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A COMPARATIVE STUDY OF EFFICACY AND SAFETY OF ONDANSETRON VERSUS PHENYLEPHRINE FOR THE PREVENTION OF SPINAL ANAESTHESIA-INDUCED HYPOTENSION IN CAESAREAN SECTION

Pharmacology

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ABSTRACT

Introduction: Spinal anaesthesia is now the effective technique for caesarean section, but hypotension is the main complication which adversely affect both mother and neonate.

Aim: To assess the efficacy and safety of prophylactic dose of ondansetron in comparison to phenylephrine to prevent spinal anesthesia- induced hypotension in caesarean section.

Materials and Methods: This prospective, randomized, parallel, double-blinded, placebo controlled unicentric clinical trial was conducted on 63 pregnant mothers who fulfilled the subject selection criterias. Patients were allocated into three groups: Group P received 100 mcg of phenylephrine intravenously, Group O received 4 mg of IV ondansetron intravenously and Group C received 10 ml of normal saline intravenously. Systolic blood pressure (SBP),diastolic blood pressure (DBP) ,mean blood pressure (MBP), heart rate (HR) were recorded in three (3) minutes interval during caesarean section and every ten (10) minutes interval after caesarean section for one hour. Adverse effects, if any were also noted during the study time. Chi-square test, Kruskall-Wallis (nonparametric) test, Friedman's ANOVA followed by Dunn's Multiple Comparison were performed by Graph Pad InStat 3 software for statistical analysis.

Result : Patients of Group P had least episode than other groups.Incidence of hypertensive episode was maximum in group C, followed by group O. rescue medication was required maximum in group C than other two group.. There was no difference between group O and group P in respect of total amount of rescue medication.

Conclusion: Prophylactic 4 mg IV ondansetron is effective and safe to prevent the spinal anaesthesia induced hypotension with minimal adverse effect.

KEYWORDS

Spinal Induced Hypotension, Ondansetron , Phenylephrine

Introduction

Spinal anaesthesia is now the effective technique for elective caesarean section. But hypotension is the main complication with this technique. Without any prophylactic measure, incidence of hypotension is 80% or more. This hypotension has detrimental effects on mother (nausea, vomiting, aspiration etc) and neonate (asphyxia, fetal acidosis etc). [1]

Intravenous fluids (IVF) before and during spinal anaesthesia is commonly used to prevent hypotension. However, fluid preloading is not so much effective; because it does not prevent spinal anaesthesia mediated decreased systemic vascular resistance. [2]

Alternative approach is to use of a vasopressor like ephedrine or phenylephrine.

Ephedrine, α and β adrenergic receptor agonist, was recommended as vasopressor for treatment of post- spinal hypotension. But due to its limited efficacy [3] (large doses is required, onset of action is slow, longer acting) and side effects [4] (Increased heart rate and contractility with or without arrhythmias) it is not used regularly.

Phenylephrine is an α adrenergic receptor agonist. It is a potent vasoconstrictor, can counteract the post-spinal related decreased vascular resistance without increasing the heart rate (HR). [5, 6] Phenylephrine is safe and effective than ephedrine seen in controlled clinical trials. Phenylephrine is a commonly used vasopressor for the treatment of spinal anaesthesia mediated hypotension. [6, 7] But side effects like nausea, vomiting, bradycardia, and sometimes hypertension are commonly seen.[8]

Ondansetron, a 5HT-3 antagonist is commonly prescribed in nausea and vomiting. [9] The antiemetic dose (4 mg IV) is also effective to attenuate the spinal anaesthesia induced hypotension by blocking Bezold Jarisch Reflex (BJR). [10]

On this background, the study was conducted to observe the efficacy and safety of ondansetron over phenylephrine for the prevention of post-spinal hypotension.

If ondansetron is found to be safe and effective than phenylephrine, then it may be used in future for its dual effects- prevention of post-spinal hypotension and nausea- vomiting in caesarean section.

