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Original Research Article

Study the effect of ondansetron on shivering under spinal anaesthesia for gynaecological surgeriesPallavi Waghalkar^{1*} and Pradnya M. Malgundkar²¹Associate Professor, ²Junior Resident,

Department of Anaesthesiology, Seth G. S. Medical College and K.E.M. hospital, Mumbai, Maharashtra, India- 400012

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***Correspondence Info:**Dr. Pallavi Waghalkar,
Associate Professor,
Department of Anaesthesiology,
Seth G. S. Medical College and K.E.M. Hospital,
Mumbai, Maharashtra, India- 400012***Article History:****Received:** 24/12/2017**Revised:** 28/12/2017**Accepted:** 30/12/2017**DOI:** <https://doi.org/10.7439/ijbr.v8i12.4546>**Abstract****Aims and Objective:** The primary aim was to study the incidence of ondansetron on shivering in patients undergoing elective gynaecological surgeries under spinal anaesthesia and secondary to record vital parameters (HR, SBP, DBP and SpO₂) and side effects, if any.**Methods:** This prospective observational study was performed on 70 ASA grade I and II female patients of 18 to 60 years of age to received either normal saline (Group NS) or Ondansetron (Group ODT) 0.15mg/kg. Spinal anaesthesia was given to all patients with Bupivacaine 15 mg. 0.5% heavy 3cc + Inj. Norphine 60 microgram L3 – L4 interspace. During surgery, a shivering score was recorded at 5, 10, 15, 20, 25, 30, 60, 120 minutes. Vital parameters in terms of HR, SBP, DBP and SpO₂ and side effects, if any were measured.**Results:** The incidence of shivering was 8.57% in ondansetron group compared to 40% patients in NS group. Also the incidence of maximum shivering score was high in group NS compared to group ODT. At 25 and 30 minutes, heart rate was significantly greater (82.14 ± 13.06 and 80.6 ± 12.55) in patients receiving normal saline after which it was constant. On the other hand, at 30 and 60 minutes the SBP, DBP and MAP was significantly greater in ondansetron group as compared to normal saline group. Hypotension was comparable in both the groups.**Conclusion:** The prophylactic administration of ondansetron (0.15mg/kg) I.V. before spinal anaesthesia produces anti-shivering effect, therefore it can be considered as a safe option to prevent post spinal anaesthesia shivering and reduce the risk of hypotension.**Keywords:** Ondansetron, Gynaecological Surgeries, Bupivacaine, Shivering score, Axillary and Tympanic Temperature, Anti-shivering effect.**1. Introduction**

Shivering is one of the most frequent complications of operation during the postanesthesia period. It occurs in more than 56.7% of patients after spinal and epidural anaesthesia [1]. Post anaesthesia shivering (PAS) was first described over fifty years ago with a worldwide incidence of 20-60%. While patients find shivering very uncomfortable, it causes artefacts in monitors and increases postoperative pain, heart rate, cardiac output, oxygen consumption by five-folds and metabolic rate by 600% [2]. These might result into

hypercarbia, myocardial ischaemia, lactic acidosis and hypoxaemia which may obscure post anaesthesia recovery. Preventing post-anaesthesia shivering may reduce morbidity and improve patient's satisfaction [3].

Different drugs and methods have been used in prevention and treatment of the postoperative shivering. These drugs belong to classes such as biogenic monoamines, endogenous peptides, cholinomimetics, cations and probably N-methyl-D-aspartate. The most efficient ways of prevention and treatment are fluid

warming and forced air warming. The pharmacological agents for combating shivering are nefopam, morphine, tramadol, ondansetron, physostigmine, fentanyl and pethidine [2,4].

