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Comparison of Preemptive Post-Intubation 15 mg/kgBW Paracetamol to 0.35 mg/kgBW Meperidine in Incidence of Post-Anesthetic Shivering

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Abstract

Post anesthesia shivering (PAS) is a repetitive involuntary movement of one or more muscle groups as a result of a decrease in core body temperature. Pharmacological therapy in preventing PAS may include meperidine and paracetamol. This study compared the effectiveness of paracetamol to meperidine in reducing the incidence of post-anesthesia shivering. This study used an experimental randomized double-blind comparative analytic design on patients underwent exploratory laparotomy surgery under general anesthesia at Dr. Hasan Sadikin General Hospital Bandung, Indonesia, from September 2021 to August 2022. Patients with 50 ASA 1-2 physical status were included and divided into two groups. One group received 15 mg/kg group paracetamol and the other received 0.35 mg/kg meperidine. Data on tympanic membrane temperature and hemodynamics before and after induction and after extubating were collected. Furthermore, data on the results of the assessment of the incidence and grade of shivering in each treatment group were also collected. The results of this study showed that there was a decrease in the frequency of PAS in patients receiving intravenous 15 mg/kg paracetamol ($p<0.05$), as well as less side effects in the form of nausea and vomiting ($p<0.05$). The incidence and degree of shivering after general anesthesia using intravenous 15 mg/kg paracetamol was lower compared to the use of 0.35 mg/kg meperidine. In the meperidine group, the decrease in body temperature was lower than in the paracetamol group, while the incidence of nausea and vomiting in the paracetamol group was lower than in the meperidine group. In conclusion, paracetamol reduces the incidence of post-anesthesia shivering better than meperidine.

Keywords: General anesthesia, meperidine, paracetamol, preemptive, shivering

Introduction

Post-anesthesia shivering (PAS) is a repetitive involuntary movement of one or several muscle groups that occurs as a mechanism due to a decrease in core body temperature.[1-4] PAS is a complication that often occurs during the recovery process from anesthesia, with the incidence of shivering after general anesthesia being 40-70%.[1,2,3] General anesthesia will change the process of normal regulation of body temperature by reducing the threshold of the vasoconstrictive response, increasing the threshold of the vasodilation response, sweating, and increasing the inter threshold range from 0,2 °C to 40 °C.[1,3,4] The direct effect of anesthetic drugs occurs in the hypothalamus.[2,3] Shivering poses a risk because of increased oxygen consumption and carbon dioxide production, catecholamines release, cardiac output, tachycardia, hypertension, and intraocular pressure.[1,2,3]

Management of PAS can be done non-pharmacologically by reducing heat loss, such as giving warm infusions, heating pads, or blankets, maintaining the operating room temperature at room temperature, warm blankets, surgical covers, and mattresses filled with warm water.[5,6,7,9] Pharmacological intervention can be done by giving opioids (meperidine, pentazocine, tramadol), α2 agonists (clonidine), magnesium sulfate, ketamine, 5-hydroxytryptamine (5-HT3) receptor antagonists, and non-steroidal anti-inflammatory drugs (NSAIDs).[5,6,7,8] Meperidine was recommended as an agent for preventing PAS, the mechanism of action occurs through the κ receptor and the μ receptor.[9] Meperidine acts as a shivering inhibitor by increasing the

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threshold of sweat response and lowering vasoconstriction.[9] The minimal effective dose of meperidine to prevent PAS is 0.35 mg/kgBW.[9,10,11] The disadvantage of meperidine as a PAS prevention agent is its side effects of nausea, vomiting, and respiratory depression.[10,11]

