الأطراف السفلية تحت التخدير النخاعى

التخدير النصفى هو تقنية آمنة وفعالة للغاية لجراحات الأطراف السفلية، و لكنها ترتبط بالعديد من الآثار الجانبية مثل إنخفاض ضغط الدم والارتعاش الذى يزعج المرضى. تشمل فوائد التخدير النصفى لجراحة الأطراف السفلية إنخفاض معدل الوفيات وتجلط الأوردة العميقة ومتطلبات نقل الدم والمضاعفات الرئوية. اقترحت عدة دراسات أن أوندانسيترون، يستخدم للوقاية والعلاج من الغثيان والقئ.

الهدف من الدراسة: الهدف من هذا العمل هو تقييم فعالية إعطاء جرعات مختلفة من الأوندانسيترون عن طريق الوريد على التخفيف من إنخفاض ضغط الدم الناجم عن العمود الفقرى كنتيجة أولية لهذه الدراسة والإرتعاش كنتيجة ثانوية خلال جراحة الأطراف السفلية.

المرضى والطرق: تم توزيع المرضى بشكل عشوائى على ثلاث مجموعات متساوية، المجموعة (C) تلقت محلول ملحى طبيعى كمجموعة تحكم، المجموعة (OL) تلقت ٤ ملغ ondansetron i.v، تلقت المجموعة (OH) 8mg ondansetron على سبيل المثال ببطء. تم تقييم المرضى للتغيرات الديناميكية الدموية، حدوث أى مضاعفات واستخدام البيثيدين والإيفيدرين.

النتائج: بالمقارنة مع متوسط ضغط الدم للمجموعات OL و OH إلى المجموعة الضابطة. كان MBP من مجموعة المراقبة أقل بكثير من المجموعة OL مباشرة بعد البحث وأيضاً فى ٥ و ١٠ و ١٥ و ٢٠ دقيقة أثناء العملية كان MBP من مجموعة التحكم أقل بكثير من المجموعة OH مباشرة بعد البحث وأيضاً فى ١٠ و ١٥ و ٢٠ و ٣٠ دقيقة أثناء العملية. كان هناك اختلاف كبير فيما يتعلق MBP بين المجموعة OL والمجموعة OH فى ٣٠ و ٦٠ دقيقة (MBP من المجموعة OH كان أعلى بكثير P. قيمة ٠.٠٢ و ٠.٠٤٣ على التوالى). كانت جرعة من البيثيدين والإيفيدرين أقل إحصائياً فى مجموعات OH من المجموعة OL من المجموعة الضابطة.

استنتاج: إعطاء جرعتين مختلفتين من أوندانسيترون عن طريق الوريد، ٤ ملغ ، ٨ ملغ ، يخفف بكفاءة إنخفاض ضغط الدم الناجم عن العمود الفقرى والارتعاش مقارنة مع مجموعة التحكم المالحة. لوحظ حدوث إنخفاض فى ضغط الدم وارتعاش أقل فى مجموعة ondansetron 8mg من مجموعة ondansetron 4mg.