Objective

To assess the efficacy and safety of prophylactic dose of ondansetron in comparison to phenylephrine to prevent spinal anesthesia- induced hypotension in caesarean section.

Material and Methods

A Prospective, randomized, parallel, double-blinded, placebo controlled unicentric clinical trial was conducted from July 2015 to September 2015 in Obstetrics and Gynaecology operation theatre of a tertiary teaching hospital after getting approval from ethics committee of College of Medicine & JNM Hospital.

A power analysis was performed by assuming an incidence of hypotension 80% in the control group and it was revealed that a sample size of 21 patients in each group had a 90% power to detect a 35% reduction of the incidence of hypotension, with type I error probability (α) of 0.05 and dropout of 10 %.Total sample size was 63 patients.

Uncomplicated singleton pregnancy more than 36 weeks,American Society of Anaesthesiologists (ASA) physical status I or II, Age between 18 – 30 years and weight - 50 kg -90 kg, scheduled to have elective caesarean section under spinal anaesthesia were recruited for this study. But, patients not interested in spinal anaesthesia or had contraindication to spinal anaesthesia having complicated pregnancy, allergy to study medications , known hypertensive or with a resting BP > 140/90 mm Hg, Known cardiovascular disease , history of any other

systemic illness , or patients on chronic medications were excluded from the study.

After obtaining signed informed consent form, the patients were randomized by a sealed-envelope technique and had a chance to get allocated in any group, to receive 100 mcg of phenylephrine[1] intravenously (**Group P**) or 4 mg of IV ondansetron [10] intravenously (Group **O**) or 10 ml of normal saline intravenously (**Group C).** All medications were freshly prepared by mixing with 10 ml normal saline (0.9% NS) for blinding.

Patients did not receive any premedication. Intravenous (I.V.) catheter of 18 gauge was placed in the vein of left forearm. Then, 500 ml ringer lactate (RL) was infused rapidly. Then, RL infusion was continued for one hour after surgery, at the rate of 4ml / kg / hour.

Ports of multichannel monitor were attached for monitoring the haemodynamic parameters- SBP (systolic blood pressure), DBP (diastolic blood pressure), MBP (mean blood pressure), heart rate (HR) and O_2 saturation (SpO_2).

Patients were placed in sitting position, after antiseptic dressing and draping, spinal needles (25 gauge) were inserted in L2-3 or L3-4 vertebral interspace. After clear cerebrospinal fluid (CSF) came out freely drop by drop, local anaesthetic agent, hyperbaric bupivacaine 0.5%, 2.5 ml was administered intrathecally. Thereafter, patients were placed in supine position with 15° angle of left lateral uterine displacement. Thereafter, according to study group, study medication was administered into the vein of left forearm for one minute. SBP, DBP, MBP, HR were recorded in three (3) minutes interval during surgery and every ten (10) minutes interval after surgery for one hour.

Hypotension was defined when SBP was <90 or a decrease of MBP more than 25% of baseline. If hypotension occurred, patients received rescue medication of IV bolus dose of phenylephrine 50 microgram (mcg) and a repeat dose after 6 minutes if needed. IV atropine 0.6 mg was injected if bradycardia (defined as HR<50 beats/minute) occurred. On requirement of more than two (2) rescue doses (either phenylephrine or atropine) continuously, the patient were excluded from the study. After delivery of shoulders of neonates, patients received 5 IU of oxytocin intravenously.Efficacy parameters were assessed through the data of SBP, MBP, DBP. Any changes in ECG, HR or any other adverse events were also noted in detail.

After the completion of case report form of last patient, statistical analysis were performed.

Data were represented as mean ± S.E.M (standard error mean). Categorical data were compared between groups by Chi-square test. As the data could not pass the normality test, numerical data between the groups were analyzed by Kruskall-Wallis (nonparametric) test, whereas within the group were analyzed by Friedman's ANOVA (nonparametric) followed by Dunn's Multiple Comparison test as post hoc test. All analyses were two-tailed and $p < 0.05$ was taken to be statistically significant. Statistical analyses were performed by Graph Pad InStat 3 software.