Ondansetron, a 5-HT₃ antagonist, is generally used as an antiemetic but its efficiency and safety in the prevention of PAS remains controversial. Consistently, several studies [1,4,5-7] have demonstrated ondansetron to prevent PAS, which has made it a promising drug for post-operative complications including PAS, nausea and vomiting. There are few studies that reported the effect of ondansetron on shivering after spinal anaesthesia but hardly any studies reporting the use of ondansetron in gynaecological surgeries. Hence, the primary aim of present study was to study the incidence of ondansetron on shivering in patients undergoing elective gynaecological surgeries under spinal anaesthesia. The secondary aim was to record vital parameters in terms of heart rate, systolic and diastolic blood pressure, peripheral oxygen saturation and side effects, if any.

2. Material and Methods

A prospective observational study was carried out in 70 female patients of ASA grade I and II [ASA II patients (those with Diabetes Mellitus, Hypertension, Bronchial asthma on regular t/t and under control)], age between 18 to 60 years undergoing any gynaecological surgery in gynaecological operation theatre under spinal anaesthesia at Seth G.S Medical College and King Edward Memorial Hospital, Mumbai. Before starting the study Institutional Ethical Committee approval and written informed consent from patients or guardians were obtained. Patients with uncontrolled hypo- or hyperthyroidism, receiving vasodilators or medications likely to alter thermoregulation, patients with uncontrolled (Not taking medication) systemic diseases leading to secondary complication (ASA III), patients refusing to be a part of this study were excluded from the study.

All patients were kept nil per oral (NBM) for 8 hours prior to the surgery. On the day of surgery on arrival of the patient in the operating room; pulseoximeter, non-invasive blood pressure, cardioscope was attached to the patient. O₂ inhalation @ 6 L/min using Hudson's mask was given to the patient. Ringer's solution was infused over at 10ml / kg, 15 min before spinal anaesthesia and before giving the IV study drugs. The temperature of the operating room during the perioperative period was kept at a set average temperature of 24°C. All these were the standard methods for achieving the secondary aim of this study. Spinal anaesthesia was given to all patients with injection

bupivacaine 15 mg, 0.5% heavy 3cc + Inj. Norphine 60 micrograms at L3 – L4 interspace. Patients were randomized into two equal groups using the random chit method to receive saline (Group S) 4cc NS I.V. and Inj. Ondansetron (Group O) 0.15mg/kg, approximately 8mg I.V.

During surgery, a shivering score was recorded at 5, 10, 15, 20, 25, 30, 60, 120 minutes. Shivering was graded according to the previous studies [26] as grade I – no Shivering, grade II – fasciculation in head and neck that is just visible, grade III – obvious tremors on head, neck and limbs and grade IV – generalised tremors. Incidence of shivering was compared in the two groups, after a prophylactic dose. Vital parameters – i.e. heart rate, systolic and diastolic blood pressure, peripheral oxygen saturation and side effects, if any were measured. Tympanic and axillary temperatures were recorded at the same time along with spinal block level in intraoperative period of gynaecological surgery. Tympanic (core) temperature was recorded using OMRON tympanic thermometer. If the observer observed pectoralis major muscle fasciculations for more than 10 seconds after subarachnoid block was complete, only then, rescue drug tramadol (50mg) I.V. diluted to 10 cc with sterile NS was administered over 10 minutes.

2.1 Statistical Analysis

Continuous variables were expressed as mean \pm standard deviation (SD) and categorical variables as frequency%. Continuous variables were analyzed using the independent t-test or Mann Whitney test. Categorical variables were analyzed using the Chi-Square test. Repeated data were analyzed using repeated measures ANOVA. P<0.05 was considered statistically significant.

