Efficacy of Prophylactic Two Different Doses of Intravenous Ondansetron in the Prevention of Spinal Anesthesia Induced Hypotension and Bradycardia in Elective Cesarean Section

Dr. Zainab M. Jaafar M. Saeed, Dr. Jaafar Hameed Mahboba, Dr. Ahmed Mohammed Rukhis

Abstract: **Background:** The most widely used regional anesthetic approach for cesarean sections is spinal anesthesia. On the other hand, hypotension and bradycardia are the most frequent side effects it is frequently seen in cases of profound circulatory collapse during neuraxial anesthesia. Researchers began investigating how ondansetron might lessen these subsequences.

Aim of the study: To evaluate the effects of two different doses of IV ondansetron on spinal anesthesia induced hypotension and bradycardia in elective cesarean section.

Patients and method: A single blind prospective randomized control trial was conducted in Al_Zahraa Teaching Hospital by enrolling 90 patients using a random sample technique. Patients were allocated into ondansetron groups (150 mcg/kg as C), (75 mcg/kg as B) and (placebo as A). Demographic data, hemodynamic parameters, and the incidence of hypotension and bradycardia.

Result: A considerable decrease in hemodynamic variables was observed in group A as compared with ondansetron groups within 30 minute time intervals (p value <0.05, the significance was more obvious in group C as compared with group B. The requests for vasopressor agents and atropine were more in group A versus ondansetron groups with a p value less than 0.001.

Conclusion: both two groups of ondansetron manifest a decrease in the incidence of hypotension and use of vasopressor or atropine but group C was exceedingly effective in the decline of hypotension after spinal anesthesia in elective cesarean section.

Keywords: spinal anesthesia, ondansetron, cesarean section, hemodynamics, hypotension, and bradycardia.

Introduction

The most common type of anesthesia for cesarean sections is spinal anesthesia with considerably fewer complications for both mothers and newborns than general anesthesia, which has a higher risk of aspiration and difficult airway **[1]**.

Spinal anesthesia has many advantages, including heavy motor block, quick onset, reliability, safety of use, and better pain management following surgery. Minimal doses of local anesthetics are needed, which decreases the possibility of systemic toxicity **[2]**.

Regardless of all of its advantages, bradycardia and hypotension are the most common side effects of spinal anesthesia. In turn, hypotension can result in nausea, vomiting, dizziness, unconsciousness, and placental hypo perfusion, which may cause fetal hypoxia and acidosis. These effects are dangerous to both the mother and the fetus **[3]**.

The following pathophysiological processes can be responsible for hypotension during spinal anesthesia: involve Aortocaval compression, quick onset of sympatholytic related to higher sensitivity of nerve fibers to local anesthetics during pregnancy, the relative dominance of the parasympathetic system, and possible activation of the Bezold Jarish reflex (BJR), and increased baroreceptor response **[4]**.

Sensory receptors in the heart are the source of BJR. As a consequence of reduced venous return of blood during spinal block, thrombocyte activation releases serotonin (5HT), which activates chemoreceptors in the heart wall in addition to stimulating cardiac mechanoreceptors. When one of these receptors is activated, BJR is produced, which results in more bradycardia, vasodilatation, and hypotension **[5]**.

After spinal anesthesia during cesarean delivery, maternal hypotension is the most common intraoperative effect (incidence as high as 50 80%) **[6]**.

Bradycardia is also frequently found in cases of significant circulatory collapse under neuraxial anesthesia and may lead to cardiac arrest. Bradycardia is often seen in 13% of non obstetric patients when they are under spinal anesthesia **[7]**.

Many studies on both non obstetric and obstetric populations indicate that 5 HT may be a key factor associated with cardiovascular responses via the BJR and that 5 HT3 receptor antagonists, such as ondansetron, can block this impact at the 5 HT3 receptor **[8]**.

Our study aims to evaluate the effects of prophylactic two different doses of intravenous ondansetron in preventing spinal anesthesia induced hypotension and bradycardia in elective cesarean section.

Spinal Anesthesia

Definition:

A type of regional anesthesia known as spinal anesthesia, frequently referred to as subarachnoid anesthesia, includes administering a local anesthetic drug into the subarachnoid space, which is the area that surrounds the spinal cord. This is an area that contains the sterile cerebrospinal fluid (CSF), a clear fluid that supports and surrounds the brain and spinal cord. An adult human has between 130 and 140 mL of CSF, continuously circulating throughout the day. However, 500 mL or more of CSF is produced daily to maintain its normal volume **[9]**.

Anatomy:

Indeed, the spine is composed of seven cervical (neck) vertebrae, 12 thoracic (upper back) vertebrae, five lumbar (lower back) vertebrae, and five fused sacral (pelvic) vertebrae. These vertebral bones are called according to their particular positions and structural features. These vertebrae sit one on top of the other, and ligaments and articulating joints connect them. The spinal canal, a hollow area between the vertebrae, is where the spinal cord resides for protection. To carry impulses to and from different body areas, the spinal nerves avoid the spinal canal through lateral gaps created between adjacent vertebrae's pedicles **[10]**.

