

Comparison of effect of prophylactic administration of ondansetron and placebo on prevention of post induction hypotension in elderly patients undergoing surgery in general anesthesia

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ABSTRACT

Background: Post-induction hypotension is a frequently encountered complication seen particularly in elderly population. Hypotension, by impairing vital organ perfusion, increases the morbidity and mortality of the patients. Studies conducted earlier showed that ondansetron, an antiemetic drug routinely used during general anesthesia for prevention of postoperative nausea and vomiting, blunts the hypotensive effect of spinal anaesthesia. This study was carried out to determine the efficacy of prophylactic use of ondansetron in preventing hypotension after induction of general anaesthesia in elderly patients aging 60 years and plus, hence getting the benefit of preventing both hypotension and postoperative nausea and vomiting by the use of a single drug.

Subjects and method: This randomized controlled clinical trial was carried out in the operation theaters of general surgery, Mayo Hospital, Lahore, from 09-09-2017 to 09-09-2018. A total of 80 patients who were to undergo general anaesthesia for elective general surgical procedures were recruited for this study. After taking informed consent, the patients were randomly divided into two groups. Patients in group A received ondansetron and those in group B received placebo prior to the induction of anaesthesia. Efficacy was labeled in terms of absence of hypotension i.e. a drop in mean arterial pressure of no more than 25% of baseline at 1, 3, 5, 9 and 11 minutes after induction of anaesthesia. The data was recorded on a predesigned proforma. Statistical analysis was done using SPSS version 21.

Results: Both groups were comparable in terms of age, gender, ASA status, BMI and weight. Efficacy was seen in 19 (47.50%) cases managed by ondansetron vs. 10 (25%) in placebo group ($p = 0.03$). There was significant difference of efficacy in patients with age between 60 to 70 years where 63.63% patients in the Group A effectively maintained their blood pressure ($p=0.02$). Patients having age 70 years or above did not show statistically significant difference. History of hypertension made no impact on the efficacy of ondansetron for maintaining blood pressure after induction ($p=0.53$)

Conclusion: Prophylactic use of ondansetron may prevent post-induction hypotension in patients of age group 60 to 70 years undergoing elective surgery under general anesthesia.

Keywords:

Ondansetron, Efficacy, Hypotension.

INTRODUCTION

Over a span of a century, the world of anesthesia has evolved enormously. Starting from a drop of ether to the most advanced and sophisticated anesthesia workstations and drugs, the magnanimous advancement seen in the specialty of anesthesia has made the anesthesia conduction much safer. Despite these advancements, complications during anesthesia are still seen. These peri-operative morbidities are multifactorial multi-factorial and patient factors and co-

morbidities plays a major role in these occurrences.¹ Some of the patients' factors can be modified and optimized while others like age are constant ones. Elderly patients are more likely to suffer from peri-operative complications due to decline in the physiological homeostasis.² Complications like hypotension, delirium, cognitive dysfunction, major adverse cardiac events are more frequently encountered in the elderly population.^{3,4} Peri-operative hypotension leads to impaired perfusion of the organs. If persistent, it can lead to end organ damage.⁴ According to Association of Anesthetists of Great Britain and Ireland, a fall in the mean arterial blood pressure of more than 30% is seen to be associated with stroke, impaired neurological outcome, myocardium infarction or acute kidney injury.⁵

Conflict of Interest: The authors declared no conflict of interest exists.

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Once evident, various options are available for the control of peri-operative hypotension. Infusing intravenous fluid or administering vasopressor drugs like ephedrine or epinephrine are commonly used to counter the hypotension, which comes with their own side effect.⁶ One of the most common time period during the conduct of anesthesia during which hypotension is commonly encountered is the time of induction of anesthesia.⁷

Anesthetic drugs, when administered, lead to fall in the blood pressure, particularly in the elderly population. Sudfeld et al concluded in their study that old age is an independent risk factor for hypotension at the induction of anesthesia.⁸ Considering the deleterious effects of hypotension as mentioned earlier, it is imperative to prevent the fall in the blood pressure at first place.

