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ORIGINAL RESEARCH REGIONAL ANESTHESIA

Comparison of granisetron 10 µg/kg vs 40 µg/kg intravenous for prophylaxis of shivering after spinal anesthesia for lower abdominal surgery

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ABSTRACT

Background & Objective: Postanesthetic shivering is one of the many complications during recovery that is marked by vasoconstriction and involuntary movements in several muscle groups and psychologically is an incredibly uncomfortable experience for the patient. The 5-HT3 receptor antagonist granisetron can potentially be used to manage postanesthetic shivering through the thermoregulation neurotransmission system. This study aims to compare the effects of administering 10 µg/kg or 40 µg/kg of granisetron intravenously on the grade of shivering post spinal anesthesia in lower abdominal surgeries.

Methodology: This study was a single-blind experimental study conducted on 30 patients who underwent spinal anesthesia for lower abdominal surgeries in Dr. Hasan Sadikin Hospital Bandung. There were no statistical differences of age, weight, height, BMI, core temperature before anesthesia, block height, room temperature, total bleeding, input volume, duration of surgery, and use of ephedrine between the two intervention groups.

Results: Administration of 40 µg/kg intravenous granisetron could maintain the body temperature above 36.56 °C , better than the 10 µg/kg intravenous granisetron with the lowest temperature at 35.31 °C. Regarding the grade of shivering, administration of 40 µg/kg granisetron IV was able to improve postanesthetic shivering up to grade 2 in 3 (20%) patients, while 10 µg/kg intravenous granisetron improved grade of shivering to grade 3 in 5 (33%) patients, these results were statistically significant ($P < 0.05$).

Conclusion: In conclusion, administration of granisetron 40 µg/kg IV reduces the incidence and severity of shivering post spinal anesthesia, and maintains a better core temperature compared to granisetron 10 µg/kg IV.

Keywords: 5-Ht3 Receptor Antagonist; Granisetron; Postanesthetic Shivering; Prophylaxis

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1. INTRODUCTION

Post-anesthesia shivering is one of anesthetic-related recovery complications. The prevalence, previously reported, was 40−70% in patients of both genders, 18–60 y old.[1,2] Shivering can increase oxygen consumption and a risk of hypoxemia, as well as other postoperative complications.[3] Shivering is usually triggered by hypothermia, which might occur even in normothermic patients during perioperative period.[1,3,4] It is characterized by vasoconstriction and involuntary activity or movement of several muscle groups.[1,5,6]

Shivering after spinal anesthesia (SA) is often encountered with an incidence rate of about 20−60%.[5,7]

Post-anesthesia shivering is a very unpleasant experience and psychologically stressful to the patient, causing several undesirable physiological consequences such as increased blood pressure, tachycardia, and increased intraocular and intracranial pressure.[1,5,7,8] Shivering can also increase aerobic metabolism which in turn causes an increase in tissue oxygen demand as much as 150%,[10] increases the synthesis of carbon dioxide and lactic acidosis which causes an increase in pulmonary ventilation capacity and cardiac workload.[14,9,10] It also increases metabolic rate up to 400%, and can cause myocardial ischemia, which is very dangerous for patients with cardiopulmonary disorders,[1,5,11–13] and interferes with the patient monitoring by causing artifacts on electrocardiographic trace, blood pressure and pulse oximetry.[1,7,9,10,14] Furthermore, shivering can exacerbate postoperative pain due to incision stretch, slow down the recovery process, prolong discharge from recovery room, thereby increasing hospital and inpatient costs.[1,2,14,15]

Several pharmacological and non-pharmacological interventions have been proposed to prevent post-anesthesia shivering.[3,10] Non-pharmacological preventive measures include fluid warmers, operating room temperature monitoring, heating blankets and surgical sterile cloths, but these are are less effective in increasing core body temperature.[1,3,13,14,16] Several pharmacological interventions such as clonidine, tramadol, neostigmine, dexmedetomidine, magnesium sulfate, ketamine and opioids have been reported to be effective but with varied success rate and potential side effects, including hemodynamic changes such as hypotension, hypertension, hallucinations, sedation, respiratory depression and nausea and vomiting.[1,4,5,10–12,16]

Recently, a 5-HT3 receptor antagonists has been suggested to prevent postoperative shivering with comparable efficacy with minimal side effects. Granisetron is a potent 5-HT3 receptor antagonist with fewer side effects than other antiemetics. Low dose granisetron significantly reduced the incidence and severity of postoperative shivering compared to normal saline. High dose granisetron significantly reduced the incidence and severity of post-spinal anesthesia shivering in lower abdominal surgery. Granisetron prophylaxis is effective in reducing the incidence and severity of perioperative shivering depending on the dose.[1,10,14,17]

We compared the prophylactic administration of granisetron 10 µg/kg and 40 µg/kg intravenously on the degree of shivering after SA for lower abdominal surgery.