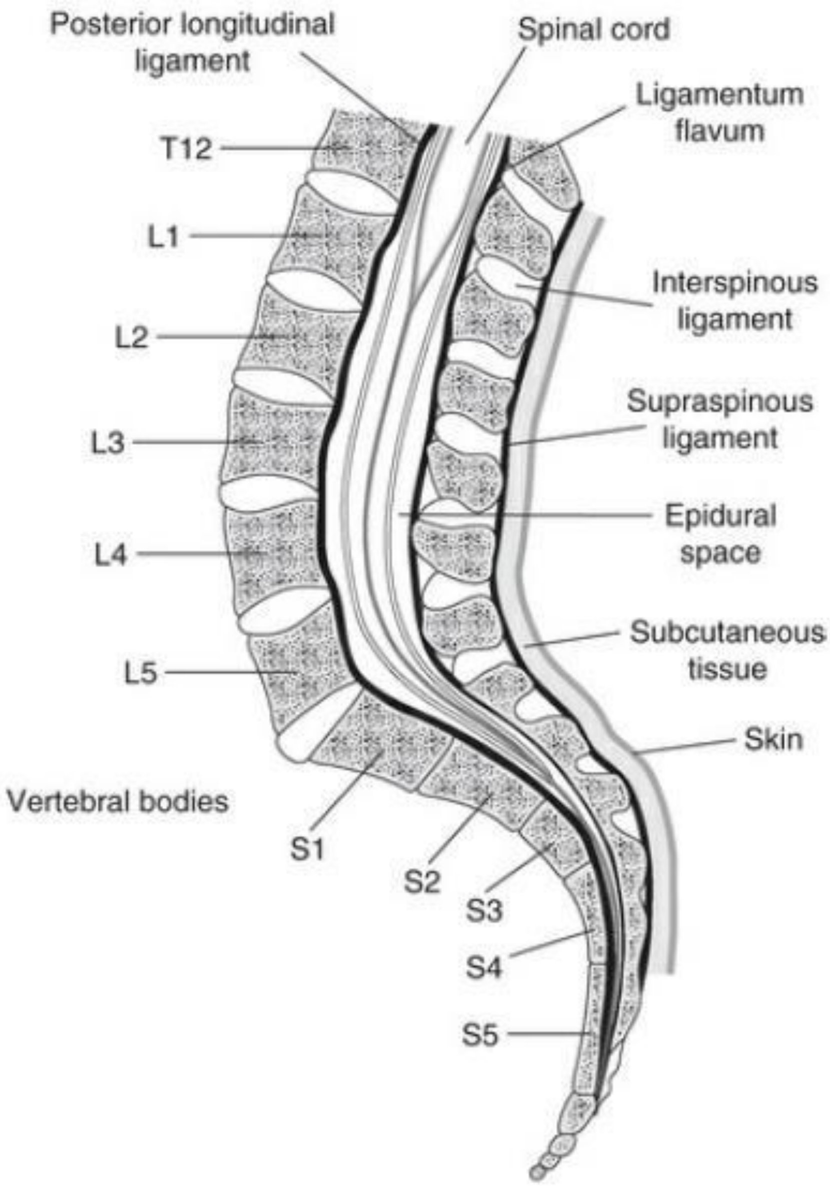

Figure 1.1: Anatomy of the spine and subarachnoid space. [Smith and Aitkenhead's Textbook of Anaesthesia, page 1232]

An experienced anesthesiologist or anesthetist normally performs the procedure. To expose the proper location for the injection, the patient is placed in a sitting or lying

down position, usually with their back arched and their legs contracted. To reduce the risk of infection, the injection site is sanitized and sterilized before injection **[11]**.

The anesthesiologist then attempts to enter the subarachnoid area by inserting a tiny, sterile needle through the skin and deeper tissues of the back. This is frequently performed in the lower back (lumbar region) between the lumbar vertebrae, the specific injection level is determined by the particular technique being carried out **[12]**.

A small amount of clear CSF fluid may be withdrawn after the needle has been properly positioned to check for accuracy and to reduce pressure in the subarachnoid space. The anesthetic drug is then administered into the subarachnoid space using the needle. Bupivacaine and ropivacaine are examples of frequently used local anesthetics **[13]**.

The drug diffuses through the CSF, covering and suppressing the spinal cord and nerve roots in the lower body. As a result, the feeling and motor function below the injection site are temporarily lost.

By changing the amount and concentration of the anesthetic drug being administered, the level of anesthesia can be regulated **[14]**.

Spinal anesthesia typically has a quick onset and its effects can be detected immediately. A warm sensation or a sense of heaviness and numbness in the lower body may be felt by the patient. Throughout the process, they stay awake and conscious, enabling them the chance to speak with the medical staff if required **[15]**.

There are various advantages to spinal anesthesia. It relieves pain by numbing a significant amount of the body without general anesthesia. It can be used for a variety of surgical operations including cesarean sections, prostate surgeries, hernia repairs, joint replacements, and surgery including the lower abdomen or lower extremities. It allows for a quicker recovery than general anesthesia **[16]**.

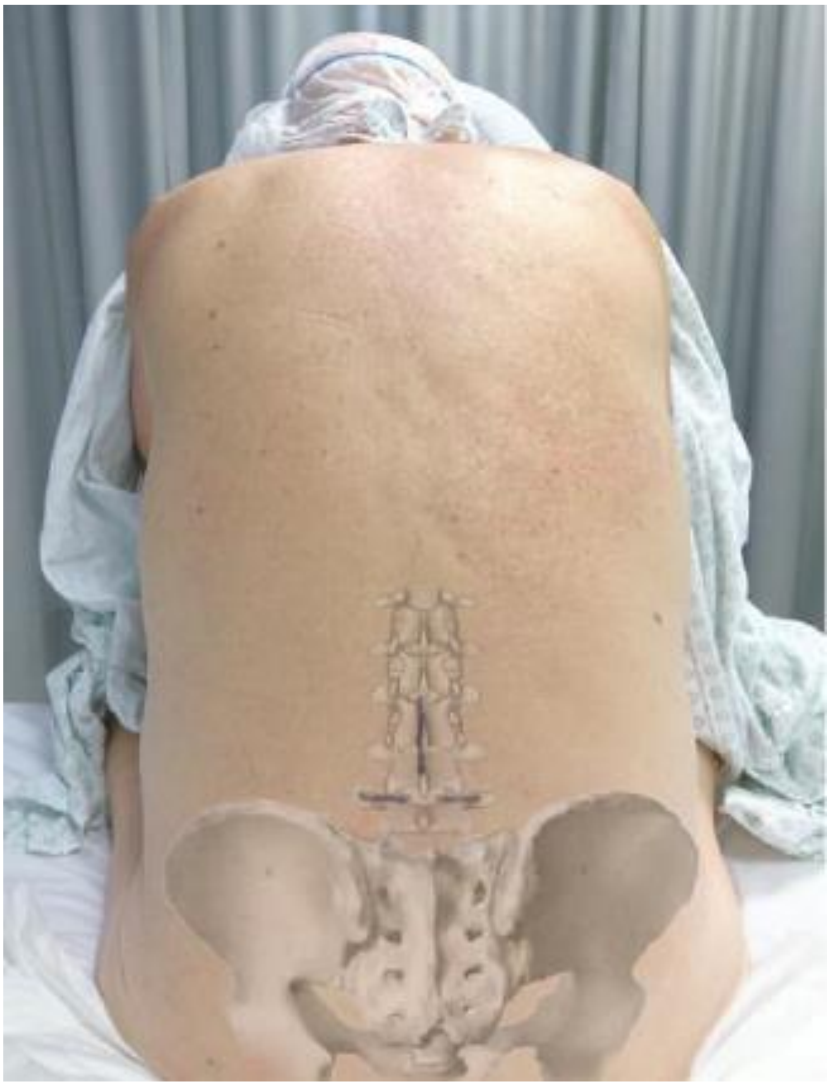

Figure 1.2: Spinal anesthesia position and technique. [Hadzics Textbook of Reginal Anesthesia and acute pain management, page 352]

