Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Evaluation of the Effect of Ondansetron on Haemodynamics under Spinal Anaesthesia.

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Received: May 2019
Accepted: May 2019

ABSTRACT

Background: Spinal anaesthesia related hypotension and bradycardia is not rare. One of the causes for post spinal hypotension is thought to be bezold-jarisch reflex (BJR) which is mediated by serotonergic 5-HT3 receptors. Ondansetron, one of the reliable drugs for nausea and vomiting, is 5-HT3 antagonist. Effect of ondansetron to attenuate hypotension has been studied in caesarean section but there is paucity of literature for general population. Aim and Objectives: In this study we aimed at evaluating the efficacy of ondansetron on haemodynamics of patients undergoing spinal anaesthesia. **Methods**: This prospective study enrolled 200 ASA I and II patients assigned into 2 groups: Group O (Ondansetron group, n=100) received injection ondansetron 0.1mg/kg intravenous, diluting the drug to make volume 10 ml 5 minutes prior to spinal anaesthesia(SA). Group P (Placebo group, n=100) received injection normal saline 10 ml intravenous 5 minutes prior to spinal anaesthesia. **Results:** Demographic data were comparable in both the groups. There was no significant difference in MAP (mean arterial pressure), HR(heart rate) & SpO2 (oxygen saturation) values in group O whereas in group P statistically significant variations in MAP, HR & SpO2 values were observed. Fewer interventions using intravenous atropine & ephedrine were required in group O as compared to group P. **Conclusion**: In conclusion, intravenous administration of ondansetron 5 minutes before spinal anaesthesia attenuates the decrease in mean arterial pressure.

Keywords: Anaesthesia, Haemodynamics, Ondansetron.

INTRODUCTION

Spinal anaesthesia is the technique of choice in abdominal and lower limb surgeries. It is easy to perform, fast to act, avoids polypharmacy and provides adequate surgical anaesthesia. Despite of these advantages, it has some known complications with hypotension and bradycardia accounting for 33% and 13% respectively being the commonest in non-obstetric cases whereas hypotension is 50-60% in non-laboring obstetric patients and incidence decreases after labour.[1,2] Sympathetic blockade cause hypotension and decreased systemic vascular resistance activating the bezold-jarisch reflex (BJR). The BJR associated with decreased venous return further cause bradycardia, vasodilatation and hypotension.[1,3] Treatment options for these pathophysiological effects of spinal anaesthesia can be intravenous fluids and vasopressors but literature suggest it is not much effective and not without side-effects.[4-7] There are many pharmacological studies and animal trials suggesting the BJR is associated with 5HT3 and receptor blockade attenuates the reflex.[8,9] Ondansetron is one of the trusted drugs used in practice for preventing nausea and vomiting, with its action on 5HT3 receptors and therefore can be used for preventing hypotension and bradycardia associated with BJR.

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Aim and Objectives

The present study is based on the assumption that ondansetron can successfully abolish the BJR and hence post spinal haemodynamic stability can be achieved that too without side effects of vasoactive drugs and chances of fluid overload.

MATERIALS AND METHODS

The present study is a randomized, prospective study which included 200 patients belonging to ASA I and II of either gender in the age group of 18-65 years posted for lower abdominal, urological, gynaecological and orthopaedic lower limb surgeries under spinal anaesthesia. Before enrolment for the

study, patients were informed about the aim, methods and potential hazards of the study.

Using a sealed envelope technique, patients were randomly allocated to two groups-

Group O (Ondansetron group, n=100) received injection(inj) ondansetron 0.1mg/kg intravenous, diluting the drug to make volume 10 ml 5 minutes prior to spinal anaesthesia.

Group P (Placebo group, n=100) received injection normal saline 10 ml intravenous, 5 minutes prior to spinal anaesthesia.

Inclusion criteria:

- ASA I and II
- Age group between 18-65 years
- Posted for surgery to be done under spinal anaesthesia
- Willing to consent

Exclusion criteria:

- Patients with contraindications to spinal anaesthesia
- Patients with contraindications to ondansetron
- Allergy to local anaesthetics used in the study
- Parturients
- History of chronic alcohol abuse
- History of hypertension
- Morbidly obese patient
- Surgeries involving major fluid shifts or blood loss more than allowable blood loss

Anaesthetic technique:

A thorough pre-operative check was conducted prior to surgery comprising detailed history and general physical examination. Routine investigations was done before surgery. Written informed consent was taken from all the participants. Pre-op advise included 8 hours of fasting, tablet pantoprazole 40 mg and tablet alprazolam 0.5 mg per oral, one at night and one in the morning of surgery.

After shifting the patients to the operation theatre, pre-induction vitals was recorded - Mean arterial pressure (MAP), heart rate (HR), oxygen saturation (SPO2). Intravenous infusion of ringer lactate was started at the rate of 10ml/kg. Depending upon the group to which patient belongs 10 ml of drug or saline was given by the anaesthesiologist blinded to the drug preparation. Group O received inj ondansetron 0.1 mg/kg intravenous, diluted to a volume of 10 ml and group P received 10 ml of normal saline.