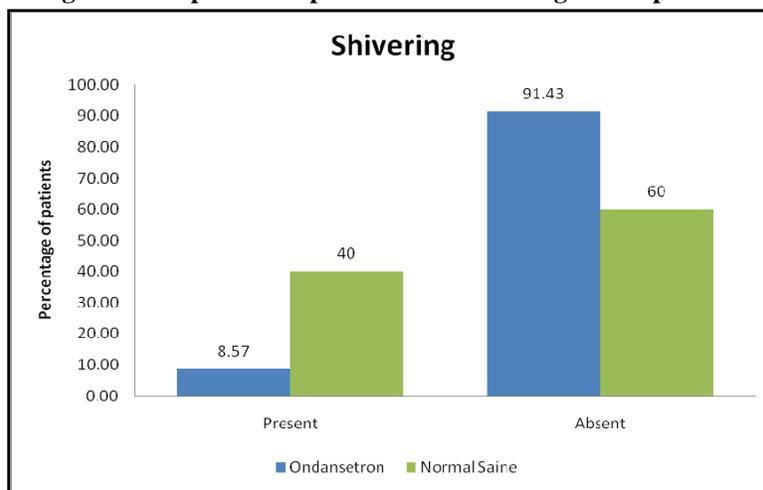
3. Observations and Results

The study enrolled total 70 ASA grade I and II female patients and divided into two equal groups to received either prophylactic 0.15 mg/kg of ondansetron or normal saline. The mean age of patients receiving ondansetron was found to be 49.17 years and for those receiving normal saline was 49.57 years. There was no significant difference between two groups with regards to mean age and ASA grade of the patients.

Table 1 show the shivering score observed in two groups. Only 3/35 (8.57%) patients in ondansetron group showed shivering as compared to 14/35(40%) patients in NS group. This indicated that significantly greater proportion of patients in normal saline group had shivering intraoperatively as compared to ondansetron group, (Figure 1).

Table 1: Comparison of Shivering score between the two groups

Shivering score	Ondansetron					Normal Saline				
	0	I	II	III	IV	0	I	II	III	IV
Pre-operative	35					35				
At Induction	35					35				
At 5 Min	35					35				
At 10 Min	35					35				
At 15 Min	33		1	1		28		1	6	
At 20 Min	32			3		21	1	1	10	2
At 25 Min	32			2	1	21	1	1	8	4
At 30 Min	34			1		25		1	7	2
At 60 Min	35					30	1	2	2	
At 120 Min	35					35				

Figure 1: Proportion of patients with shivering intra-operative

The heart rate was observed to be constant in both the groups for pre-operative period, at induction and up to 20 minutes after induction. However, at 25 and 30 minutes the heart rate was significantly greater in patients receiving normal saline after which it was constant. SBP, DBP and

MAP were found to be constant for pre-operative period, at induction, at 5, 10, 15, 20, 25 and 120 minutes. On the other hand, at 30 and 60 minutes the SBP, DBP and MAP was significantly greater in ondansetron group as compared to normal saline group (Table 2).

Table 2: Comparison of vital parameters between two groups

Time interval	Heart Rate		Systolic BP		Diastolic BP		MAP	
	ODT	NS	ODT	NS	ODT	NS	ODT	NS
Pre-operative	82.05±13.56	77.94±2.25	121.17±11.92	126.05±16.46	80.63±6.72	81.49±3.44	94.14±5.85	96.37±5.85
At Induction	84.97±11.43	80.46±7.85	122.06±11.8	121.34±12.33	78.34±7.32	78.37±6.33	92.94±8.30	93.06±7.49
At 5 Min	85.89±9.30	82.31±8.74	111.54±8.44	113.54±8.8	72.29±7.96	72.54±6.56	85.43±7.56	86.14±6.24
At 10 Min	84.51±8.11	84±9.18	103.66±6.18	106.2±7.91	68.34±6.99	68.66±6.37	80.09±6.27	81.14±6.07
At 15 Min	81.65±9.54	84.09±10.96	101.2±7.42	102.34±7.19	65.77±6.28	65.63±7.19	77.63±6.22	77.91±6.49
At 20 Min	79.2±10.03	83.09±12.02	99.89±6.84	100±6.54	64.69±5.13	64.88±7.16	76.31±5.11	76.46±6.42
At 25 Min	73.49±9.50	82.14±13.06	102.34±7.95	100.46±5.6	68.11±7.58	65.48±7.35	79.57±7.28	77.11±6.39
At 30 Min	72.89±8.67	80.6±12.55	110.51±9.71	104.14±7.07	72.06±8.67	66.46±8.61	84.97±7.93	78.68±7.48
At 60 Min	76.6±9.19	76.4±8.15	124.94±16.02	113.4±12.47	77.66±9.12	70.74±9.34	93.46±10.73	84.8±9.82
At 120 Min	77.71±8.49	76.14±6.23	121.91±9.38	117.94±10.17	72.6±8.31	71.11±8.68	89.09±8.06	86.66±8.30
P value	p<0.01	p<0.05	p<0.01	p<0.01	p<0.01	p<0.01	p<0.01	p<0.01