Indications of spinal anesthesia [17]:

1. Cesarean sections.
2. Hip, knee, tibia, pelvic, and ankle orthopedic surgery.
3. Vascular procedures for the legs.
4. Operations for hernias.
5. A hemorrhoid scission.
6. Cystectomy.

7. Nephrectomy.

8. Transurethral resection of prostate tumors.

9. Urology conditions.

Contraindications of spinal anesthesia [18]:

Absolut:

1. Patient refusal.

2. An injection site infection.

3. Coagulopathy.

4. Extreme hypovolemia.

5. Increase intracranial pressure.

Relative:

1. Sepsis.

2. The patient is uncooperative.

3. Neurological problems.

4. Demyelinating lesions.

5. Moderate to Mild stenotic valve disease.

6. Hypertrophic obstructive cardiomyopathy.

7. A severely deformed spine.

Controversial:

1. Previous back surgery at the injection site.

2. Complicated operations.

3. Longer operations.

Spinal Anesthesia during cesarean section:

The use of spinal anesthesia during cesarean birth provides multiple advantages such as a simple technique, quick induction, and dependability, Minimization of aspiration risks, an awake pregnant woman, and limited fetal exposure to the drugs **[19]**.

The disadvantages of spinal anesthesia for cesarean delivery include the high incidence of hypotension, post lumbar puncture headache, decreased duration of action, intraoperative pain, and the risk of neurologic and cardiac toxicity from the local anesthetic **[20]**.

Hypotension during spinal anesthesia:

The two main perioperative complications that affect the secure and effective use of spinal anesthesia are bradycardia and hypotension. The prevalence of hypotension ranges from 15% to 33%. It is well established that hypotension episodes and death are related **[21]**.

Many pathophysiological reasons explain spinal anesthesia induced hypotension, the most important of which is the rapid start of sympatholytic response resulting from nerve fibers' increased sensitivity to local anesthetics during pregnancy **[22]**.

The level of blocking of the sympathetic chain is related to the degree of cerebral spread of the local anesthetic inside the subarachnoid space **[23]**.

Cesarean section:

A cesarean section, often known as a C section, is a surgical procedure achieved by making surgical incisions in the mother's abdomen and uterus to deliver the fetus when natural birth is not safe and the mother's or the child's life is at risk, a cesarean delivery is necessary **[24]**.

It is a commonly performed procedure with a maternal mortality rate much higher than vaginal delivery; complications including preeclampsia, pulmonary thromboembolism, amniotic fluid embolism, obstetric hemorrhage, and heart disease are the primary causes of mortality **[25]**.

Currently, the most common operation in the US is a cesarean delivery, accounting for about 30% of all deliveries. 1 million are performed yearly; the rate of cesarean delivery in other developed countries ranges from 15% to 30% **[26]**.

There is a high risk of infection, severe hypotension, hemorrhage, ruptured uterus, organ injury, venous thromboembolism, aspiration, and hypoxia following a cesarean section **[27]**.

These complications are all related to maternal problems, which raise healthcare costs, increase hospital stays, and increase maternal mortality and morbidity **[28]**.

Hypotension during cesarean section:

Hypotension during cesarean section done under spinal anesthesia has been studied for almost 50 years and studies show that between 7.4% and 74.1% of patients have hypotension following spinal anesthesia for a cesarean delivery **[29]**.

The major causes of the increased risk and severity of hypotension in pregnant women as compared to non obstetric patients include higher sensitivity to local anesthetics and aortocaval compression of the pregnant uterus **[30]**.

The sympathetic nervous system is more active in pregnant women than the parasympathetic nervous system. Sympatholytic leads to a greater level of peripheral vasodilatation and a higher level of parasympathetic activity, which reduces the venous return and cardiac preload, resulting in bradycardia **[31]**.

The decreased preload leads to a decrease in cardiac output (CO), which in turn causes systemic hypotension. This statement becomes aggravating due to aortocaval compression **[32]**.

Increased sympathetic block consequently reduces the degree of compensatory responses through baroreceptors and raises the risk of cardioinhibitory events like the Bezold Jarisch reflex, which can lead to cardiac arrest and death **[33]**.

When maternal blood pressure drops rapidly and for a long period, she may have a reduced consciousness. This is uncommon when treatment begins immediately **[34]**.

Ondansetron

Mechanism of action:

Ondansetron is one of the group of drugs known as serotonin 5 HT3 receptor antagonists. Serotonin is a substance that occurs naturally and has the potential to induce nausea and vomiting. Ondansetron works by blocking its activity and is a selective antagonist of the 5 HT3 subtype of serotonin receptors **[35]**.

Cytotoxic chemotherapy and radiation therapy release serotonin (5 HT) from small intestines, stimulating the vomiting reflex by activating 5 HT3 receptors on vagal afferents. Ondansetron may prevent this reflex from occurring. A central release of serotonin from the region postrema's chemoreceptor trigger zone lies on the fourth ventricle's floor, and can also occur from the activation of vagal afferents **[36]**.

Ondansetron's antiemetic effect is thus likely due to the specific antagonistic action of 5 HT3 receptors on neurons found in the central nervous system, peripheral nervous system, or both **[37]**.