2. METHODOLOGY

This analytic experimental study was conducted from November to March 2021, in Hasan Sadikin General Hospital. Ethical approval was obtained from Health Research Ethics Committee Universitas Padjadjaran Indonesia, with registration number LB.02.01/X.6.5/137/2020. The subjects were patients with ASA PS-I to II, who could undergo regional SA, aged 18−60 y, had normal body mass index between 20−30 kg/m^2, and listed for lower abdominal surgery, such as appendectomy, uterine prolapse repair and inguinal hernia repair etc. The exclusion criteria were; cesarean sections, fever or preoperative hypothermia, body temperature > 38°C or < 36.5°C, the duration of surgery for more than 2 h, and intraoperative blood transfusion. The drop-out criteria for the study were failure of spinal blockade, allergy to the drugs used in the study, and conversion of the SA to general anesthesia.

A total of 30 patients were enrolled in the study. Patients were randomly divided into two groups, through sealed envelope method; Group G-10 patients to receive granisetron 10 µg/kg IV, and Group G-40 to receive granisetron 40 µg/kg IV.

Patient was positioned on the operating table and standard monitors plus a temperature probe were connected to the patient. Supplemental oxygen was administered through a nasal cannula @ 3 L/min. Five minutes before the SA procedure, the patient was given granisetron 10 µg/kg IV or granisetron 40 µg/kg intravenously which were both diluted with aqua pro injection to 5 ml. SA was performed using a Quincke Spinocan® 25G spinal needle without an introducer at a level of L3−L4. After free flow of spinal fluid was established, hyperbaric bupivacaine 0.5% 12.5 mg was injected. A pinprick test was carried out to ensure that the spinal blockade had reached the desired dermatome level, T5−T6. Blood pressure, pulse rate, body temperature, room temperature and degree of shivering were monitored every 5 min from right after SA, till the completion of surgery, and until the patient was discharged from the recovery room. Hypotension (MAP < 65 mmHg or a drop of 20−30% of the baseline MAP), boluses of ephedrine 5 mg IV were given until the blood pressure reached baseline.

Data recording and statistical analysis were performed using Statistical Packaged for Social Science Version 16 (SPSS Inc., Chicago, IL).

3. RESULTS

A total of 30 subjects participated in the study. There was no significant difference in the subjects' demographic characteristics between the Group G-10

Table 1: Comparative demographic data of the two groups

Characteristics	Group G-10 (n = 15)	Group G-40 (n = 15)	p-value
Age (year)	50.27 ± 5.22	52 ± 4.55	0.340 [a]
Height (cm)	154.87 ± 2.26	155.33 ± 3.27	0.653 [a]
Weight (kg)	52.73 ± 2.66	53.8 ± 3.08	0.382 [b]
Body Mass Index (BMI)	21.99 ± 1.07	22.3 ± 1.26	0.468 [a]
ASA			
○ I	13 (86.7)	11 (73.3)	0.326 [c]
○ II	2 (13.3)	4 (26.7)	

Note: Data presented are in Mean ± SD or n (%); P-values were obtained from: a) two-group unpaired t-test (normally distributed data), b) Mann Whitney test (data not normally distributed), c) Fisher's exact test; P < 0.05 is considered to be significant.

Table 2: Comparative study characteristics

Characteristics	Group G-10 (n = 15)	Group G-40 (n = 15)	P-value
Input volume (ml)	853.33 ± 112.55	866.67 ± 134.52	0.894 [b]
Total bleeding (ml)	150 ± 37.8	175.33 ± 36.62	0.088 [b]
Room temperature (ºC)	20.93 ± 0.88	21.2 ± 0.68	0.377 [b]
Systolic BP (mmHg)	119.53 ± 12.15	128.13 ± 11.28	0.054 [a]
Diastolic BP (mmHg)	73.93 ± 9.84	72.07 ± 8.91	0.590 [a]
Block height			
○ T5	2 (13.3)	4 (26.7)	0.326 [c]
○ T6	13 (86.7)	11 (73.3)	
Duration of surgery (min)			
Mean ± SD	70.0 ± 11.3)	71.3 ± 9.2)	0.624 [b]
Min-max (median)	60−90 (70)	60−90 (70)	
Use of ephedrine			
○ 0 (mg)	7 (46.7)	10 (66.7)	0.305 [b]
○ 5 (mg)	2 (13.3)	2 (13.3)	
○ 10 (mg)	6 (40)	3 (20)	

Note: Data presented are in Mean ± SD or n (%); P-values were obtained from: a) two-group unpaired t-test (normally distributed data), b) Mann Whitney test (data not normally distributed), c) Fisher's exact test; P < 0.05 is considered to be significant.

Table 3: Comparison of incidence and degree of shivering

Degree of shivering	Group G-10 (n = 15)	Group G-40 (n = 15)	P-value
Not shivering	10 (67)	12 (80)	0.017*
2nd degree shivering	0 (0)	3 (20)	
3rd degree shivering	5 (33)	0 (0)	
Total	15 (100)	15 (100)	

Note: The data presented n (%); with P-values obtained from the Chi Square test. P < 0.05 is considered to be significant.significant.

