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SPINAL ANAESTHESIA;

COMPARISON BETWEEN PROPHYLACTIC LOW DOSE KETAMINE AND ONDANSETRON FOR PREVENTION OF SHIVERING DURING SPINAL ANAESTHESIA IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES

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ABSTRACT… Perioperative shivering is a common problem during spinal anaesthesia. It causes tremendous deleterious effects on metabolism of body. Despite of re-warming and raising the ambient temperature, several drugs are under research to evaluate their preventive role in shivering during anaesthesia like tramadol, butorphanol, midazolam, ketamine and ondansetron. The present study was conducted to evaluate the effect of prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. **Objective:** To compare prophylactic low dose ketamine with ondansetron for prevention of shivering during spinal anaesthesia in patients undergoing lower abdominal surgeries. **Study Design:** Randomized controlled trial. **Setting:** Department of Anaesthesia, Nishtar Hospital Multan. **Period:** November 2012 to May 2013. **Material and methods**: A total of 256 patients were included in the study divided into two equal groups. **Results:** In this study basic demographics like age, gender, mean weight and height and type of surgery patients underwent were similar, having no significant difference in both groups, while on comparison in both groups, the frequency of shivering revealed 4.69%(n=6) in K Group and 11.72%(n=15) in O Group while remaining 95.31%(n=122) in K and 88.28%(n=113) in O Group had no findings of the morbidity, p value was calculated as 0.03, which showed significant difference. **Conclusion:** The result of the study concluded that prophylactic intravenous administration of low dose ketamine (0.25mg/kg) is significantly more effective than ondansteron (4 mg) for prevention of shivering during spinal anesthesia in patients undergoing lower abdominal surgeries.

Key words: Spinal anaesthesia,Shivering, thermoregulation, Ketamine, Ondansetron.

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INTRODUCTION

Perioperative shivering is a common problem during spinal anaesthesia and its incidence is almost 33 %[1]. Spinal anaesthesia causes vasodilatation due to sympathetic blockade and leads to redistribution of heat. It also alters the thermoregulatory system in the hypothalamus and causes hypothermia. Shivering leads to increased metabolic activity and increased O_2 consumption up to 200-500%. It causes arterial hypoxia and has been shown to correlate with increased risk of myocardial ischemia. It increases intraocular and intracranial pressure. The other effects are increase in cardiac output, peripheral vascular resistance, CO_2 production, prolonged coagulation, stress response and lactic acidosis[2]. It also interferes with ECG monitoring and pulse oximetry due to motion artifacts.

Perioperative hypothermia and shivering is usually prevented by physical methods like surface warming[3] and pharmacologically by drugs like pethidine[4], tramadol[5], corticosteroids, clonidine[6], doxapram, dexmedetomidine[7], butorphanol and midazolam.

Recently Ketamine and Ondansetron have been tried to prevent shivering during anaesthesia with good results. Ketamine is a competitive N-Methyl-D-Aspartate (NMDA) receptor antagonist and has a role in thermoregulation at various levels. NMDA receptors modulate noradrenergic and serotoninergic neurons in locus coeruleus. It has been used as anti-shivering agent in dose of 0.5-0.75 mg/kg IV but even these doses cause adverse effects like drowsiness, hallucinations and delirium.[8] Ketamine when used in epidural

anaesthesia for transurethral resection of prostate also has anti-shivering effect.[9]

Ondansetron is 5-HT3 receptor antagonist which is widely used as an anti-emetic. According to thermo-regulator effect of intra-hypothalamic serotonin (5-HT), 5-HT antagonist like ondansetron also has effect on thermoregulation. It has been successfully used for prevention of shivering in a dose of 8mg IV without any side effects.[10]

In a study conducted in India in 2010 by B Shakya, A Chaturvedi and BP Sah, the effect of low dose ketamine, ondansetron and saline on patients undergoing surgery under spinal anaesthesia, for control of perioperative shivering concluded that shivering was 2.5% in ketamine group, 10% in ondansetron group and 42.5% in placebo group showing superiority of low dose ketamine with $p<0.05$ for control of perioperative shivering.[11] Ketamine prevents shivering by nonshivering thermogenesis at the level of hypothalamus or the beta adrenergic action of norepinephrine.

Ketamine being easily available, economical and Ondansetron used as routine antiemetic compelled us for this study to compare the efficacy and safety of two drugs for control of perioperative shivering to find out the one with better efficacy and cost effectiveness.