Bezold Jarisch reflex (BJR) is triggered by the activation of intracardiac receptors, such as chemoreceptors and mechanoreceptors. All of the heart's chambers contain mechanoreceptors, and when venous return is reduced, these receptors become stimulated and BJR is activated. Chemoreceptors are essential in inducing BJR during hypotension and hypovolemia because they are sensitive to serotonin, which is generated by activated thrombocytes. This results in an increase in efferent vagal signals, which causes hypotension and bradycardia **[38]**.

Ondansetron is a 5 hydroxyl tryptamine (5HT3) receptor antagonist that inhibits BJR and is effective correctly in keeping patients undergoing elective cesarean sections (CS) from developing spinal induced hypotension **[39]**.

Different ondansetron dosages have been reported to have variable effects in decreasing the incidence of maternal hypotension **[40]**.

Absorption: Ondansetron IV infusions of 4 mg injected over 5 minutes produce peak plasma concentrations of around 65 ng/ml maximum dose is 16mg.

Distribution: plasma protein binding of ondansetron is 70 76% and VD is 2 L/kg.

Metabolism: Ondansetron is metabolized by the liver using multiple types of P450 enzymes (CYP1A2, CYP2D6, and CYP3A4) when it enters the systemic circulation.

Execration: In the urine, less than 5% of the drug is excreted unchanged. The half

life of elimination is three hours, and the clearance is 6.3 ml/kg/min **[41]**.

1.5. Management of hypotension during spinal anesthesia

When spinal anesthesia was first used, several scientific and medical studies focused on the prevention and treatment of spinal anesthetic induced hypotension during cesarean sections due to the potentially serious consequences for both the mother and the fetus **[42]**.

To reduce the adverse hemodynamic effects caused by spinal anesthesia during a cesarean section, it has been shown that reducing the local anesthetic dose to 5 7 mg of bupivacaine can result in adequate anesthesia **[43]**.

Vasoactive drug administration is important. Dopamine was one of the first drugs to be used, then ephedrine, and more recently, norepinephrine and phenylephrine **[44]**.

When spinal anesthesia was used, ephedrine was first given as a bolus to treat hypotension. However, later guidelines allowed for continuous infusion of the drug **[45]**.

Administration of phenylephrine was related to a decreased incidence of fetal acidosis and maternal nausea and vomiting, even though ephedrine and phenylephrine had similar impacts on the prevention and treatment of hypotension in pregnant women during spinal anesthesia **[46]**.

It recommends co loading with 1000 2000 mL of crystalloids and a continuous infusion of phenylephrine at 25 50 mcg/min immediately following spinal anesthetic

injection to obtain the best blood pressure control during spinal anesthesia for cesarean sections **[47]**.

The aim of the study

To evaluate the prophylactic effects of two different doses of IV ondansetron on spinal anesthesia induced hypotension and bradycardia in elective cesarean section.

Patients & Method

A prospective randomized controled trial was started from January 2023 to November 2023 in Al_Zahraa Teaching Hospital. The ethical permission was obtained from the Iraqi local committee of the Scientific Council of Anesthesia and Intensive Care before the start of the study. Verbal also written informed consent was taken from all participants. American Society of Anesthesia (ASA) II under elective cesarean section under spinal anesthesia were involved in the current study.

Inclusion criteria:

1. Age between 18-45 years old.
2. BMI >18 and < 35 kg/m2.
3. Elective cesarean section under spinal anesthesia.
4. ASA II

Exclusion criteria:

1. History of allergy to ondansetron or local anesthesia.
2. Placenta Previa and acreta
3. Parturient with preeclampsia.
4. Any contraindications to spinal anesthesia.
5. Droped cases that need blood transfusion.

Every parturient had a preoperative evaluation one day before the procedure and was placed on NPO for 12 hours. Before providing spinal anesthesia, the patient's presence in the operating room was marked by the application of the ASA standard monitoring, which included recording their heart rate, noninvasive blood pressure, ECG, and oxygen saturation levels. An 18 gauge cannula was used to secure peripheral venous access.

Ninety participants in the research study were allocated into three groups (30 in each), the control group which received a placebo (10 ml normal saline) considered group A, group B received ondansetron (75mcg/kg diluted with 10 ml normal saline), and group C received ondansetron (150 mcg/kg diluted with 10 ml normal saline), the normal saline and the study drug doses were given 10 minutes before performed spinal anesthesia slowly maximum dose was 16mg.

Subarachnoid block (spinal anesthesia) was given under sterile techniques in the sitting position using hyperbaric Marcaine 0.5% (12.5 mg), between L3 L4 interspace using a Quincke's spinal needle 25 gage, following the administration of a local anesthetic intrathecal, the parturient assumes a supine position with 15° pelvic lift, 20 mL/kg normal saline runs quickly as co loading following spinal anesthesia. HR, SPO2, and baseline maternal blood pressure (SBP, DBP, and MAP) were documented.

6 mg IV ephedrine boluses were administered to treat hypotension, which was defined as a drop in SBP of more than 20% from the baseline. 0.6 mg IV atropine boluses were used to treat bradycardia, which was defined as a heart rate of less than 50 bpm.

Hemodynamic parameters such as (SBP, DBP, MAP, HR, and SpO2), adverse effects (hypotension, bradycardia), and the need for atropine and ephedrine were recorded. Hemodynamic parameters which were considered as a primary outcome were documented at 5 minute intervals following performed spinal anesthesia for the first 30 minutes.

Results

90 parturients enrolled in this study under cesarean section under spinal anesthesia, allocated into 3 groups A, B, and C, with 30 parturients in each group. Table (1) showed there were insignificant differences among the three groups or B and C groups regarding age, BMI, and primary cesarean section, with a p value greater than 0.05.

Mean ages were 27, 25, and 25 years, with a standard deviation of 4.8, 4.2, and 3.9 for each A, B, and C respectively. Mean BMI was 25.7, 25.5, and 25. 8 kg/m, with a standard deviation of 3.08, 2.3, and 1.6 for A, B, and C respectively.

The percentage of primary cesarean sections were 70%, 76%, and 66% for each A, B, and C respectively, the other remaining percentages were for parturients who had a second time of cesarean section.

Table 3.1: Demographic characteristics.