Table 4: Comparative core temperatures intwo groups

Recording Time (min)	Group G-10 (n = 15)	Group G-40 (n = 15)	P-value
Before induction	36.38 ± 0.36	36.29 ± 0.39	0.531 [a]
0 min	36.09 ± 0.39	36.46 ± 0.28	0.006* [a]
5 min	36.02 ± 0.36	36.14 ± 0.34	0.543 [b]
10 min	35.93 ± 0.37	36.56 ± 0.28	0.000* [a]
15 min	36.18 ± 0.36	36.60 ± 0.38	0.004* [a]
20 min	36.08 ± 0.37	36.77 ± 0.16	0.000* [b]
25 min	35.73 ± 0.37	36.56 ± 0.28	0.000* [a]
30 min	35.31 ± 0.33	36.67 ± 0.16	0.000* [b]
35 min	36.08 ± 0.36	36.56 ± 0.28	0.000* [a]
40 min	35.90 ± 0.38	35.89 ± 2.61	0.001* [b]
45 min	35.48 ± 0.31	36.64 ± 0.25	0.000* [a]
50 min	35.42 ± 0.35	36.65 ± 0.26	0.000* [a]
55 min	35.48 ± 0.36	36.57 ± 0.27	0.000* [a]
60 min	35.88 ± 0.36	36.70 ± 0.29	0.000* [b]
65 min	35.78 ± 0.36	36.18 ± 0.27	0.002* [a]

Note: The P-values were obtained by: a) t-test of two unpaired groups (normally distributed data), b) Mann Whitney's test (data not normally distributed). The difference is significant if P < 0.05.

and Group G-40 (Table 1). Comparison of the hemodynamic data and the study characteristics are presented in Table2.

In this study, 5 subjects (33%) from granisetron 10 µg/kg group had 3rd degree shivering while only 2 subjects (20%) from granisetron 40 µg/kg had 2nd degree shivering. Granisetron 40 µg/kg group had better incidence and degree of shivering compared to granisetron 10 µg/kg group (P < 0.05; Table 3).

There was not any significant difference of the initial temperature before induction between the two groups. However, the core temperature of Group G-40 tended to be higher than the Group G-10 throughout from min 0 to the min 65 with significant differences (P < 0.05) except at min 5 (P > 0.05) as shown in Table 4.

4. DISCUSSION

Thirty patients were enrolled in this study. The baseline demographic and clinical parameters, including age, weight, height, BMI, core temperature before anesthesia, block height, room temperature, total blood loss, fluid input, duration of surgery, and use of ephedrine, were not significantly different (P > 0.05). This showed that the subjects in this study were relatively homogenous and comparable.

SA is the anesthesia of choice for lower abdominal surgery due to its fast onset and easy to perform, but it might alter blood pressure and cause hypotension and bradycardia. One of the post-SA side effects is shivering. Shivering after SA occurs due to disruption of central and peripheral thermoregulation with increased threshold range, increased sweating threshold and decreased shivering and vasoconstriction thresholds.[7]

This study compared the use of granisetron 40 µg/kg with 10 µg/kg before SA as prophylaxis for shivering. The result of this study showed that administration of granisetron 40 µg/kg can decrease the incidence and degree of shivering more effectively, as compared to granisetron 10 µg/kg. This result is in accordance with several previous studies which stated that granisetron 40 µg/kg is an effective prophylaxis to prevent shivering in SA and was as effective as meperidine 0.4 mg/kg and was slightly more effective than hydrocortisone 2 mg/kg in reducing the incidence and intensity of shivering under SA.[1,10,14,17,18]

This study showed fluctuating core body temperature with significant differences between two of the groups at certain time points. The granisetron 40 µg/kg tended to maintain core body temperature better than granisetron 10 µg/kg. A previous study stated that core body temperature can decrease by 0.5−1ºC after neuraxial anesthesia, therefore vasoconstriction and shivering occur above the block level. Intraoperative hypothermia is divided into three phases. The first phase is a rapid decrease in core body temperature after induction of anesthesia due to the result of heat redistribution of the core compartment to the outer layers of the body. The next phase is a slower and linear decrease in core temperature, lasting several hours. The last phase is where the body temperature remains unchanged until surgery is finished. In this study, it is shown that the post-anesthesia core body temperature changes sharply in the first 20−30 min, then the temperature drops slowly in the next 20−40 min and the temperature tends to remain constant in the next 20−30 min, then the temperature slowly returns to normal. Other studies showed the same pattern of temperature changes, which showed sharp decrease in the first 30 min followed by a sloppy temperature change, after which it remained above the linear value.[15,19]

5. CONCLUSION

Prophylactic administration of granisetron 40 µg/kg intravenously can reduce the incidence and degree of shivering after spinal anesthesia and maintain core body temperature better than granisetron 10 µg/kg.

6. Data availability

The numerical data generated during this research is available with the authors.

7. Acknowledgement

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8. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

9. Authors' contribution

WR: Concept, Conduct of study, Supervision, Manuscript editing

EP: Literature review, results analysis, manuscript writing

MAP: Provision of personnel, space, financial resources and equipment necessary for the work

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