Ondansetron, 5HT receptor blocker, is commonly used for the prevention and treatment of postoperative nausea and vomiting. Studies conducted by Owczuk et al. and Sahoo et al. showed that it also blunts the hypotensive response of spinal anesthesia. Possible mechanism of this effect is the enhancement of cardiac contractility and stability of systemic vascular resistance (SVR) by blocking 5HT receptors in the heart and the blood vessels.^{9,10}

However, little is known about the role of ondansetron for prevention of post induction hypotension in patients receiving general anesthesia. We conducted this study to observe and find the role of this drug in preventing post-induction hypotension addressing the elderly population so that the low blood pressure at anesthesia induction and its harmful effects could be effectively avoided.

SUBJECTS AND METHODS

After taking approval from the ethical committee of KEMU/Mayo hospital, Lahore, 80 patients were recruited for this randomized controlled trial. The study was carried out in the East and West operation theaters of general surgery, Mayo Hospital, Lahore, from 09-09-17 to 09-09-18. The patients included in this study belonged to ASA class 1 and 2, were above 60 years of age, of either gender, undergoing elective general surgical procedures under general anaesthesia e.g. cholecystectomy, laparotomy, hernia repair, and hysterectomy. Patients who were already on vasoactive drugs, having cardiovascular disease, respiratory diseases, diabetes mellitus or having difficult airway were excluded from the study. After taking informed consent from the patients, their demographic data

including age, gender and procedure to be performed was recorded on a specified proforma. The patients were divided into two groups A and B, using random allocation software. Patients in group A received intravenous Ondansetron 4mg in 10ml of normal saline while those in group B received equal volume of normal saline as placebo 20 minutes before induction of anaesthesia. Ondansetron and placebo were prepared in identical syringes, each labeled with a unique code according to the allocation list. The person administering anaesthesia, handling syringes and the person collecting data were not aware of the allocation list. Standard monitors including NIBP, ECG, pulse oximeter and capnogram were applied and base line readings were recorded. Anaesthesia was induced using 1.5mg per kg of propofol. Atracurium 0.5mg per kg was used for muscle relaxation. Analgesia was provided by using nalbuphine 0.1mg per kg at the time of induction. Patients were ventilated with face mask for 3 minutes and then intubated. Anaesthesia was maintained with isoflurane 1% in a 50/50 mixture of oxygen and nitrous oxide. Mean blood pressure was measured using noninvasive blood pressure cuff with Data Scope cardiac monitors at 1, 3, 5, 7, 9 and 11 minutes to note any anaesthesia induced hypotension (more than 25% drop in the baseline mean arterial pressure within 10 minutes of induction of general anaesthesia). Patients experiencing hypotension after induction of anesthesia were given injection ephedrine to maintain their blood pressure.

Data was analyzed using software SPSS version 21. Both groups were compared by applying chi square test for efficacy with p value of equal to or less than 0.05 was considered as statistically significant.

RESULTS

Patients in both groups were comparable in terms of age, gender, height, BMI, history of hypertension and ASA functional classification (Table 1). Statistically significant number of patients maintained their blood pressure post induction in group A as compared to group B (47.5% vs. 25%) with p value of 0.03. Blood pressure was effectively maintained in patients belonging to age group 60 to 70 years in group A while no difference was seen in the efficacy of maintaining blood pressure between two groups with patient's age beyond 70 years (Table 2). Presence or absence of hypertension makes no impact on the efficacy of ondansetron for maintaining blood pressure after induction (Table 3).

Table 1: Comparison of baseline data between group A and Group B.