Variable	Group	Mean ± SD	P-value All	P-value B&C
Age	Group A	27±4.8	0.143	0.90
	Group B	25±4.2		
	Group C	25±3.9		
BMI	Group A	25.7±3.08	0.421	0.185
	Group B	26.5±2.3		
	Group C	25.8±1.6		
Primary N (%)	Group A	21 (70)	0.685	0.45
	Group B	23 (76)		
	Group C	20 (66)		

BMI: body mass index, **N:** number, **%**: percentage

Table (2) showed there were significant differences regarding systolic blood pressure between the three groups in the baseline, 0, 5, 10, 15, 20, 25, and 30 minutes, with a p value lower than 0.001.

As compared between groups (B&C). Group C (150 mcg/kg ondansetron) showed better maintained systolic blood pressure over 30 minutes after performing spinal anesthesia with a p value less than 0.05.

Table 3.2: Comparison of study groups regarding Systolic Blood pressure.

-	Time(min)	Group A (N= 30)	Group B (N= 30)	Group C (N= 30)	p-value All	p-value B&C
SBP(mmHg)	Baseline	122.2±7.9	124.1±5.9	120.8±5.9	< 0.001	0.032
SBP(mmHg)	0	117.2±15.8	112.3±13.8	119.3±4.6	< 0.001	0.011
SBP(mmHg)	5	92.1±16.2	92.6±14.7	109.2±6.5	< 0.001	< 0.001
SBP(mmHg)	10	86.9±12.5	87.2±15.1	105.8±8.08	< 0.001	< 0.001
SBP(mmHg)	15	91.8±12.3	95±9.8	102.1±7.7	< 0.001	< 0.001
SBP(mmHg)	20	108.2±11.1	105.8±6.3	114.6±9.7	< 0.001	0.026
SBP(mmHg)	25	116.2±7.4	113.7±8.4	125.9±7.2	< 0.001	0.001
SBP(mmHg)	30	118.7±8.2	115.8±7.4	125.4±6.5	< 0.001	< 0.001

SBP: systolic blood pressure, **min:** minute, **N:** number

Data are expressed as mean± standard deviation.

P-value > 0.05 is considered non-significant.

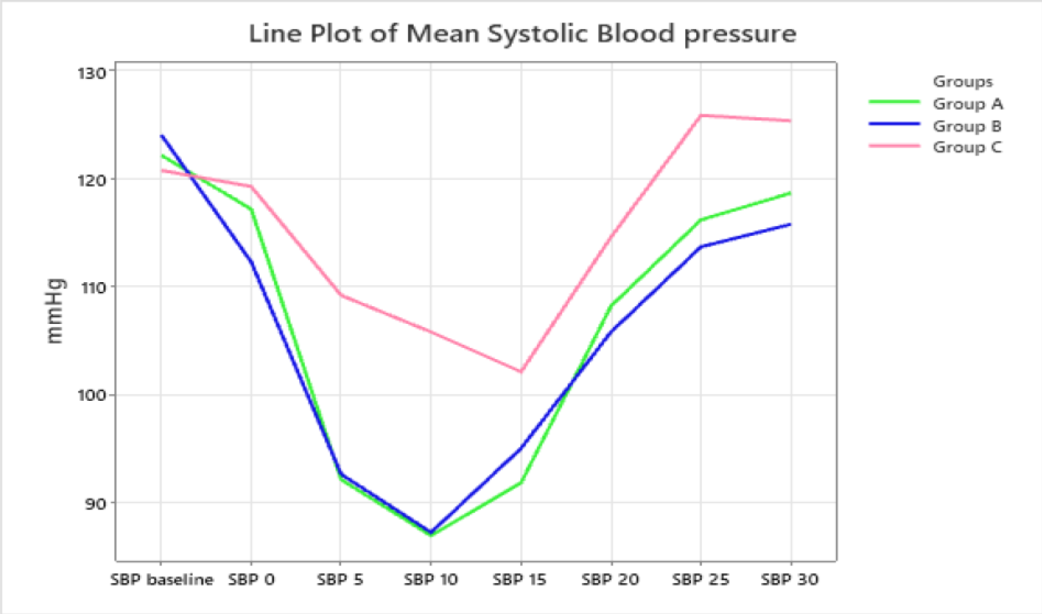

Figure 3.1: Line plot of mean systolic pressure.

Table (3) showed there were significant differences regarding diastolic blood pressure between the three groups in the baseline, 0, 5, 10, 15, 20, 25, and 30 minutes, with a p value lower than 0.001.

In comparison between groups (B&C). Group C (150 mcg/kg) showed better

maintained diastolic blood pressure in the 5, 10, 15, 20, and 25 minutes, with a p value lower than 0.05. Otherwise, there were insignificant in between B&C in the baseline, 0, and 30 minutes, with a p value > 0.05.

Table 3.3: Comparison of study groups regarding Diastolic Blood pressure.

-	Time(min)	Group A (N= 30)	Group B (N= 30)	Group C (N= 30)	p-value	
					All	B&C
DBP(mmHg)	**Baseline**	76.8±6.3	73.9±6.2	71.5±4.6	< 0.001	0.92
DBP(mmHg)	**0**	70.2±9.1	68.6±9.1	70.2±4.3	< 0.001	0.391
DBP(mmHg)	**5**	59±11	56.2±14.7	65.2±5	< 0.001	< 0.001
DBP(mmHg)	**10**	56.3±8.7	52±10	61.2±4.4	< 0.001	< 0.001
DBP(mmHg)	**15**	60.2±8.8	56.7±7.4	64.6±4.2	< 0.001	0.016
DBP(mmHg)	**20**	68.4±11.1	59.2±6.5	70.3±5.2	< 0.001	0.011
DBP(mmHg)	**25**	66.1±6.1	63±6.3	74.8±4.6	< 0.001	0.05
DBP(mmHg)	**30**	62±6.5	64.8±6.4	67.1±4.8	< 0.001	0.118

DBP: diastolic blood pressure, mean± standard deviation.

Data are expressed as mean± standard deviation.

P-value > 0.05 is considered non-significant.

Figure 3.2: Line plot of mean diastolic blood pressure.