Significant hypotension was observed in 19/35 patients (54.29%) of ondansetron group which was comparable to 24/35 patients (68.57%) of normal saline group. There was no significant difference observed between two groups.

At induction the axillary temperature was significantly higher (37.22±0.25 with p 0.0008) in

ondansetron group compared to NS group (37.42 ± 0.21). After 10 min up to 120 min the axillary temperature was observed to be constant. In case of tympanic temperature, at 60 min the tympanic temperature was significantly greater 37 ± 0.37 with p 0.0044 in ondansetron group as compared to normal saline group. Before and after this time period it was found to be comparable in both the groups (Figure 2).

Figure 2: Comparison of axillary and tympanic temperature between the two groups

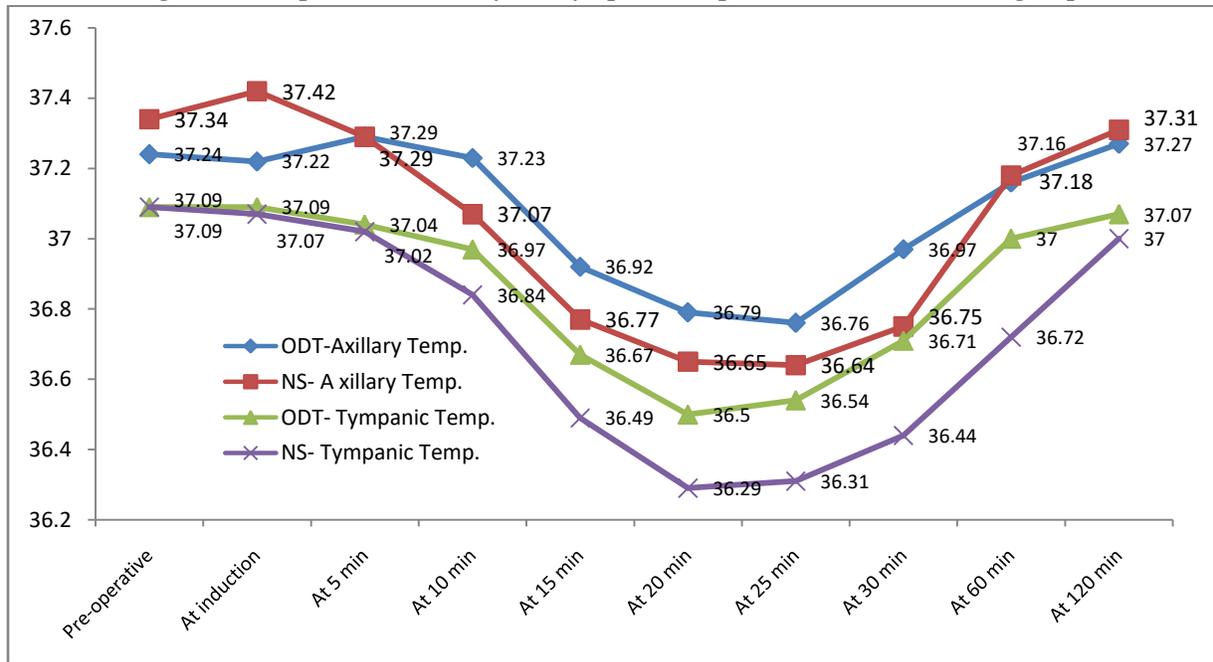
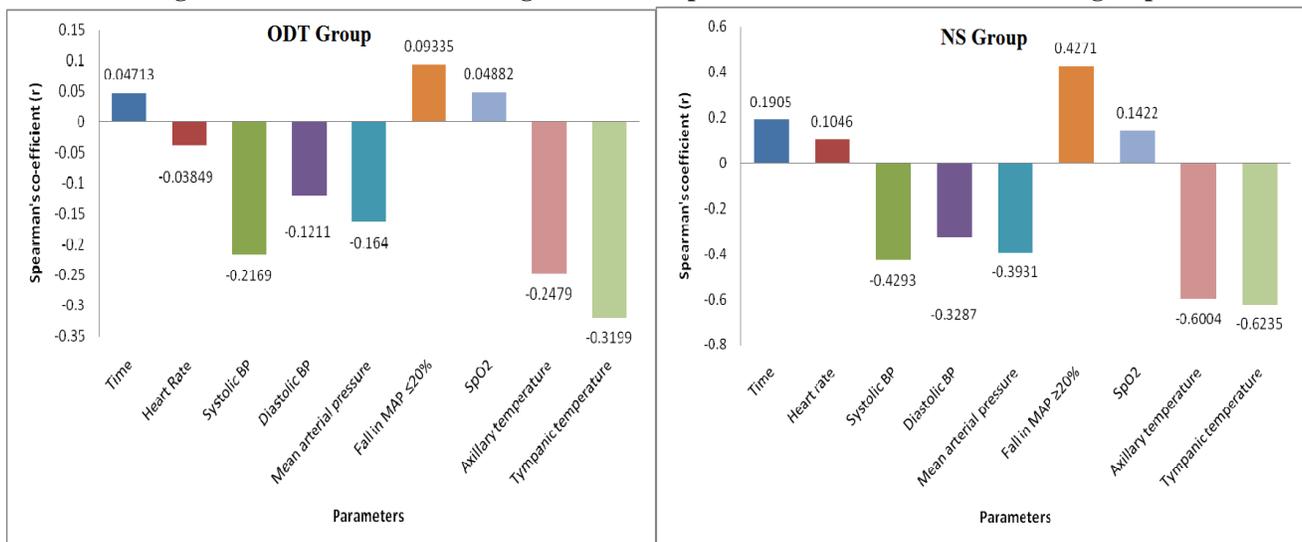