Parameter	Group A N=40	Group B N=40	p-value
Age in years (mean ±SD)	68.25±5.07	67.58±4.69	0.54
Height in meter (mean ±SD)	1.81±0.35	1.79±0.31	0.78
Weight in kg (mean ±SD)	72.46±11.47	75.13±10.89	0.28
BMI (Kg/m ²) (mean ±SD)	29.67±4.31	28.41±4.13	0.18
Patients with H/O hypertension (%age)	8 (20%)	10 (25%)	0.59
Gender			
Male	21 (52.5%)	22 (55%)	0.82
Female	19 (47.5%)	18 (45%)	
ASA CLASS distribution of patients			
ASA I	10 (25%)	12 (30%)	0.61
ASA II	30 (75%)	28 (70%)	

Table 2: Efficacy in terms of maintaining blood pressure at the induction of anaesthesia

Parameter	Group a N=40	Group b N=40	p-value
Maintained BP at induction of anaesthesia	19 (47.5%)	10 (25%)	0.03
Maintained BP at induction of anaesthesia			
60-70 yrs. age	7/11(63.63%)	5/22 (22.72%)	0.02
71 yrs. age & onwards	12/29 (41.37%)	4/18 (22.22%)	0.18

Table 3: Efficacy in terms of maintaining blood pressure at the induction of anaesthesia in hypertensive patients

Parameter	Hypertensive patients n=18	Normotensive patients n=62	p-value
Efficacy of ondansetron in maintaining blood pressure in hypertensive patients	38.8% 7 patients	50% 31 patients	0.53

DISCUSSION

Hypotension is a common yet a very significant occurrence seen after the induction of general anaesthesia. Its significant is more marked in elderly population in which end organs are very susceptible to even slight ischemia due to underlying atherosclerosis.¹¹

Loading the elderly patients with volume to prevent hypotension or giving vasopressors to treat hypotension may increase the cardiovascular risks in these patients. Adequate preventive measures, therefore, become a very important step. Turner et al concluded in their study that preloading with crystalloid solution does not prevent fall in the blood pressure after induction of anaesthesia with propofol and fentanyl.¹² In another study carried out by Chiu et al, metaraminol was used to attenuate the hypotension caused by the induction of anaesthesia using propofol. They concluded that prophylactic use of metaraminol does not effectively prevent the post induction hypotension.¹³ In the present study the efficacy in the form of prevention of hypotension after induction of anaesthesia was seen in 19 (47.50%) cases managed by prophylactic Ondansetron as compared to 10 (25%) with placebo having significant difference with p value of 0.03.

The results of our study were comparable to the one conducted by Golparvar M et al in which patients in ondansetron group effectively maintained blood

pressure after induction of anaesthesia as compared to those who received placebo. However, in their study 16% of the patients in ondansetron group developed post induction hypotension while 52.5% in our study developed post induction hypotension.¹⁴

Efficacy of ondansetron for maintenance of blood pressure during spinal anaesthesia has been seen in various studies. Owczuk R et al concluded in their study that ondansetron is effective in maintaining diastolic and mean blood pressure in elderly population during spinal anaesthesia (p < 0.05). They recruited 53 patients older than 70 years of age for their study. Also, the dose given was 8mg as compared to 4 mg used in our study.¹⁵ In our study, the efficacy of ondansetron for maintaining blood pressure was seen in age group 60 to 70 years only whereas no significant difference was seen in age group beyond 70 years which is in contrast to the results of the study carried out by Owczuk R et al.

In another randomized-placebo controlled trial carried out in Pakistan by Shah et al found that ondansetron given before spinal anaesthesia in elderly population, aged 50 to 80 years, effectively prevents hypotension and bradycardia (p=0.02). Here again ondansetron was given in a dose of 8mg to the patients in the study group.¹⁶

Similar efficacy was seen when ondansetron was used for the prevention of spinal induced hypotension

in patients undergoing caesarean section in Indian population. 4mg of the drug was given 5 minutes before the spinal anesthesia. Significantly less number of patients in the study group needed vasopressor as compared to the patients in control group with p value of 0.009.¹⁷