Table (4) showed there were significant differences regarding mean arterial pressure between the three groups in the baseline, 0, 5, 10, 15, 20, 25, and 30 minutes, with a p

value lower than 0.001. As compared between groups (B&C). Group C (150 mcg/kg ondansetron) showed better control mean arterial pressure over 30 minutes after performing spinal anesthesia with a p value less than 0.05.

Table 3.4: Comparison of study groups regarding MAP.

-	Time(min)	Group A (N= 30)	Group B (N= 30)	Group C (N= 30)	p-value	
					All	B&C
MAP(mmHg)	**Baseline**	91.6+6.5	90.3+6.2	87.7+4.4	< 0.001	0.051
MAP(mmHg))	**0**	88.1+9.4	82.4+9.4	86.2+3.9	< 0.001	0.049
MAP(mmHg)	**5**	66.2+12.2	68+10.7	79.6+6	< 0.001	< 0.001
MAP(mmHg)	**10**	66.2+9.6	63.3+11.4	74.7+5.2	< 0.001	< 0.001
MAP(mmHg)	**15**	70.7+10.3	69.2+7.7	76.8+5.1	< 0.001	0.016
MAP(mmHg)	**20**	76.3+8	72.8+5.4	81.6+6.6	< 0.001	0.009
MAP(mmHg)	**25**	80.3+6.3	76.5+6.5	87.5+5.6	< 0.001	0.017
MAP(mmHg)	**30**	80.9+6.4	78.1+6.4	86.9+5.2	< 0.001	0.014

MAP: mean arterial pressure

Data are expressed as mean± standard deviation.

P-value > 0.05 is considered non-significant.

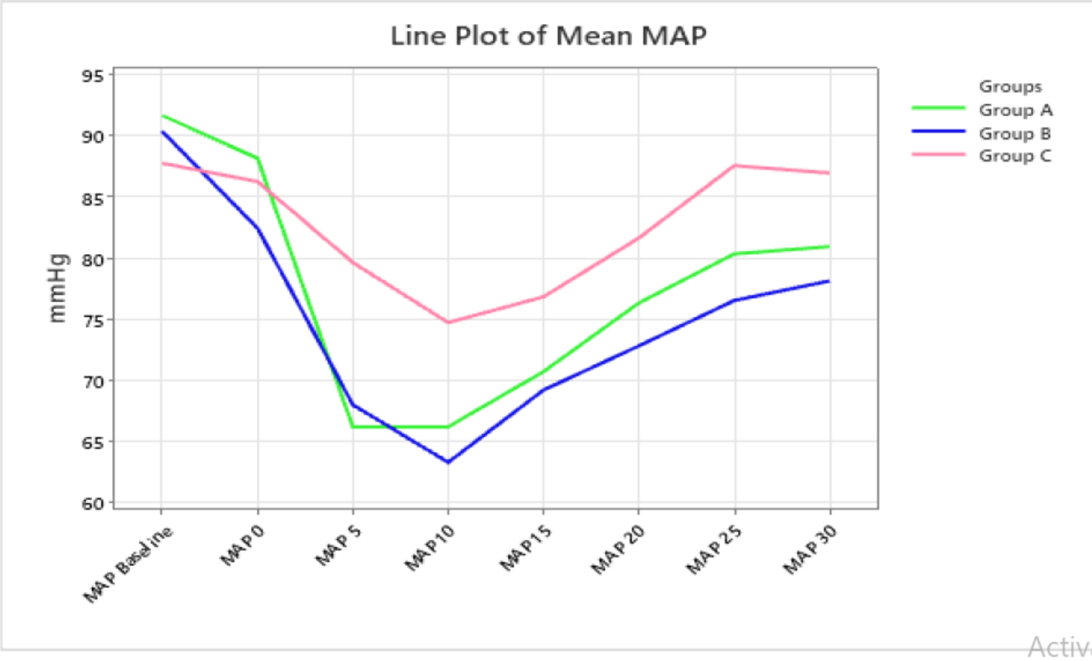

Figure 3.3: Line plot of mean MAP.

The attained results showed the heart rate in the three study groups decreased from the baseline over the period with slightly being higher in group C, with a p value less than 0.001.

Comparing the mean heart rate between groups B&C, heart rate was significantly higher in group C as compared with group B at intraoperative times 0, 5, 10, 15, and 20 minutes with a p value < 0.05, however, there were insignificant in the 25, and 30 minutes with a p value greater than 0.05, table (5).

Table 3.5: Comparison of study groups regarding Heart Rate.

-	Time(min)	Group A (N= 30)	Group B (N= 30)	Group C (N= 30)	p-value	
					All	B&C
HR (mmHg)	**Baseline**	91.2±11.9	109.6±11.1	120.6±8.9	< 0.001	< 0.001
HR (mmHg)	**0**	93.5±14	105.8±12.5	119.1±6.8	< 0.001	< 0.001
HR (mmHg)	**5**	83.5±18.7	94±21	116.1±6	< 0.001	< 0.001
HR (mmHg)	**10**	75.9±23.5	81.4±19.8	107.2±11.6	< 0.001	< 0.001
HR (mmHg)	**15**	70.4±17.2	73.1±20.4	100±10.5	< 0.001	0.016
HR (mmHg)	**20**	71.3±9.4	80.6±12.5	92.9±10.8	< 0.001	0.009
HR (mmHg)	**25**	80.4±6.8	83.8±10.3	87.3±5.2	< 0.001	0.098
HR (mmHg)	**30**	83.2±6.6	84.2±8.7	86±4.6	< 0.001	0.145

HR: heart rate.

Data is expressed as mean± standard deviation.

P-value > 0.05 is considered non-significant.