Figure 3 show the correlation of shivering with various parameters in ondansetron and NS group. In the ondansetron group, there was no correlation between time, heart rate, fall in MAP \geq 20% and SpO₂with shivering. However, for SBP, DBP and MAP there was mild and

negative correlation with shivering. Moreover, for axillary and tympanic temperature there was significant moderate negative correlation observed for axillary and tympanic temperatures respectively.

Figure 3: Correlation of shivering with various parameters in ondansetron and NS group



4. Discussion

Shivering, the “big little problem” during anesthesia has an incidence of 30%–40% following regional anesthesia. The etiology of shivering is not clearly understood. The mechanisms chiefly responsible for shivering in patients undergoing surgery are intraoperative temperature loss, increased sympathetic tone, pain, and

systemic release of pyrogens. The best way to avoid the intraoperative and postoperative shivering induced complications is to prevent shivering. Perioperative hypothermia and shivering are usually prevented by physical methods such as surface warming and pharmacologically by drugs such as pethidine, tramadol, ondansetron, clonidine, and ketamine [8].

Ondansetron is a specific 5-HT₃ antagonist that is usually recommended for prevention and treatment of nausea and vomiting during or after surgery. Previous studies have demonstrated that a biological amine found in the brain and spinal cord, serotonin (5-HT), plays a role in neurotransmission, and several studies have confirmed that the serotonergic system plays an important role in the control of PAS [9-11]. Ondansetron could therefore affect perioperative thermoregulation and prevent PAS. The detailed mechanism by which 5-HT₃ antagonists act in the regulation of body temperature and the prevention of PAS has not been clarified but it might be related to encouraging the inhibiting effect of serotonin reuptake on the preoptic anterior hypothalamus region [12,13].