OBSERVATIONS AND RESULTS

Sixty three patients (63) were randomized during the period of July, 2015 to September 2015. Out of those,fifty five patients (55) completed the study as per protocol, 19 patients in group O (ondansetron 4 mg IV treated group) , 19 patients in group P (phenylephrine 100 mcg IV),and 17 patients group C (0.9% normal saline). 2 patients of group O, 2 patients of group P, and 4 patients of group C did not complete the study ((due to hypotension even after rescue medication), were declared as dropout.

PROFILES OF STUDY PATIENTS

All study patients were recruited on an ambulatory (out-patient) basis. The patients in all groups had comparable demographic profile, laboratory parameters and baseline efficacy parameters are represented in table 1. Data are presented as mean ± standard error of mean (SEM).

TABLE 1. Shows demographic parameters, laboratory parameters, efficacy parameters

Parameters	Group O (N= 19)	Group P (N=19)	Group C (N=17)	P value
Demographic parameters				
Age (yrs)	23.68 ± 0.63	22 ± 1.06	24.38 ± 1.2	0.22
Gestational age (weeks)	37.26 ± 0.16	37.56 ± 0.24	37.6 ± 0.18	0.47
Height (cm)	149.84 ± 0.675	150.11 ± 1.49	148.9 ± 0.64	0.66
Weight (kg)	6.68 ± 1.93	58.22 ± 1.15	61.53 ± 0.85	0.06
Laboratory parameters				
Hemoglobin (gm %)	10.06 ± 0.22	10.1 ± 0.3	10.2 ± 0.21	0.79
FBS (mg/dl)	80.1 ± 1.91	75.56 ± 1.72	83.8 ± 3.18	0.16
PPBS (mg/dl)	118.47 ± 2.07	108.78 ± 6.4	122.54 ± 4.25	0.08
Urea (mg/dl)	24.21 ± 1.07	24.11 ± 1.36	25.84 ± 1.07	0.47
Creatinine (mg/dl)	0.70 ± 0.03	0.67 ± 0.04	0.66 ± 0.02	0.65
Efficacy parameters (baseline)				
SBP(mm of Hg)	121.16 ± 2.77	118 ±3.37	124 ± 2.5	0.43
DBP (mm of Hg)	81.41 ± 1.45	76.33±2.92	82 ± 2.1	0.26
MBP (mm of Hg)	94.67 ± 1.78	90.11 ± 2.89	96.15± 1.98	0.20
HR (beats/min)	96 ± 4.31	82 ± 5.02	91.23 ± 2.94	0.12

p value for comparison of the study groups was from Kruskal Wallis H test (non parametric test).
p value <0.05 is consider significant.

SYSTOLIC BLOOD PRESSURE (SBP)

TABLE 2. Shows SBP in various time period of three groups- Group O , Group P, Group C.

SBP		DURING SURGERY (INTRA-OPERATIVE)								AFTER SURGERY (POST OPERATIVE)						
GROUPS		Baseline	SBP-1 (1+3=4 mins after drug administration)	SBP-2 (3+4=7 mins after drug administration)	SBP-3 (7+3=10 mins after drug administration)	SBP-4 (10+3=13 mins after drug administration)	SBP-5 (13+3=16 mins after drug administration)	SBP-6 (16+3=19 mins after drug administration)	SBP-7 (19+3=22 mins after drug administration)	SBP-8 (22+3=25 mins after drug administration)	SBP-10 (10 mins after surgery)	SBP-20 (20 mins after surgery)	SBP-30 (30 mins after surgery)	SBP-40 (40 mins after surgery)	SBP-50 (50 mins after surgery)	SBP-60 (60 mins after surgery)
GROUP O	Mean ± SEM	121.16 ± 2.77	116.67 ± 3.18	111.42 ± 3.46	107.42 ± 3.67 *	109.25 ± 3.25	110.83 ± 2.55	110.92 ± 2.21	110.44 ± 2.8	113.75 ± 5.6	114.16 ± 2.24	115.66 ± 2.1	117.58 ± 1.96	117.83 ± 2.3	119.33 ± 2.07	120.33 ± 1.87
	P value		>0.05	>0.05	<0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
GROUP P	Mean ±SEM	118 ±3.37	116.78 ± 4.06	111.22 ± 2.68	111.44 ± 3.85	108.22 ± 4.15	106 ± 4.72	107.22 ± 4.99	107.16 ± 4.49	119 ± 1.0	112.16 ± 3.05	112.66 ± 3.52	114.08 ± 3.21	115.83 ± 2.93	117.67 ± 2.23	118.25 ± 2.15
	P value		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