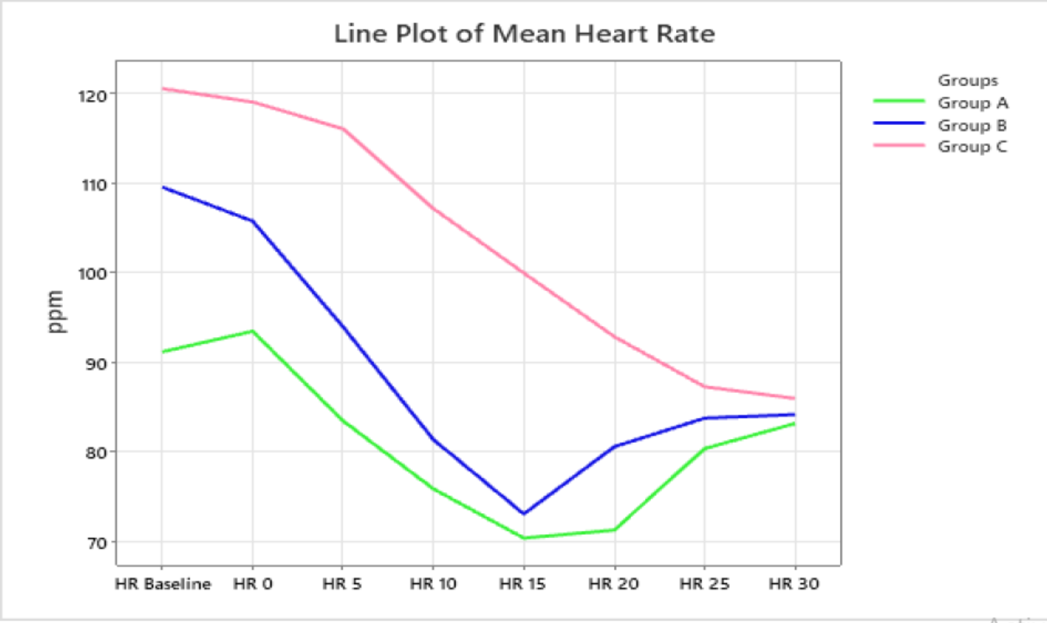

Figure 3.4: Line plot of mean heart rate.

Table (6) shows there was a significant difference among the three study groups, with a p value less than 0.001, while the SPO2 was still over 97%.

However, there were statistically insignificant differences in both B&C groups regarding SPO2 over 30 minutes, with a p value more than 0.05. Figure (5).

Table 3.6: SPO2 distribution at different times among the three groups.

-	Time(min)	Group A (N= 30)	Group B (N= 30)	Group C (N= 30)	p-value	
					All	B&C
SPO2 (mmHg)	**Baseline**	97.8±1.1	97±1.2	97.8±0.8	< 0.001	0.004
SPO2 (mmHg)	**0**	97.8±1.2	97±1	97.4±0.9	< 0.001	0.106
SPO2 (mmHg)	**5**	97.7±1.6	97.7±1.7	97.4±1.1	< 0.001	0.102
SPO2 (mmHg)	**10**	98.9±1	97.3±1.6	98±1.1	< 0.001	0.068
SPO2 (mmHg)	**15**	98.6±1.6	97.4±1.1	98±1.2	< 0.001	0.065
SPO2 (mmHg)	**20**	99.1±0.6	97.9±0.8	98.3±1.1	< 0.001	0.103
SPO2 (mmHg)	**25**	99.2±0.8	98.4±0.6	98.5±1.1	< 0.001	0.891
SPO2 (mmHg)	**30**	99±0.5	98.6±0.7	98.6±1.2	< 0.001	0.901

SPO2: saturation of peripheral oxygen.

Data are expressed as mean± standard deviation.

P-value > 0.05 is considered non-significant.

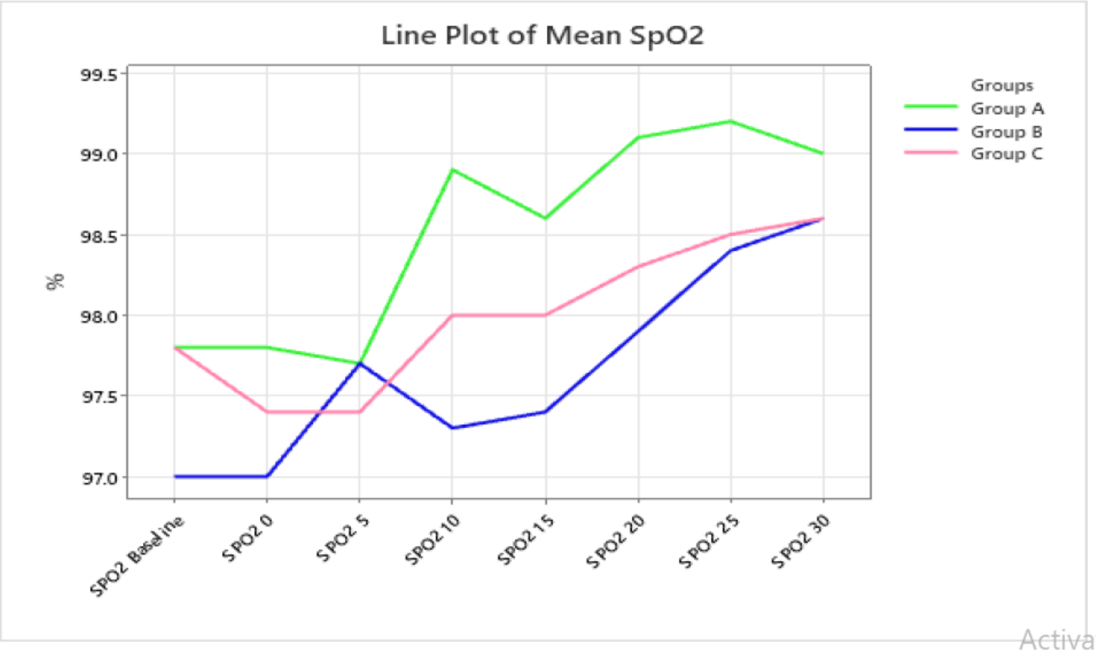

Figure 3.5: Line plot of mean SPO2.

Table (7) shows the incidence of bradycardia intraoperative times in the three study groups, the incidence was higher in the control group (63.4%) as compared with other groups 40%, and 0% for groups B and C respectively, with p values < 0.001.

Statistical differences between groups B and C were higher in the prevalence of bradycardia 40% for group B and 0% for groups C, with a p value equal to 0.005.

Table 3.7: Incidence of bradycardia among three study groups.

