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ONDANSETRON VERSUS LOW DOSE KETAMINE IN SUBARACHNOID BLOCK INDUCED HYPOTENSION AND SHIVERING – WHICH IS BETTER?

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ABSTRACT

Back ground: subarachnoid block (SAB) is a safe anesthestic technique commonly practiced in world wide. However it is associated with hypotension (33%), bradycardia (13%) and shivering whish are due to hypovolemia, sympathetic blockde and Bezold- zarisch reflexthrough intracardiac serotonin (5HT3) receptors and vagus nerve.

Objective: The aim of the study was to evaluate the efficacy of Ondansetron versus low dose Ketamine in prevention of hypotension and shivering during subarachnoid block.

Methods: 120 patients scheduled for elective surgeries were randomly allocated in to two groups. 5 min before induction of subrachnoid block group O (n=60) received 4 mg of Ondansetron and group K (n-60) received 0.25 mg/kg Ketamine intravenously. HR, MAP,shivering , bromage scale and sedation were assessed every 5 min after SAB.

Results: decreases in HR significantly lower in group K than in group O after SAB, 2, 8, 15, 25 and 40 min (P – 0.001). Decrease in MAP was significantly lower in group K than in group O.

Conclusion: Administration of intravenous ondansetron and ketamine prior to SAB prevents the drop in heart rate,MAP, and also prevents intraoperative shivering effectively.

INTRODUCTION

Spinal Anaesthesia is one of the standard methods of providing anaesthesia for various surgeries. Despite its popularity and ease of use, this procedure is associated frequently with haemodynamic instability and shivering. The incidence of hypotension and bradycardia in non-obstetric patients has been reported to be 33% and 13%, respectively[1].

Reduction in vascular resistance by sympathetic nerve blockade is the main reason for hypotension. Relative dominance of the parasympathetic system, activation of Bezold Jarish reflex (BJR) and increased baroreceptor activity may lead to bradycardia and some degree of hypotension. Apart from mechanoreceptors, chemoreceptors sensitive to serotonin (5HT3 receptors) participate in systemic responses to volume changes2. Studies have illustrated that BJR could be decreased by 5-HT3 antagonists3. Vasopressors are highly effective in preventing hypotension but may result in cardiac arrhythmias and myocardial ischemia[4].

Due to the relative safety and beneficial effects on cardiovascular function ketamine is hypothesized to be used as an anaesthetic agent for poor risk patients. ketamine induces increase heart rate and blood presure due to sympathetic activation therefore reduces hypotension and bradycardia following subarachnoid block.

Ondansetron is selective 5-hydroxytryptamine 3 (5-HT3) receptor antagonists, and thus may be beneficial for preventing bradycardia and hypotension[5].

Shivering, the "big little problem" during anesthesia has an incidence of 30%–40% following regional anesthesia6 Shivering not only causes psychological stress to the patient but also physiologically leads to an increase in oxygen consumption by 200%–600% and increased carbon dioxide production, increased chances of myocardial ischemia. It also produces hypoxemia, lactic acidosis, increased intra ocular,cranial pressure, and interferes with ECG, NIBP and SpO2.

Many studies explained that the serotonergic system plays an important role in the pathogenesis of perioperative shivering7. Apart from physical warming and pharmacological agents, ondansetron and low dose ketamine is being used for the prevention of shivering with good results.

Due to ketamine's sympathetic stimulation and vasoconstriction, it can decrease core-to-peripheral redistribution of heat8. It is used as antishivering agent in dose of 0.5-0.75mg kg-1 IV9. Serotonin (5-HT) is a critical thermoregulatory neuro transmitter. Ondansetron a 5HT3 blocker decreases core temperature attenuation that triggers shivering10. This study was conducted to evaluate and compare the relative efficacy and safety of low dose ketamine (0.25 mg kg-1) and ondansetron (4 mg) for prevention of Hypotension and shivering during spinal anaesthesia.

MATERIAL AND METHODS

After the approval of the institute's ethics committee (No: PESIMSR/IHEC/110/2017-18) and obtaining written informed consent 120 adult patients of ASA physical status I&II, aged 18 – 60 years,undergoing elective lower abdominal surgical procedures (general and gynaecological surgery) under subarachnoid block were included in this prospective randomized study. The study was conducted in Department of Anaesthesiology at PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh from January 2018 to July 2019.Exclusion criteria were the following:

1. Patients with thyroid disorder, cardiopulmonary, liver and kidney diseases
2. History of epilepsy, bronchial asthma
3. Pregnancy
4. History of allergy to the agents to be used
5. Initial core temperature <36.5 or >37.5c
6. Use of vasodilators, patients on selective serotonin reuptake inhibitors and monoamine oxidase inhibitors

7. Patients with severe bradycardia and hypotension and
8. Contraindications to spinal anaesthesia.

Selected patients were investigated and pre anaestetic evaluation conducetd. Patients were then randomly allocated to 2 groups containing 60 patients each according to the study drug; Ondansetron 4mg group (Group O) and Ketamine 0.25 mg kg-1group (Group K).The allocation to each group was done using randomisation through random number generator application method. Group- K received 0.25mg/kg of IV ketamine just five minutes before assuming the correct lateral decubitus position for spinal anaesthesia and 15 min after the first dose while Group- O received 4mg of IV ondansetron .