GROUP C	Mean ±SEM	124 ± 2.5	118.07 ± 4.16	106.53 ± 4.16 **	104.07 ± 3.28**	103.23 ± 2.91***	103.23 ± 4.21 ***	103.36 ± 3.47 **	107.6 ± 3.24 *	111.8 ± 4.40	11.76 ± 3.02	113.15 ± 2.63	111.15 ± 3.28	114.23 ± 2.01	117.07 ± 2.04	118.46 ± 1.47
	P value		>0.05	<0.01	<0.01	<0.001	<0.001	<0. 01	<0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

Statistical analysis for comparisons of SBP within the group (with baseline comparison) were performed by nonparametric Friedman's ANOVA followed by post-hoc analysis by Dunn multiple comparison test.

p value <0.05 considered significant different with baseline.***= p<0.001, ** =p<0.01, * =p<0.05

Least fluctuation of SBP was seen in Group P followed by Group O.

DIASTOLIC BLOOD PRESSURE (DBP)

TABLE 3. Shows DBP in various time period of three groups- Group O , Group P, Group C.

DBP		DURING SURGERY (INTRA-OPERATIVE)									AFTER SURGERY (POST OPERATIVE)					
GROUPS		Baseline	DBP-1 (1+3=4 mins after drug administration)	DBP -2 (3+4=7 mins after drug administration)	DBP -3 (7+3=10 mins after drug administration)	DBP -4 (10+3=13 mins after drug administration)	DBP -5 (13+3=16 mins after drug administration)	DBP -6 (16+3=19 mins after drug administration)	DBP -7 (19+3=22 mins after drug administration)	DBP -8 (22+3=25 mins after drug administration)	DBP - 10 (10 mins after surgery)	DBP - 20 (20 mins after surgery)	DBP - 30 (30 mins after surgery)	DBP - 40 (40 mins after surgery)	DBP - 50 (50 mins after surgery)	DBP - 60 (60 mins after surgery)
GROUP O	Mean ± SEM	81.41 ± 1.45	77.5 ± 1.48	67.67 ± 2.87**	78.17 ± 1.18	79.17 ± 1.23	79.67 ± 1.66	77.58 ± 1.37	77.22 ± 1.58	79.75 ± 1.03	76.91 ± 1.71	75.5 ± 1.89	77.67 ± 1.77	78.75 ± 1.32	79.75 ± 1.42	79.83 ± 1.46
	P value		>0.05	<0.01	<0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
GROUP P	Mean ±SEM	76.33±2.92	71.33± 4.66	72.56 ± 4.09	67.89 ± 3.39	65.55 ± 4.13	62.89± 3.96	65.11 ± 3.10	64 ± 3.67	71.5 ± 4.5	68.44 ± 2.79	70.22 ± 2.96	72 ± 2.66	74 ± 2.13	74 ± 1.97	75.33 ± 1.97
	P value		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
GROUP C	Mean ±SEM	82 ± 2.1	76.15 ± 3.12	69.3 ± 3.48	63.46 ± 3.07**	62.69 ± 3.67***	60.46 ± 2.89 ***	59.8 ± 3.38 **	60.8 ± 2.74 **	66.85 ± 3.68	66.46 ± 4.03	70.84 ± 3.36	70.23 ± 3.57	71.84 ± 3.04	75.15 ± 2.3	78 ± 1.58
	P value		>0.05	>0.05	<0.01	<0.001	<0.001	<0. 01	<0.01	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

Statistical analysis for comparisons of DBP within the group (with baseline comparison) were performed by nonparametric Friedman's ANOVA followed by post-hoc analysis by Dunn multiple comparison test.

p value <0.05 considered significant different with baseline.***= p<0.001, ** =p<0.01, * =p<0.05

Least fluctuation of DBP was seen in Group P followed by Group O.