MATERIALS AND METHODS

This prospective randomized controlled study was carried out in the Department of Anaesthesia at Nishtar Hospital Multan from November 2012 to May 2013. After approval from ethical committee of the institute and obtaining written informed consent in detail, a total of 256 patients with ASA Grade I, II admitted for elective lower abdominal surgical procedures to be done under spinal anaesthesia were included in the study. Surgical procedures included hernioplasty, vesicolithotomy, vaginal / abdominal hysterectomy and elective caesarean section. Exclusion criteria were patients with cardiopulmonary diseases, obesity, thyroid disease, abnormal psychological profile, on medications likely to alter thermoregulation, allergic to any of the study drug, and patients requiring blood transfusion.

Selected patients were randomly allocated to two equal groups containing 128 patients in each.

Group K received 0.25 mg/kg ketamine IV and group O received 4 mg ondansetron IV.
All patients did not receive any pre-medication. On arrival in operation theatre, all patients had an 18 G venous cannula inserted. All patients were preloaded with 500 ml of 6% Haesteril. 3.0 ml of 0.5% heavy bupivacaine was injected in L3-4 interspace intrathecally with 27 G pencil point needle. Patients in group K was given 0.25 mg / kg ketamine and group O was given 4 mg ondansetron intravenously. Level of motor and sensory blockade was assessed. Grades of shivering were noted intraoperatively and 30 minutes postoperatively and recorded.

RESULTS

A total of 256 cases(128 in each group) were enrolled after fulfilling the inclusion/exclusion criteria to compare prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia in patients undergoing going lower abdominal surgeries.Sex distribution of the patients showed female patients in majority in both groups i.e. 61.72%(n=79) in K Group and 64.84%(n=83) in O Groups while remaining 38.28%(n=49) in K and 35.16%(n=45) in O Group were male. Mean weight of the patients in both groups showed 56.21+3.61 kg in K group and 55.43$\pm$2.87 kg in O Group. Mean height of the patients in both groups was measured and recorded, where 158.32$\pm$5.11 cm in K and 157.79$\pm$6.27 cm were in O Group.

As per age distribution, majority of the patients were between 31-40 years in both the groups i.e. 37.5%(n=48) in K Group and 35.94%(n=46) in O Group, next were between 20-30 years 30.47%(n=39) in K Group and 32.81%(n=42) in O Group while those between 41-50 years of age were 32.03%(n=41) in K Group and 31.25%(n=40) in O Group, mean and SD was calculated as 38.43+3.54 years in K and 37.32$\pm$4.14 years in O Group. (Table-I)

Age (years)	Group-K		Group-O	
	Patients	%age	Patients	%age
20-30	39	30.50	43	32.81
31-40	48	37.47	46	35.94
41-50	41	32.03	40	31.25
Total	128	100.0	128	100.0
Mean ± SD	**38.43 + 3.54**		**37.32 ± 4.14**	

Table-I. Age distribution (n=256)

Types of surgery in both groups was recorded, 17.97%(n=23) in K and 13.28%(n=17) in O Group had hernioplasty, 39.84%(n=51) in K Group and 33.59%(n=43) in O Group had elective caesarean section, 14.06%(n=18) in K Group and 16.41%(n=21) in O Group had cystolithotomy, 18.75%(n=24) in A Group and 21.09%(n=27) had vaginal hysterectomy while 9.38%(n=12) in K Group and 15.63%(n=20) in O Group had abdominal hysterectomy.(Table-II)

Type of surgery	Group-K		Group-O	
	No.	%age	No.	%age
Elective Caesarean Section	51	39.84	43	33.60
Vaginal Hysterectomy	24	18.75	27	21.10
Hernioplasty	23	17.97	17	13.28
Cystolithomy	18	14.06	21	16.40
Abdominal Hysterectomy	12	09.38	20	15.62
Total	**128**	**100**	**128**	**100**

Table-II. Typeof surgery in both groups (n=256)

Comparison of frequency of shivering in both groups revealed as 4.69%(n=6) in K Group and 11.72%(n=15) in O Group while remaining 95.31%(n=122) in K and 88.28%(n=113) in O Group had no findings of such morbidity, p value was calculated as 0.03. (Table-III)

Shivering	Group-K (128)		Group-O (128)	
	No.	%age	Patients	%age
Yes	6	4.69	15	11.72
No	122	95.31	113	88.28
Total	128	100	128	100

Table-III. Comparison of frequency of shivering (n=256)