Spinal anaesthesia was given under all aseptic precautions in sitting position in intervertebral space L3-4 or L4-5 with 26 gauze Quincke needle using Injection bupivacaine 0.5% hyperbaric 3 ml. Assessment of sensory blockade was done using alcohol swab and motor blockade using modified bromage score. Vitals including MAP, HR, SPO2 was recorded at 2 minutes interval up to 20 minutes and then every 5 minutes interval till completion of the surgery. Patient was shifted to post anaesthesia care unit and was monitored 2 hourly intervals to a total of 8 hours. Hypotension was defined by decrease of mean arterial pressure by 30% from baseline and was treated with injection ephedrine 6 mg bolus. Bradycardia was defined as heart rate less than 20% from baseline and was treated with injection atropine 0.5 mg. Intravenous fluids was used to replace blood loss and maintenance. Total number of interventions made and complications if any, were noted down at the end of the surgery.

RESULTS

Demographic data: 100 patients in each were allotted in group O & group P. Demographic data is presented in [Table 1-3]. There were no significant differences in patient's age, body weight, gender & nature of surgery.

Haemodynamic parameter variations: The changes in the MAP, HR & SpO2 values in both patient groups which were recorded before blockade & at 5 minutes interval after the block, are presented in the [Table 4-6]. Decrease in MAP & HR were observed in both the groups, but in group O the decrease was not statistically significant. MAP was significantly higher in the ondansetron group up to 20 minutes. These differences vanished at the 20th minute after SA (spinal anaesthesia).

If we refer to the table of pharmacological intervention, we will see that in group O, intervention with ephedrine/atropine was required only up to 18 minutes compared to group P were intervention was required up to 20 minutes

Table 1: Demographic Profile.

	Ondan		Placebo		t	p-value
	Mean	SD	Mean	SD		
Age	43.11	11.82	41.57	10.63	0.969	0.334
Weight	64.37	7.70	63.11	7.00	1.211	0.227

Table 2: Gender Distribution.

		Group		Total	Chi-square value	p-value
		Ondan	Placebo			
Gender	F	52	49	101	0.18	0.671
	M	48	51	99		
Total		100	100	200		

Table 3: Nature of operation.

		Group		Total	Chi-square value	p-value
		Ondan	Placebo			
Nature of operation	General Surgery	31	40	71	5.359	0.069
	Gynaecology	38	23	61		
	Orthopaedics	31	37	68		

Table 4: Changes of Mean Arterial Pressure.

Time interval(min)	Group O		Group P		t	p-value
	Mean	SD	Mean	SD		
T0_MAP	97.47	10.42	98.08	10.60	-0.410	0.682
T2_MAP	94.45	10.65	94.11	10.87	0.223	0.823
T4_MAP	93.08	9.44	89.78	12.01	2.160	0.032
T6_MAP	92.63	9.01	88.64	11.46	2.738	0.007
T8_MAP	90.93	8.95	87.39	11.50	2.430	0.016
T10_MAP	89.54	8.97	86.23	9.28	2.565	0.011
T12_MAP	90.07	8.80	87.04	10.66	2.193	0.029
T14_MAP	88.60	8.35	85.57	10.67	2.236	0.026
T16_MAP	87.53	8.84	84.04	10.63	2.525	0.012
T18_MAP	87.27	7.66	83.80	9.54	2.836	0.005
T20_MAP	87.40	8.23	84.32	9.11	2.508	0.013
T2h_MAP	88.07	6.43	86.79	6.78	1.369	0.172
T4h_MAP	88.67	6.72	87.42	7.09	1.280	0.202
T6h_MAP	89.86	6.56	88.56	6.88	1.367	0.173
T8h_MAP	90.36	6.04	88.91	6.22	1.660	0.099

Table 5: Changes in Heart Rate.

	Group O		Group P		t	p-value
	Mean	SD	Mean	SD		
T0_HR	77.83	14.56	79.18	15.57	-0.633	0.527
T2_HR	78.20	13.78	76.69	16.72	0.697	0.487
T4_HR	75.49	12.89	75.60	14.88	-0.056	0.955
T6_HR	76.35	11.56	71.61	15.82	2.419	0.016
T8_HR	76.42	12.49	72.08	16.61	2.089	0.038
T10_HR	73.80	11.33	69.56	15.73	2.187	0.030
T12_HR	72.41	9.42	69.07	12.58	2.125	0.035
T14_HR	73.83	10.63	68.57	11.28	3.394	0.001
T16_HR	71.22	10.78	67.17	11.82	2.531	0.012
T18_HR	70.33	10.10	70.68	12.37	-0.219	0.827
T20_HR	69.67	8.36	71.01	11.09	-0.965	0.336
T2h_HR	71.28	7.14	70.66	8.60	0.555	0.580
T4h_HR	73.55	7.67	72.56	7.76	0.907	0.365
T6h_HR	75.45	7.28	74.57	9.57	0.732	0.465
T8h_HR	76.87	7.40	75.32	9.15	1.295	0.197

Table 6: Changes of Oxygen Saturation.