MEAN BLOOD PRESSURE (MBP)

Statistical analysis for comparisons of MBP within the group (with

TABLE 4. Shows MBP in various time period of three groups- Group O , Group P, Group C.

MBP		DURING SURGERY (INTRA-OPERATIVE)									AFTER SURGERY (POST OPERATIVE)					
GROUPS		Baseline	MBP-1 (1+3=4 mins after drug administration)	MBP -2 (3+4=7 mins after drug administration)	MBP -3 (7+3=10 mins after drug administration)	MBP -4 (10+3=13 mins after drug administration)	MBP -5 (13+3=16 mins after drug administration)	MBP -6 (16+3=19 mins after drug administration)	MBP -7 (19+3=22 mins after drug administration)	MBP -8 (22+3=25 mins after drug administration)	MBP - 10 (10 mins after surgery)	MBP - 20 (20 mins after surgery)	MBP - 30 (30 mins after surgery)	MBP - 40 (40 mins after surgery)	MBP - 50 (50 mins after surgery)	MBP - 60 (60 mins after surgery)
GROUP O	Mean ± SEM	94.67 ± 1.78	90.41 ± 1.89	82.25 ± 2.82	87.83 ± 1.68	89.08 ± 1.58	90.25 ± 1.44	88.67 ± 1.40	72.27 ± 10.86	91 ± 2.35	89.33 ± 1.76	88.83 ± 1.80	90.91 ± 1.63	91.75 ± 1.28	93 ± 1.50	93.14 ± 1.47
	P value		>0.05	<0.01	<0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
GROUP P	Mean ±SEM	90.11 ± 2.89	86 ± 4.03	84.78 ± 3.19	82.45 ± 3.38	78.78 ± 3.95	77.23 ± 4.16	77.23 ± 4.16	79.33 ± 3.78	78 ± 3.95	87 ± 3.1	82.22 ± 2.64	83.56 ± 3.05	85.45 ± 2.73	87.55 ± 2.93	87.89 ± 1.93
	P value		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
GROUP C	Mean ±SEM	96.15 ± 1.98	89.92 ± 3.25	81.76 ± 3.59	76.84± 3.06***	76.61± 3.39***	74.23± 3.18***	74.7± 3.36***	75.3± 2.57***	81.5 ± 4.08	81.46± 3.70*	82.61 ± 3.69	84.69 ± 3.09	85.46 ± 2.56	89.15 ± 2.17	91.07 ± 1.54
	P value		>0.05	>0.05	<0.001	<0.001	<0.001	<0.001	<0.001	>0.05	<0.05	>0.05	>0.05	>0.05	>0.05	>0.05

baseline comparison) were performed by nonparametric Friedman's ANOVA followed by post-hoc analysis by Dunn multiple comparison test.

p value <0.05 considered significant different with baseline.***= p<0.001, ** =p<0.01, * =p<0.05

Least fluctuation of MBP was seen in Group P followed by Group O.

HEART RATE (HR)

TABLE 5. Shows HR in various time period of three groups- Group O , Group P, Group C.