Bradycardia		Group A	Group B	Group C	P-value	
					All	B&C
No	N	11	18	30	< 0.001	0.005
	%	36.6	60	100		
Yes	N	19	12	0		
	%	63.4	40	0		

Table (8) shows the atropine requests in the three study groups, the requests were higher in the control group (63.4%) as compared with other groups 40%, and 0% for groups B and C respectively, with a p value < 0.001.

Statistical differences between groups B and C were higher regarding atropine requests 40% for group B and 0% for group C, with a p value = 0.005.

Table 3.8: Atropine requests among three study groups.

Atropine		Group A	Group B	Group C	P-value All	P-value B&C
No	N	11	18	30	< 0.001	0.005
	%	36.6	60	100		
Yes	N	19	12	0		
	%	63.4	40	0		

Table (9) showed the incidence of hypotension intraoperative times in the three study groups, the incidence was higher in the control group (100%) as compared with other groups 73.4%, and 0% for groups B and C respectively, with a p value < 0.001.

Statistical differences between groups B&C were higher in the incidence of hypotension 73.4% for group B and 0% for groups C, with a p value equal to 0.005.

Table 3.9: Incidence of hypotension among three study groups.

Hypotension		Group A	Group B	Group C	P-value All	P-value B&C
No	N	0	8	30	< 0.001	0.005
	%	0.	26.6	100		
Yes	N	30	22	0		
	%	100	73.4	0		

Table (10) shows the vasopressor requests in the three study groups, the requests were higher in the control group (100%) as compared with other groups 66.6%, and 0% for groups B and C respectively, with a p value < 0.001.

Statistical differences between groups B&C were higher regarding atropine requests 66.6 % for group B and 0% for group C, with a p value < 0.001.

Table 3.10: Vasopressor requests among three study groups.

Vasopressor		Group A	Group B	Group C	P-value	
					All	B&C
No	N	0	10	30	< 0.001	< 0.001
	%	0	33.4	100		
Yes	N	30	20	0		
	%	100	66.6	0		

Discussion

spinal anesthesia is the preferred method of anesthesia for cesarean deliveries and has decreased maternal mortality. But in 80 83 percent of parturient, it has been associated with maternal hypotension **[48]**. Hypotension after the sub arachnoid block is caused by a combination of decreased cardiac output and decreased systemic vascular resistance as a result of sympathetic nerve blockage **[49]**.

An extremely potent and selective 5 HT3 receptor antagonist called ondansetron can reduce BJR by preventing 5 HT from attaching to chemoreceptors. Along with promoting venous return to the heart, it also inhibits peripheral vessel expansion **[50]**. The dose dependent effect of ondansetron on lowering maternal hypotension is still unclear and requires more research, even though 4 mg of ondansetron preloading has been frequently used to prevent it **[50 54]**.

Whenever compared statistically with the control group, the mean maternal SBP, DBP, and MAP among the ondansetron groups were very slightly influenced in group B but were statistically significant at a maximum number of time points in group C. Significantly fewer vasopressors were used in the ondansetron groups as well. Nonetheless, at different time intervals, there was a statistically significant difference in HR between the ondansetron groups and the control group, and the patient experienced a bradycardia episode that prompted atropine.

4 mg of ondansetron can successfully attenuate maternal hypotension during cesarean section under spinal anesthesia, according to studies by Sahoo et al. **[50]**, Wang et al. **[51]**, Trabelsi et al. **[52]**, and Shabana et al. **[53]**. However, all of these researchers only used one specific dose of the study drugs, whereas our study incorporated two different doses of ondansetron.

Compared to our study but with different doses, Oratiz and his groups **[55]**. Compared two doses (2mg and 4 mg) of ondansetron with control, they found that injection of ondansetron before spinal anesthesia has little effect on the incidence of hypotension, which disagrees with our result, and these differences might be due to different sample sizes and different anesthetic techniques.

Comparing two dosages of ondansetron (4 mg and 8 mg) in 150 parturients was also conducted by Bhiwal et al. **[56]**, using normal saline as the control. They discovered that preemptive ondansetron use reduced the need for vasopressors and helped minimize maternal hypotension, with 8 mg of ondansetron requiring less vasopressor. This result was consistent with our research, which also showed that high doses of 150/kg were useful for avoiding maternal hypotension.

Intravenous ondansetron decreased the incidence of maternal hypotension, n, according to Potdar et al.'s **[57]** comparison of two dosages (4 mg and 8 mg) with a control (normal saline). However, there was no benefit to using 8 mg of ondansetron instead of 4 mg, which is in contrast with our research study we found that high doses of 150 mcg/kg were associated with reducing maternal hypotension as compared with 75 mcg/kg. The observed disparity could perhaps be attributed to variations in the anesthetic approach employed in the two studies (our study utilized 12.5 mg of bupivacaine, whereas Potdar et al.'s study used 12 mg and 60 µg of fentanyl).

Sumedha Vashishth and his group reported that 6mg and 8mg were more effective in preventing spinal induced maternal hypotension as compared with 2mg and 4 mg which supported our research study **[58]**.

The limitation of our study was that we recorded blood pressure after spinal anesthesia was performed every 5 min for 30 min. If hypotension occurred, ephedrine was administered immediately until the MAP reached the lower limit of baseline level, which influenced our recording variables.

Conclusion

Maternal hypotension and bradycardia caused by sub arachnoid block is a major risk during surgical management of pregnancy. Regarding maternal hemodynamic stability, all two groups of patients who received ondansetron showed a decrease in the incidence of hypotension, bradycardia, use of ephedrine, and atropine. However, group C was greater effective in minimizing spinal induced hypotension in parturients undergoing cesarean section.

Recommendation

1. Uses of 150 mcg/kg ondansetron in elective cesarean section with ASA I&II if no contraindication rather than 75 mcg/kg or without.
2. More study is needed to use ondansetron with a BMI of more than 35kg/m2 and ASA III or IV
3. Uses of ondansetron with another type of surgery under spinal anesthesia to reduce the incidence of spinal-induced hypotension
4. Further study is needed for real-time accurate monitoring of blood pressure invasively to detect actual variation of hemodynamic parameters.

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