In the operating room routine standard monitoring was done for all patients. Baseline vitals were recorded,temperature of the operating room was maintained at 21°C to 22°C. Irrigation and i.v. Fluids were administrated at room temperature without inline warming. Ringer lactate solution given at a rate of 500 ml/20 min i.v as a rapid infusion when spinal anaesthesia was induced and then at 7 ml/kg/h i.v. The hemodynamic parameters of the patients were studied at different intervals; once in two minutes for the first ten minutes and once in five minutes for the next twenty minutes. Parameters such as heart rate, mean arterial pressure was recorded and compared. 0.6 mg iv atropine was administered whenever heart rate fell below 50 bpm. Hypotension treated with 6 mg Mephentermine via IV bolus and then with further iv infusion of lactated Ringer's solution as required. The quantity of Mephentermine given in each group recorded. 10 mg i.v metoclopramide was administered for patients who developed nausea and vomiting.

Shivering was graded based on the Bedside Shivering Assessment Scale (BSAS).

Table: 1 Bedside Shivering Assessment Scale (BSAS).

BSAS 0	None	No Shivering
BSAS 1	Mild	Shivering localised to neck/thorax may be seen only as an artefact on ECG or felt by palpation
BSAS 2	Moderate	Intermittent involvement of the upper extremities +/-thorax
BSAS 3	Severe	Generalised shivering or sustained upper/lower extremity shivering

Statistical analysis

Statistical analysis done through STATA 14. Numerical data like Mean arterial pressure and Heart rate compared and analysed using Unpaired t-tests between the groups. Shivering was compared using contingency tests. This graded data were analysed using the chi-square test. P values <0.05 was considered to be significant. The data collected were presented as Mean & SD with 95% confidence intervals for quantitative observations and proportions (%) for qualitative observations.

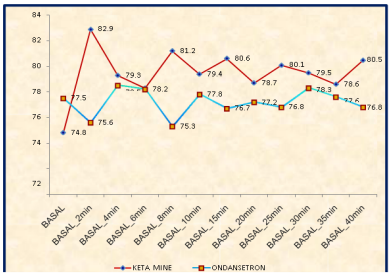
RESULTS

The study was conducted on 120 patients who were posted for elective surgical procedures. The demographic characteristics such as Age, Gender, Weight and ASA physical classification I, II were comparable in both groups (p > 0.05). There was no statistical significance in both the groups.

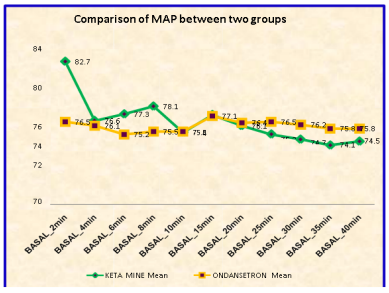
Decrease in heart rate were significantly lower in group K than in group O after 2 min (0.001), 8 min (0.001), 15 min (0.0031), 25 min (0.0115) and 40 min (0.0037) of subarachnoid block. (Graph: 1)

Decreases in Mean arterial pressure were significantly lower in group K than group O. patients in group K had significantly less requirement of vasopressor. There were no statistically significant differences between the two groups after 2 min of SAB. MAP was increased at 2 min time interval in Ketamine group comparative with Ondansetron group with a p-value <0.05 showing a high statistical significance. (Graph: 2)

Shivering was not observed in any patient in both the groups within 20 min time interval. While 70 % (42) of patients in group K had shivering with grade 1 (p < 0.001) compared to 36.7 % (22) of patients in group O (Table: 2).