Paracetamol is an NSAID drug that affects core body temperature through the hypothalamus by affecting prostaglandin synthesis. Paracetamol inhibits cyclooxygenase (COX), which plays a role in the synthesis of prostaglandins in the brain; the substrate is responsible for regulating the set point temperature in the hypothalamus, thereby causing an increase in the threshold for vasodilation and sweating. Paracetamol can be used as antipyretic and postoperative analgesia to reduce opioid consumption. In addition, paracetamol does not have a respiratory depression effect.[10-15] In 2018, research in Iran found that 15 mg/kg BW intravenous paracetamol effectively reduced the incidence of PAS to 9.1% in patients undergoing section cesarean under general anesthesia. [5,6] A study in Japan in 2019 found that 15 mg/kgBW intravenous paracetamol effectively prevented PAS in about 22.2% of patients with gynecologic laparotomy surgery.[7,8]

The study aimed to Compare paracetamol 15 mg/kg BW intravenously with meperidine 0.35 mg/kg BW in terms of the incidence of shivering after general anesthesia.

Methods

In this randomized, double-blinded prospective study, fifty patients underwent laparotomy procedures with general anesthesia in Dr. Hasan Sadikin General Hospital's operating theater from September until December 2021. The criteria for enrollment were patients between 18–60 years old, American Society of Anesthesiologists (ASA) physical status I, II, and surgery duration from one to three hours. Patients who consumed prophylactic drug that affects thermoregulation, history of allergy, elevated liver enzyme, obesity, fever, and or hypothermia were excluded from this study. The study protocol was explained to all patients, and written informed consent was obtained. The Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung approved the study protocol under the ethical clearance number LB.02.01/X.6.5/325/202. The standard operating room monitoring, including noninvasive blood pressure, electrocardiogram, and pulse oximetry, was performed for all patients. The patients were randomized into two groups based on random allocation. The 1st group received paracetamol 15 mg/kgBW (paracetamol group, n=25), and the 2nd group received meperidine 0.35 mg/kgBW (meperidine group, n=25). Patients were observed for nausea, vomiting, and shivering, and grades were recorded for each patient. The person observing in the postoperative ward was blind to the group allocation. Data recorded age, sex, body mass index (BMI), PAS, body temperature, ASA, room temperature, fluid maintenance, surgery duration, and blood loss volume. Statistical analysis was performed with SPSS 22 for windows and chi-square, and the Fisher test (categorical variables), t-test, and Mann-Whitney (numerical variables) were used. The $p<0.05$ was considered significant.

Results

The statistical analysis results showed no differences in patient characteristics between the two groups in the baseline study. (Table 1) This shows that the research subjects are

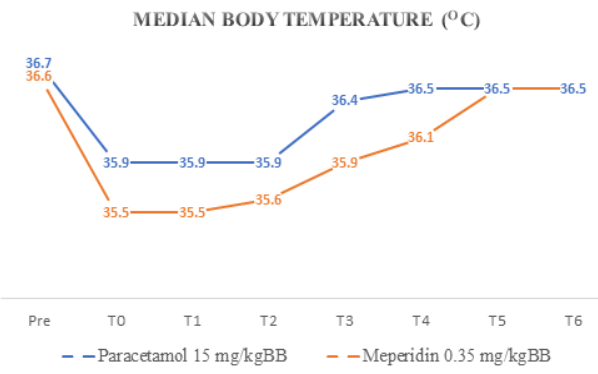

Figure Core Temperature between Two Groups

Table 1 Demographics and Characteristics of Patients

Variables (n=50)	Paracetamol group (P)	Meperidine group (M)	P value
Sex			
Male (%)	4 (16.0)	2 (8.0)	0.667[a]
Female (%)	21 (84.0)	23 (92.0)	
Age (years)			
Mean ± SD	41±8	40±10	0.853[b]
BMI (kg/m^2)			
Median (Range)	22.3 (19.5–30.3)	21.8 (19.6–31.0)	0.382[c]
Duration of surgery (min)			
Median (Range)	135 (120 – 190)	145 (120 – 180)	0.778[c]
Fluid maintenance (mL)			
Median (Range)	1500 (500–1500)	1500 (1000–1500)	0.449[c]
Volume of blood loss (mL)			
Mean ± SD	408±262	464±236	0.428[b]
Room temperature (^{0}C)			
Median (Range)	25.5 (23.5–25.5)	25.5 (23.4–25.5)	0.233[c]
ASA			
I (%)	2 (8.0)	1 (4.0)	1.000[a]
II (%)	23 (92.0)	24 (96.0)	