Stratification for comparison of shivering with regards to age of the patients was done with the results that out of 6 cases in K Group 16.67%(n=1) had age between 20-30 years, 50%(n=3) between 31-40 years and 33.33%(n=2) between 41-50 years while in O Group out of 15 cases of shivering 20%(n=3) between 20-30 years, 60%(n=9) between 31-40 years, and 20%(n=3) between 41-50 years of age, p value in each age group was insignificant. (Table-IV)

Age (years)	Group-K (6)		Group-O (15)		P. value
	No.	%age	No.	%age	
20-30	1	16.7	3	20.0	0.68
31-40	3	50.0	9	60.0	0.52
41-50	2	33.3	3	20.0	0.44
Total	6	100.0	15	100.0	0.03

Table-IV. Comparison of shivering regarding age of the patients

Stratification for comparison of shivering regarding sex of the patients was done with the result that out of 6 cases in K Group 66.67%(n=4) were female and 33.33%(n=2) were male, while in O Group 60%(n=9) female and 40%(n=6) were male, p value was calculated as 0.59 (Table-V)

Sex	Group-K (6)		Group-O (15)		P. value
	No.	%age	No.	%age	
Male	4	66.7	9	60.0	0.68
Female	2	33.3	6	40.0	0.52

Table-V. Comparison of shivering regarding sex of the patients

P-value = 0.03

DISCUSSIONS

Shivering is an involuntary, repetitive activity of skeletal muscles. The mechanisms of shivering in patients undergoing surgery are mainly intraoperative heat loss, increased sympathetic tone, pain, and systemic release of pyrogens[12]. Spinal anesthesia significantly impairs the thermoregulation system by inhibiting tonic vasoconstriction, which plays a significant role in temperature regulation[13]. Spinal anesthesia also causes redistribution of core heat from the trunk (below the block level) to the peripheral tissues. These two effects predispose patients to hypothermia and shivering.[14] The median incidence of shivering related to regional anesthesia observed in a review of 21 studies is

55%[11]. Shivering increases oxygen consumption, lactic acidosis, carbon dioxide production, and metabolic rate by up to 400%.[15,16] Therefore, shivering may cause problems in patients with low cardiac and pulmonary reserves. The best way to avoid these intraoperative and postoperative shivering-induced increases in hemodynamic and metabolic demands is to prevent shivering in the first place.[12] Recently Ketamine and Ondansetron have been tried to prevent shivering during anaesthesia with good results.

Low dose ketamine is economical, easily available and easy to administer while no study in our hospital was conducted before however, we planned this study to compare the efficacy of two drugs for control of perioperative shivering so that drug which is cost effective and has better efficacy will be used in future in our setting.

Basic demographics like age, gender, mean weight and height and type of surgery patients underwent were similar and having no significant difference in both groups, while on comparison of frequency of shivering in both groups revealed, 4.69%(n=6) in K Group and 11.72%(n=15) in O Group while remaining 95.31%(n=122) in K and 88.28%(n=113) in O Group had no findings of the such morbidity, p value was calculated as 0.03, which shows significant difference.

The findings of our study are in agreement with an Indian study by Shakya B and co-workers who studied the effect of low dose ketamine, ondansetron and saline on patients undergoing spinal anaesthesia for control of perioperative shivering and concluded that shivering was 2.5% in ketamine group, 10% in ondansetron group and 42.5% in placebo group showing superiority of low dose ketamine with $p<0.05$ for control of perioperative shivering.[11] Multiple researchers found that ketamine 0.5 mg per kg IV was effective like pethidine 20-25 mg IV. Ketamine prevents shivering by non-shivering thermogenesis at the level of hypothalamus or by the beta adrenergic action of norepinephrine. Nausea and vomiting was low in this group, may be due to low dose of ketamine.

Dal et al studied that ketamine 0.5mg kg $^{-1}$ was effective in prevention of post anaesthetic shivering in patients undergoing general anaesthsia.[17] Sagir et al also found that 0.5mg kg $^{-1}$ of ketamine was effective in prevention of shivering during spinal anaesthesia.[18]

In our study, the effectiveness of ondansetron and ketamine was compared, ketamine was found to be more effective in prevention of shivering, $p< 0.05$. Ketamine has sympathetic stimulation and vaso-constrictive effect which explains the less incidence of hypotension with lesser requirement of vasopressor. Mild sedative effect was observed in ketamine group which was considered as an advantage during surgery under spinal anaesthesia.

In our study, we found the hypothesis “Efficacy of prophylactic intravenous administration of low dose ketamine (0.25mg/kg) is more as compared to ondansetron in prevention of shivering during spinal anaesthesia” is justified and ketamine may be used in patients undergoing lower abdominal surgeries.