Marashi et al compared two different doses of ondansetron for attenuation of hypotensive response, 6mg and 12mg, but found no statistically significant difference between the two groups (p=0.06).¹⁸

Here it must be kept in mind that mechanism of hypotension in general anesthesia is different from that of spinal anesthesia. Hypotension brought by spinal anesthesia is due to the blockade of sympathetic outflow and Bezold-Jarisch reflex (BJR). BJR is mediated by mechanoreceptors present in the left ventricle of heart. These receptors are activated by 5HT in response to low left ventricular volume and leads to bradycardia and further drop in the blood pressure. Hence, by blocking BJR, 5HT antagonists like ondansetron steadies the cardiovascular system, thus maintaining blood pressure during SA.¹⁹ On the contrary, the hypotension brought about by general anesthesia have different mechanisms including vasodilation and direct myocardial depressant effects of the intravenous or volatile anesthetic agents.⁷ Vascular endothelial 5HT receptors mediate both vasodilation and vasoconstriction depending upon their distribution and subtypes.²⁰ Therefore, the exact mechanism by which ondansetron prevents hypotension during general anesthesia is not well understood and more studies are needed to discover the mechanism of this effect.

In our study we used ondansetron in a dose of 4mg as compared to 8mg used in various other studies for prevention of hypotension. 4mg is the recommended dose of ondansetron used for the prophylaxis of post-operative nausea and vomiting²¹. In our set up we follow the same recommendation for PONV prophylaxis. However, various studies have been done comparing the 4mg dose with the 8mg dose for better prevention of PONV with varying results^{22,23}. Further studies need to be done to see if 8mg dose could prove to be more beneficial for the prevention of post-induction hypotension as compared to the dose used in our study i.e. 4mg.

However, there are many strengthening points as well; as this study highlighted a very important age group which is more fragile and prone to post-induction hypotension. Also, in our study, we checked the effect of ondansetron for prevention of post-

induction hypotension in hypertensive population as well.

CONCLUSION

Prophylactic use of ondansetron may prevent post-induction hypotension in patients of age group 60 to 70 years undergoing elective surgery under general anesthesia.

REFERENCES

1. Steadman J, Catalani B, Sharp C, Cooper L. Life-threatening perioperative anesthetic complications: major issues surrounding perioperative morbidity and mortality. *Trauma Surg Acute Care Open*. 2017;2:e000113.
2. Strøm C, Rasmussen LS, Steinmetz J. Practical Management of Anaesthesia in the Elderly. *Drugs Aging*. 2016;33:765-77.
3. Strøm C, Rasmussen LS, Sieber FE. Should general anaesthesia be avoided in the elderly? *Anaesthesia*. 2014;69 Suppl 1:35-44.
4. Wickham A, Highton D, Martin D, Pan London Perioperative Audit and Research Network (PLAN). Care of elderly patients: a prospective audit of the prevalence of hypotension and the use of BIS intraoperatively in 25 hospitals in London. *Perioper Med (Lond)*. 2016;5:12.
5. Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. *Anesthesiology*. 2013;119:507-15.
6. Lonjaret L, Lairez O, Minville V, Geeraerts T. Optimal perioperative management of arterial blood pressure. *Integr Blood Press Control*. 2014;7:49-59.
7. Reich DL, Hossain S, Krol M, Baez B, Patel P, Bernstein A, et al. Predictors of hypotension after induction of general anesthesia. *Anesth Analg*. 2005;101:622-28.
8. Südfeld S, Brechnitz S, Wagner JY, Reese PC, Pinnschmidt HO, Reuter DA, et al. Post-induction hypotension and early intraoperative hypotension associated with general anaesthesia. *Br J Anaesth*. 2017;119:57-64.
9. Owczuk R, Wenski W, Polak-Krzeminska A, Twardowski P, Arszułowicz R, Dyleczyk-Sommer A, et al. Ondansetron given intravenously attenuates arterial blood pressure drop due to spinal anesthesia: a double-blind, placebo-controlled study. *Reg Anesth Pain Med*. 2008;33:332-9.
10. Sahoo T, SenDasgupta C, Goswami A, Hazra A. Reduction in spinal-induced hypotension with ondansetron in parturients undergoing caesarean section: a double-blind randomised, placebo-controlled study. *Int J Obstet Anesth*. 2012 ;21:24-8.
11. Iqbal A, Ahmed A, Rudra A, Wankhede RG, Sengupta S, Das T, et al. Prophylactic granisetron vs. pethidine for the prevention of postoperative shivering: A randomized control trial. *Indian J Anaesth*. 2009;53:330-4.
12. Turner RJ, Gatt SP, Kam PC, Ramzan I, Daley M. Administration of a crystalloid fluid preload does not prevent the decrease in arterial blood pressure after induction of anaesthesia with propofol and fentanyl. *Br J Anaesth*. 1998;80:737-41.
13. Chiu CL, Tew GP, Wang CY. The effect of prophylactic metaraminol on systemic hypotension caused by induction of anaesthesia with propofol in patients over 55 years old. *Anaesthesia*. 2001;56:893-7.
14. Golparvar M, Saghaei M, Saadati M. Effect of ondansetron on prevention of post-induction hypotension in elderly patients