P value tested with [a] Fisher Exact, [b] t-test, [c] Mann-Whitney test

Table 2 Incidence of PAS

Variables	Paracetamol group (%)	Meperidine group (%)	p-value	RR (95% CI)
Yes (scale 2–4)	2 (8.0)	8 (32.0)	0.034*	0.185 (0.035 – 0.983)
No (scale 0–1)	23 (92.0)	17 (68.0)		

RR=Relative Risk. CI=Confidence Interval. p<0.05 compared with the other groups using the Chi-Square test*

homogeneous and deserve to be compared. The number of PAS is significantly less in the paracetamol group compared to the meperidine group, as shown in Table 2 (p<0.05), with the efficacy of paracetamol being 81.5%.

There were significant differences in postoperative nausea and vomiting or no side effects between the two groups, as shown in Table 3 (p<0.05). Based on Figure, the meperidine group had lower core body temperature post-intubation (p<0.05).

Table 3 Side Effects Between Two Groups After Extubation

Variables	Paracetamol group (%)	Meperidine group (%)	P value
Nausea	1 (4.0)	4 (16.7)	0.015*
Vomiting	0 (0.0)	5 (20.8)	
No side effect	24 (96.0)	15 (62.5)	

*p<0.05 compared with the other groups using the Chi-Square test

Discussion

Postanesthetic shivering is a harmful condition caused by general anesthesia. The side effects can cause hypoxia, pain, and lactic acidosis. Thus, the prevention of shivering is important. This study studied two groups of 25 patients, each candidate for exploratory laparotomy under general anesthesia. The incidence of PAS can be influenced by several factors, including age, BMI, duration of surgery, type of amount of fluid that enters intraoperatively, and operating room temperature.[5,10] In this study. that variable was not significantly different. but this result was the same as other studies.[5,6,7,8] This result may be obtained because the same criteria were set in this study to reduce research bias due to other risk factors. In another study with a larger and more diverse sample size, it was found that the incidence of postanesthetic shivering was influenced by body mass index, duration of surgery, and blood loss.[3]

This study showed that the incidence of PAS was higher in the meperidine group. Based on the result, the researchers concluded that intravenous paracetamol was a more effective prevention drug than meperidine intravenous in preventing PAS due to general anesthesia. This result was similar to the previous study, where paracetamol was more effective than saline infusion. Based on paracetamol's mechanism of action on thermoregulating the core body temperature by affecting the synthesis of Prostaglandin.[5.6] Another study reported that perioperative paracetamol administration can prevent postoperative severe shivering in patients scheduled for gynecological laparotomy. It might be because the drug prevented body temperature from increasing.[7] Until now, no other studies have compared paracetamol with meperidine..

For side effects between the two drugs, results show the meperidine group had more incidence of side effects during the study, and the paracetamol group mostly had no side effects at all. Many studies have reported side effects for other anti-shivering medications, between meperidine and paracetamol. Paracetamol had fewer side effects as an advantage. Meperidine can produce sedation, nausea, vomiting, or respiratory distress.[5] When compared with other anti-shivering drugs. Meperidine has fairly good effectiveness with fewer side effects but still affects respiratory distress.[9.10]

According to this study, patients receiving paracetamol had lower core temperatures than the control group. Still, the two groups had no significant differences, which is consistent with the findings in other studies.[6] This might be that the effects of paracetamol prevented body temperature from increasing. Maintaining core temperature during surgery was important for preventing PAS.[7]

Limitations of this study were the small sample size. Most of the patients were in higher ASA and also limited time for the study. That point can be improved in further studies.

The conclusion of the study is that in addition to maintaining body temperature during surgery. Paracetamol, as a pre-emptive drug in general anesthesia, could help prevent PAS. Besides having fewer side effects, it can also be a postoperative analgesic. More studies should be done on the efficacy of intravenous paracetamol as a preventive agent of PAS.

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