CONCLUSION

The result of the study conclude that prophylactic intravenous administration of low dose ketamine (0.25mg/kg) is significantly more effective than ondansteron during spinal anesthesia for prevention of perioperative shivering in patients undergoing lower abdominal surgeries.

REFERENCES

1. Aitkenhead AR, Smith G, Rowbotham DJ. Textbook of Anesthesia. 5th ed. **Metabolism ,the stress response to surgery and perioperative thermoregulation.** Churchill Livingstone Publication Philadelphia; 2007:414.

2. Morgan jr GE, Mikhail MS, Murray MJ. **Clinical Anaesthesiology.** 4th ed. Patient Monitors McGraw-Hill Medical Publishing Division USA;2006;148-50.

3. Kimberger O, Ali SZ, Markstaller M, Zmoos S, Lauber R, Hunkeler C, etal. **Mepridine and skin surface warming additively reduces the shivering threshold.** Crit Care. 2007;11(1):R29.

4. Kamalipour H, Avestimehr S. **A comparative study on the effect of Tramadol and Pethidine on postoperative shivering.** Anesth Pain Intens Care. 2007;11(2):84-8.

5. Javaherforoosh F, Akhondzadeh R, Aein KB, Olapour A, Samimi M. **Effects of Tramadol on shivering post spinal anaesrhesia in elective cesarean section.** Pak J Med Sci. 2009;25(1):12-17.

6. Shukhla U, Malhotra K, Prabhakar T. **A comparative study of the effect of clonidine and tramadol on post spinal anaesthesia shivering.** Indian J Anesth. 2011;55(3):240-6.

7. Usta B, Gozdemir M, Demircioglu RI, Muslu B, Sert H, Yaldiz A. **Dexmedetomidine for prevention of shivering during spinal anaesthesia.** Clinics (Sao Paulo). 2011;66(7):1187-91.

8. Laiq N, Kham MN, Nasir N, Khan S. **Prevention of postoperative shivering by prophylactic ketamine in patients undergoing major surgeries under general anaesthesia.** Ann Pak Inst Med Sci. 2006;2(3):163-6.

9. Han DY, Jeong HJ, Lee C, Choi DH. **The efficacy of epidural ketamine on shivering during transurethral resection of the prostate under epidural anaesthesia.** IntNeurolurol J. 2010 Aug;14(2):105-11.

10. Kelsaka E, Sibel B, Deniz K, Binnur S. **Comparison ofondansetron and meperidine for prevention of shiveringin patients undergoing spinal anesthesia.** RegAnesthPain Med 2006; 31: 40-45.

11. Shakya S, Chaturvedi A, Sah BP. **Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia.** J AnesthesiolClinPharmacol. 2010 Oct-Dec;26(4):465-9.

12. Crowley LJ, Buggy DJ. **Shivering and neuraxial anesthesia.** RegAnesth Pain Med.2008;33:241–52.

13. Glosten B, Sessler DI, Faure EA, Karl L, Thisted RA. **Central temperature changes are poorly perceived during epidural anesthesia.** Anesthesiology. 1992;77:10–6.

14. Ozaki M, Kurz A, Sessler DI, Lenhardt R, Schroeder M, Moayeri A, Noyes KM, Rotheneder E. **Thermoregulatory thresholds during epidural and spinal anesthesia.** Anesthesiology. 1994;8:282–8.

15. Tsai YC, Chu KS. **Acomparisonoftramadol, amitriptyline, and meperidine for postepidural anesthetic shivering in parturients.** AnesthAnalg. 2001;93:1288–92.

16. Macintyre PE, Pavlin EG, Dwersteg JF. **Effect of meperidine on oxygen consumption, carbon dioxide production, and respiratory gas exchange in postanesthesia shivering.** AnesthAnalg. 1987;66:751.

17. Dal D, Kose A, Honca M, Akinci SB, Basgul E, Aypar U. **Efficacy of prophylactic ketamine in preventing postoperative shivering.** Br J Anaesth 2005; 95: 189-92.

18. Sagir O, Gulhas N, Toprak H, Yucel A, Begec Z, Ersoy O. **Control of shivering during regional anaesthesia: prophylactic ketamine and granisetron.** ActaAnaesthesiolScand 2007; 51: 44-49.

PREVIOUS RELATED STUDY

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Shaukat Raza, Hasan Raza, Humayun Munir Tarar. SPINAL ANAESTHESIA; EFFECTS OF ADDING PETHIDINE WITH BUPIVACAINE (Original) Prof Med Jour 13(4) 651-656 Oct, Nov, Dec, 2006.

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