HR		AFTER SURGERY (POST OPERATIVE)									DURING SURGERY (INTRA-OPERATIVE)					
GROUPS		Baseline	HR-1 (1+3=4 mins after drug administration)	HR -2 (3+4=7 mins after drug administration)	HR -3 (7+3=10 mins after drug administration)	HR -4 (10+3=13 mins after drug administration)	HR -5 (13+3=16 mins after drug administration)	HR -6 (16+3=19 mins after drug administration)	HR -7 (19+3=22 mins after drug administration)	HR -8 (22+3=25 mins after drug administration)	HR -10 (10 mins after surgery)	HR -20 (20 mins after surgery)	HR -30 (30 mins after surgery)	HR -40 (40 mins after surgery)	HR -50 (50 mins after surgery)	HR -60 (60 mins after surgery)

GROUP O	Mean ± SEM	96 ± 4.31	93.36 ± 4.2	92.45 ± 3.74	94.27 ± 3.81	96 ± 3.28	99.27 ± 2.94	98.18 ± 3.72	97.5 ± 4.73	106.67 ± 2.90	93.81 ± 2.55	90.9 ± 1.98	89.27 ± 1.67	88.54 ± 1.93	85.63 ± 1.69	85.54 ± 1.62
	P value		>0.05	<0.01	<0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
GROUP P	Mean ±SEM	82 ± 5.02	77.22± 5.03	82.45 ± 3.88	85.78 ± 3.80	90.89 ± 4.49	91.56 ± 2.76	97.12 ± 2.5	95.28 ± 2.21	98.5 ± 3.5	91.89 ± 2.3	89.67 ± 2.84	87.11 ± 2.12	85.33 ± 2.11	84.11 ± 1.65	83.33 ± 1.52
	P value		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
GROUP C	Mean ±SEM	91 ± 2.94	88.23 ± 5.35	93 ± 4.83	96.92 ± 4.72	94.61 ± 4.07	96.38 ± 3.87	93.9 ± 4.4	93.7 ± 5.08	93.67 ± 7.25	92 ± 1.34	88.23 ± 2.73	88.07 ± 3.06	88.38 ± 2.84	86.76 ± 2.4	83.76 ± 1.98
	P value		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

Statistical analysis for comparisons of HR within the group (with baseline comparison) were performed by nonparametric Friedman's ANOVA followed by post-hoc analysis by Dunn multiple comparison test.

p value <0.05 considered significant different with baseline.***= p<0.001, ** =p<0.01, * =p<0.05

Least fluctuation of MBP was seen in Group P and Group C.

INCIDENCE OF HYPOTENSION

TABLE 6. Shows the incidence of hypotension in different groups

GROUPS	ONCE	TWICE	THRICE	4 TIMES	5 TIMES
GROUP O	**1**	**4**	**1**	**0**	**0**
GROUP P	**1**	**4**	**0**	**0**	**0**
GROUP C	**0**	**3**	**1**	**2**	**3**

It is seen that least incidence of spinal induced hypotension is seen in Group P patients followed by Group O patients.

RESCUE MEDICATION

Frequency of rescue medication intake

Table 7. Shows number of patients received rescue medication in different groups

Rescue medication received	GROUP O (N=19)	GROUP P (N=19)	GROUP C (N=17)
Yes	6 (31.58 %)	5 (26.31%)	9 (52.94 %)
No	13 (68.42 %)	14 (73.69%)	8 (47.06 %)

GROUP-WISE COMPARISON

Table 8. shows p value between the groups

Comparison	P Value
Group O Vs Group P	0.72
Group O Vs Group C	0.33
Group P Vs Group C	0.19

It is seen that there is no difference of frequency of rescue medication intake.

Total requirement of rescue medication

Table 9. Shows requirement of total rescue medication in different groups

GROUPS	GROUP O	GROUP P	GROUP C
Mean ± SEM	92.86 ± 13.04	90 ±10.1	183.33 ± 20.41

Table 10.shows p value between groups

Comparison	P Value
Group O Vs Group P	> 0.05
Group O Vs Group C	<0.05
Group P Vs Group C	<0.05

Total requirement of rescue medication is more in group C than group O and group P.

ADVERSE EVENTS

Only adverse event was nausea, vomiting. There was no incidence of hypertension or bradycardia was seen during the study period of any group.

Table 11. Shows incidence of adverse events in various groups.