Graph: 1 Comparison of HR between studied groups



Graph: 2 comparision of MAP between two groups

Table: 2COMPARISONOF SHIVERING SCALE

SHIVERING SCALE		GROUP				P-value
		KETA MINE		ONDANSETRON		
	F	%	F	%		
BASAL	0	60	100	60	100	-
BASAL - 5min	0	60	100	60	100	-
BASAL - 10min	0	60	100	60	100	-
BASAL - 15min	0	60	100	60	100	-
BASAL - 20min	0	60	100	60	100	-
BASAL - 25min	0	18	30	38	63.3	*<0.001
	1	42	70	22	36.7	
BASAL - 30min	0	30	50	28	46.7	0.715
	1	30	50	32	53.3	
BASAL - 35min	0	38	63.3	44	73.3	0.239
	1	22	36.7	16	26.7	
BASAL - 40min	0	30	50	42	70	0.025
	1	30	50	18	30	

* Significant difference

DISCUSSION

Systemic hypotension is the most common complication of spinal anaesthesia with an incidence of 20% in the elderly11.Symptoms of Hypotension include nausea, vomiting, dizziness, and decreased consciousness12. Spinal-induced bradycardia is multifactorial but is in part due to the Bezold–Jarisch reflex, which is mediated by serotonin receptors within the wall of the ventricle in response to systemic hypotension13. It is thought that the stimulation of these peripheral 5-hydroxytryptamine subtype 3 (5-HT3) receptors results in increased parasympathetic activity and decreased sympathetic activity, resulting in bradycardia, vasodilatation, and hypotension[14].

Ketamine is NMDA receptor antagonist is known to produce

Dissociative anaesthesia. It increases the blood pressure by central stimulation of sympathetic nervous system and inhibition of norepinephrine reuptake. Ondansetron, a widely used antiemetic and serotonin antagonist, has been safely used to blunt the Bezold–Jarisch reflex, resulting in less bradycardia and hypotension in humans undergoing spinal anesthesia[15].

In our study we investigated the comparative efficacy and safety of prophylactic low dose of ketamine and ondansetron (with different mechanism of action) for prevention of Hypotension and shivering during spinal anaesthesia. There was no difference among the 2 groups in relation to hemodynamic parameters. These results were consistent with previous studies by Sagir et al16 and Kelsaka et al17. In line with our results, Sahoo et al18 concluded that i.v.ondansetron at 4 mg given prophylactically can attenuate the decreases in blood pressure following spinal anesthesia. Owczuk et al19 reported that 8 mg i.v.ondansetron attenuates the fall of systolic and mean blood pressure but does not have an influence on DBP or HR. In addition, the study by Ortiz-Gómez et al20 showed that prophylactic ondansetron at 2, 4, or 8 mg i.v. had little effect on the incidence of hypotension in healthy parturients undergoing spinal anesthesia with bupivacaine and fentanyl for elective cesarean delivery. In a study conducted by Rashad21 and Farmawy in 60 parturient females undergoing elective cesarean section, they concluded that patients who received i.v. ondansetron 4 mg before subarachnoid block significantly decreased both the hypotension and the doses of vasopressors consumption (P = 0.005).

In this study, shivering was graded using a scale that was validated by Tsai and Chu8. Our results were differ with the findings of Shakya et al24, who suggested that the prophylactic administration of lowdose ketamine (0.25 mg/kg) and ondansetron (4 mg) produces signifi cant antishivering effect in comparison with placebo in patients undergoing spinal anesthesia and that ketamine (0.25 mg/kg) is significantly more effective than ondansetron (4 mg).

Kelsaka et al. study said that 8mg of i.v Ondansetron effectively prevents the postspinal shivering compared to the control group, which was very similar to our results.
Sagir et al. concluded that prophylactic use of ketamine and granisetron separately and in combination was effective in preventing shivering developed during regional anesthesia that emphasizes the effect of a serotonin 5-HT3 receptor antagonist on the prevention of shivering.

In our study, very low dose of ketamine (0.25mg kg-1) was used to minimize the side effect and we found that it was significantly effective and only grade 1 shivering was observed after 25 min initial dose in 42 patients out of 60 (70%). Dal et al25 showed that ketamine 0.5mg kg-1was effective in prevention of post anaesthetic shivering in patients receiving general anaesthsia. Sagiret al showed that 0.5mg kg-1of ketamine was also effective in prevention of shivering during spinal anaesthesia. The shivering was not observed in any patients receiving ketamine. In our study, 0.25mg kg-1of ketamine was also as effective as 0.5mg kg-1of ketamine.

One limitation of our study was we used fixed dose of ondansetron 4 mg in all patients irrespective of weight of patients. Another limitation was we monitored NIBP; probably invasive blood pressure monitoring would have been more reliable. The use sympathomimetics such as Mephenteramine for treatment of hypotension which has a tendency to increase both blood pressure and HR would have masked the incidence of bradycardia. Hence, this could possibly one of the reasons for not getting significant values in the incidence of bradycardia.

CONCLUSION

Based on the present comparative study between ondansetron and low dose ketamine we concluded that,

- Intravenous ketamine 0.25mg/kg resulted in better prophylaxis against hypotension.
- Single-dose of Ondansetron 4mg intravenous bolus resulted in better prophylaxis against shivering.
- No significant side effects observed for both groups during the study.

Acknowledgements

Conflicts of interest none declared.

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