- undergoing general anesthesia: A randomized, double-blind placebo-controlled clinical trial. *Saudi J Anaesth.* 2015; 9: 365–69.
15. Owczuk R, Wenski W, Twardowski P, Dylczyk-Sommer A, Sawicka W, Wujtewicz MA, et al. Ondansetron attenuates the decrease in blood pressure due to spinal anesthesia in the elderly: a double blind, placebo-controlled study. *Minerva Anesthesiol.* 2015;81:598-607.
 16. Shah SA, Naqvi SS, Abbas MA. Efficacy of prophylactic intravenous administration of ondansetron for prevention of spinal anesthesia induced hypotension in elderly patients. *Anaesth Pain Intes Care.* 2016;20:17-20.
 17. Sahoo T, SenDasgupta C, Goswami A, Hazra A. Reduction in spinal-induced hypotension with ondansetron in parturients undergoing caesarean section: a double-blind randomised, placebo-controlled study. *Int J Obstet Anesth.* 2012;21:24-8.
 18. Marashi SM, Soltani-Omid S, Soltani Mohammadi S, Aghajani Y, Movafegh A. Comparing Two Different Doses of Intravenous Ondansetron With Placebo on Attenuation of Spinal-induced Hypotension and Shivering. *Anesth Pain Med.* 2014;4:e12055.
 19. Raghu K, Kumar S, Rajaram G, Nikhil N, Damodar P Effect of ondansetron in the prevention of spinal anesthesia-induced hypotension. *J Sci Soc.*2018;45:125-28.
 20. Gamoh S, Hisa H, Yamamoto R. 5-hydroxytryptamine receptors as targets for drug therapies of vascular-related diseases. *Biol Pharm Bull.* 2013;36:1410-5.
 21. Hanumanthaiah D, Sudhir V. Comment: Ondansetron: Timing and dosage. *Indian J Anaesth.* 2013;57:429-30.
 22. Paventi S, Santevecchi A, Ranieri R. Efficacy of a single-dose ondansetron for preventing post-operative nausea and vomiting after laparoscopic cholecystectomy with sevoflurane and remifentanyl infusion anaesthesia. *Eur Rev Med Pharmacol Sci.* 2001;5:59-63.
 23. Kovac AL, O'Connor TA, Pearman MH, Kekoler LJ, Edmondson D, Baughman VL, et al. Efficacy of repeat intravenous dosing of ondansetron in controlling postoperative nausea and vomiting: a randomized, double-blind, placebo-controlled multicenter trial. *J Clin Anesth.* 1999;11:453-9.