Time interval(min)	Group O		Group P		Z	p-value
	Mean	SD	Mean	SD		
T0_SPO2	99.77	0.69	99.64	1.10	-0.034	0.973
T2_SPO2	99.75	1.10	99.85	0.66	-0.081	0.936
T4_SPO2	99.75	0.89	99.73	0.93	-0.455	0.649
T6_SPO2	99.83	0.67	99.63	1.27	-0.417	0.676
T8_SPO2	99.78	0.88	99.73	0.93	-0.243	0.808
T10_SPO2	99.69	1.13	99.80	0.88	-0.311	0.756
T12_SPO2	99.80	0.88	99.85	0.86	-0.666	0.506
T14_SPO2	99.81	0.68	99.78	0.77	-0.250	0.803
T16_SPO2	99.76	0.89	99.91	0.51	-1.790	0.073
T18_SPO2	99.69	1.13	99.88	0.69	-1.790	0.073
T20_SPO2	99.78	0.88	99.71	1.00	-0.270	0.787
T2h_SPO2	100.00	.000a	100.00	.000a	0.000	1.000
T4h_SPO2	100.00	.000a	100.00	.000a	0.000	1.000
T6h_SPO2	100.00	.000a	100.00	.000a	0.000	1.000
T8h_SPO2	100.00	.000a	100.00	.000a	0.000	1.000

Table 7: Pharmacological Intervention.

Time interval		Group		Total	Chi-square value	p-value
		O	P			
T4_INTERVENTION	N	92	95	187	0.740	0.390
	Y	8	5	13		
T6_INTERVENTION	N	100	81	181	20.994	0.000
	Y	0	19	19		
T8_INTERVENTION	N	100	85	185	16.082	0.041
	Y	0	15	15		
T10_INTERVENTION	N	95	86	181	4.711	0.051
	Y	5	14	19		
T12_INTERVENTION	N	100	87	187	13.904	0.000
	Y	0	13	13		
T14_INTERVENTION	N	100	92	192	8.333	0.007
	Y	0	8	8		
T16_INTERVENTION	N	100	83	183	18.576	0.000
	Y	0	17	17		
T18_INTERVENTION	N	100	87	187	13.904	0.000
	Y	0	13	13		
T20_INTERVENTION	N	96	91	187	2.057	0.251
	Y	4	9	13		

DISCUSSION

The most significant observation in the present study is that intravenous ondansetron prior to spinal anaesthesia may help prevent hypotension. In the studied group, we observed higher values of mean arterial pressure in those who received ondansetron, but there were no substantial changes in HR & SpO2. The haemodynamic effects of spinal anaesthesia are frequently observed & the most frequent is hypotension, while bradycardia is observed less often. The first side effect is mainly connected with vasodilatation due to sympathetic fibre blockade, which spreads higher than motor & sensory blockades.[10] The same mechanism may be an infrequent cause of bradycardia, mainly in individuals with a strong spinal block. A substantial decrease in the HR is a consequence of the BJR & the increased baroreflex activity. Prophylactic vasopressors are not always effective at preventing hypotension during spinal anaesthesia & could cause hypertension & tachycardia.[11] The latter complication may follow atropine or glycopyrrolate administration, both of which are used for attenuation of hypotensive response after spinal anaesthesia in geriatric population.

Considering the aforementioned problem, ondansetron is an attractive alternative for older methods of spinal anaesthesia associated hypotension attenuation. The influence of ondansetron on HR & blood pressure is irrelevant, even when it is administered via rapid intravenous infusion.[12]

This drug is widely used for post op nausea vomiting (PONV) prevention & in the treatment for both children & adults.[13]

The effect of ondansetron on hypotension following spinal anaesthesia has been described in a mixed population 9 & in parturient undergoing caesarean section.[14]

We observed that ondansetron exerts substantial effects on the mean arterial blood pressure. It is difficult to explain how 5 - HT3 blockade with ondansetron influences vascular resistance, especially that the antiemetic administration in normal setting is not connected with any substantial changes in HR & arterial blood pressure.[15] Although it is known that serotonin has relevant influence on the vascular tone, there are sparse data about the role of 5 – HT3 receptors in those mechanisms regulation.+[16]

In conclusion, intravenous administration of ondansetron before spinal anaesthesia attenuates the decrease in mean arterial pressure without significantly affecting HR & SpO2. Though other effects of ondansetron, like decrease frequency of PONV, Post-dural puncture headache & shivering associated with spinal anaesthesia, were not included in the study; however, these effects add more advantages to its use in spinal anaesthesia.

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How to cite this article: Kaur K, Gupta SK, Kaur M. Evaluation of the Effect of Ondansetron on Haemodynamics under Spinal Anaesthesia. Ann. Int. Med. Den. Res. 2019; 5(4):AN17-AN21.

Source of Support: Nil, **Conflict of Interest:** None declared