The results of present study show that ondansetron can significantly reduce the risk of PAS compared with normal saline and it was significantly associated with a lower risk of hypotension. The basic demographics like age and proportion of ASA grade I and II were similar and having no significant difference in both groups. The incidence of shivering was significantly higher in normal saline group as compared to ondansetron group, this result was correlated with previous studies [1,3,4,14,15]. Shivering score had remarkable variation in both the groups. The incidence of maximum shivering score was high in group NS compared to group ODT. Our results were compared with the study of Safavi *et al* [1] and Chagaleti *et al* [3].

The heart rate was observed to be constant in both the groups for preoperative period, at induction and up to 20 minutes after induction. However, at 25 and 30 minutes the heart rate was significantly greater in patients receiving normal saline. After which the heart rate was stable at 60 minutes and at 120 minutes in both the groups. SBP and DBP were found to be constant for pre-operative period, at induction at 5, 10, 15, 20, 25 and 120 minutes but MAP was constant for preoperative, at induction and up to 25 minutes after induction. On the other hand, at 30 and 60 minutes the SBP, DBP and MAP was significantly greater in ondansetron group as compared to normal saline group. However, at 120 minutes MAP was normal and no significant difference was observed in both the groups. Mean SpO₂ was similar in both the groups throughout the study. After reaching 100% at 10 min it was observed to be constant till 120 min. In our study, HR, SBP, DBP, MAP, SpO₂ and ASA score showed that ondansetron had better anti-shivering effect compared to NS. These results was correlated with previous studies [1,4,14]. Significant hypotension was comparable between two groups and found no significant difference in the proportion of patients.

According to Safavi *et al* [1] nine patients were from control group (22.5%), three patients from group

ondansetron (7.5%) reported to have hypotension. According to a study by Shakya *et al* [15] hypotension was seen in 9 cases (22.5%) in ondansetron group and 8 cases (20%) in NS group

The axillary and tympanic temperature was maintained by ondansetron. At induction the axillary temperature was significantly higher in ondansetron group compared to NS group. After 10 min up to 120 min the axillary temperature was observed to be constant whereas tympanic temperature was comparable in both the groups till 30 min and at 120 min. At 60 min the tympanic temperature was significantly greater in ondansetron group as compared to normal saline group. The tympanic temperature varied in the individual groups throughout the time period. Our study agreement with the previous studies [1,4,15]. 20 minutes onwards, spinal block achieved was the same in both the groups. At 120 minutes, spinal block level in ondansetron group was L1 and in normal saline group it was T12.

There was no correlation in the age of the patient and ASA grade with incidence of shivering. In ondansetron group, there was no correlation between time, heart rate, fall in MAP $\geq 20\%$ and SpO₂ and shivering. However, for SBP, DBP and MAP there was mild and negative correlation with shivering. Moreover, for axillary and tympanic temperature a significant moderate negative correlation with shivering was observed. In the NS group, there was no correlation between heart rate shivering. However, for time, mild negative correlation was observed between time of anaesthesia and shivering. There was moderate negative correlation between SBP, DBP, MAP, axillary and tympanic temperatures with shivering. Moreover, for fall in MAP $\geq 20\%$ a significant moderate positive correlation was observed and for SpO₂ there was mild negative correlation with shivering.

Few of the limitations of study were that no positive control group such as tramadol, ketamine, meperidine, midazolam was used for comparison of ondansetron. This was because data is already available on the efficacy of these drugs. Moreover, the variables such as type of surgery and duration of surgery were not taken into account. This would have added an advantage to the study and the results could be interpreted in more confirmative way. Moreover, only 1 dose of ondansetron was used for the study. The dose variability can be used as a future prospect which may efficiently improve the study results.

5. Conclusion

The findings of present study suggested that prophylactic administration of injection ondansetron (0.15mg/kg) I.V. before spinal anaesthesia produces anti-shivering effect in patients undergoing spinal anaesthesia

for gynaecological surgeries. So, Ondansetron can be considered as a safe option to prevent post spinal anaesthesia shivering.

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