NAUSEA,VOMITING	GROUP O (N=19)	GROUP P (N=19)	GROUP C (N=17)
YES	1	4	9
NO	18	15	8

Table 12.shows p value between different groups

Comparison	P value
GROUP O Vs GROUP P	0.33
GROUP O Vs GROUP C	0.004
GROUP P Vs GROUP C	0.1

It is seen that incidence of adverse events (nausea, vomiting) is more in group C that both group O and group P.

DISCUSSION

The present study was a randomized controlled clinical trial to evaluate the efficacy and safety of ondansetron over phenylephrine for the prevention of spinal anaesthesia-induced hypotension in caesarean section

They are assigned to three groups by randomization.

The groups were comparable at baseline with respect of demographic parameters (age, gestational age, weight, and height), laboratory parameters (urea, creatinine, hemoglobin, fasting & post prandial blood sugar) and baseline efficacy parameters (SBP, DBP, MBP, HR).

In group O, SBPs were maintained throughout the time periods (except SBP-3), and in group P, the SBPs were maintained (no variability) throughout the surgery and also throughout one hour of post-operative period. But in group C had maximum fluctuation of SBPs in respect to group O and group P.

In group O, DBPs were maintained throughout the time periods (except DBP-2). In group P had no variability throughout the time period. But in group C had maximum fluctuation during the time periods that were statistically significant.

In group O and group P had maintained the MBP throughout the time period, but group C had maximum fluctuation of MBPs during that period that was statistically significant.

It was seen that, group O , group P and group C maintained the HR throughout the surgery and even after one hour of surgery.

Incidence of hypertensive episode was maximum in group C, followed by group O. Group P had least episode than other groups.

It was seen that rescue medication was required maximum in group C than other two group that was statistically significant. There was no difference between group O and group P in respect of total amount of rescue medication.

Only adverse effects were seen; nausea and vomiting. There was no episode of rise of blood pressure or bradycardia. In this respect, group C had maximum incidence of nausea and vomiting than group O and group P what was statistically significant.

So from the result it can be said that 100 mcg IV phenylephrine and 4 mg IV ondansetron can be effective to prevent spinal anaesthesia induced hypotension.

This result correlates with other previous studies.

In a study of comparison between phenylephrine and ephedrine in preventing hypotension during spinal anesthesia for cesarean section, it was seen that 100 mcg IV phenylephrine was effective to prevent spinal anaesthesia induced hypotension.[1]

In another study of comparison the effect of ephedrine and phenylephrine in treatment of hypotension after spinal anesthesia during cesarean section, it was observed that 100 mcg IV phenylephrine was effective to prevent spinal anaesthesia induced hypotension.[11]

In another RCT of reduction in spinal-induced hypotension with ondansetron in parturients undergoing caesarean section: A double-blind randomised, placebo-controlled study,it was observed that 4 mg IV ondansetron reduced the incidence of spinal anaesthesia induced hypotension and requirement of vessopressor.[10]

A study on comparing two different doses of intravenous ondansetron with placebo on attenuation of spinal-induced hypotension and shivering ,it was seen ondansetron 6 mg and 12 mg, significantly attenuates spinal induced hypotension, compared to the control saline group. [12]

The present study had some limitation

1. Effect of phenylephrine and ondansetron on fetus was not assessed (umbilical arterial cord pH for fetal acidosis, APGAR score)
2. Higher dose group of ondansetron (8mg IV) was not included in this study
4. Height of blockage was not seen
5. Drug concentration was not measured

Although there are few limitations in the study, but it can be said that 100 mcg IV phenylephrine and 4 mg IV ondansetron is effective to prevent spinal anaesthesia induced hypotension with minimal side effects.

CONCLUSION

To conclude, it can be concluded that prophylactic 4 mg IV ondansetron is effective and safe to prevent the spinal anaesthesia induced hypotension with minimal adverse effect. But it is less effective than 100 mcg phenylephrine, although ondansetron is more effective to prevent incidence of nausea, vomiting in caesarean section.

Further study will be needed with larger population (without the above limitations) to detect the ideal IV dose of ondansetron that will be maximally effective for the prevention of spinal anaesthesia induced hypotension, with minimal side effect.

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