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Research Article

A STUDY ON BENZODIAZEPINES CLASS OF DRUG AND NON-BARBITURATE CLASS OF DRUGS: SYNERGISTIC ANAESTHESIA EFFECTS AMONG CARDIO-VASCULAR PATIENTS

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ABSTRACT

By administering a small dose of midazolam during induction at the trachea, this study aims to reduce the amount of propofol administered and prevent cardiovascular changes. Elective surgery was performed on 40 patients over the age of 60. The general anaesthesia was provided by combining remifentanil with propofol or midazolam. Induction was performed with 0.9% NaCl 0.03 ml/kg, propofol 1.2 mg/kg, and remifentanil for group P (n = 20). Group MP (n = 20) received midazolam 0.03 mg/kg, propofol 0.8 mg/kg, and remifentanil to induce anaesthesia. The time to reach a bispectrality index score (BIS) was recorded at the time of loss of consciousness (LOC). Rocuronium 0.8 mg/kg was administered after LOC to induce tracheal intubation. We measured mean blood pressure (MBP) and heart rate three minutes after induction and before intubation as baseline values, and immediately after intubation. In groups P and MP, the mean blood pressure decreased significantly ($P< 0.05$) at 3 minutes after intubation. A significant difference was found between group MP and group P in MBP decreases before intubation, immediately after intubation, and three minutes after intubation ($P < 0.05$). In comparison with group P, MP reached LOC significantly faster ($P < 0.05$). Midazolam and propofol were co-administered during tracheal intubation and avoided a marked decrease in patient blood pressure during the procedure.

Keywords: - Midazolam, propofol, Cardiovascular effects.

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INTRODUCTION

Due to deteriorating organ function, changes in the autonomic nervous system, and increased sensitivity to drugs, elderly patients require special attention and observation during anesthesia induction and endotracheal intubation. Even with an adult dose, they may experience a high frequency of side effects [1]. Moreover, elderly patients should avoid any serious decreases in pulse rate (HR), since even temporary drops in blood pressure (BP) and heart rate (HR) can increase the risk for cardiac ischemia, cerebral infarction, and cerebral ischemic stroke. In elderly patients and under general anaesthesia, propofol is recommended due to its rapid onset time. The anaesthetic effects of propofol are stronger in aged patients, however, due to its increased sensitivity to the brain. [2]. Propofol can also cause a problem when used to induce anaesthesia, where the systolic pressure may decrease by 15-40% in the elderly [3].

When elderly patients suffer from severe hemodynamic changes, it is recommended that they be co-induced with an intravenous anaesthetic agent [4,5]. As the name suggests, co-induction involves reducing the dose of the induction agent by administering sedatives or

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another anaesthetic agent alongside the anaesthetic agent. When two or more drug agents are combined, it reduces side effects associated with anaesthesia induction and provides comparable or better results than when just one drug agent is used. [4].

There is evidence that midazolam and propofol synergize and can reduce propofol dosage in elderly patients during anaesthesia induction [5,8], but no reports have been published describing cardiac changes associated with midazolam and propofol used in elderly patients. When elderly patients are admitted to the hospital for general anaesthesia, propofol doses can be reduced with co-administration of propofol and remifentanil. It is also possible to reduce the amount of propofol needed to induce anaesthesia by co-administering midazolam and propofol prior to and after endotracheal intubation.

MATERIALS AND METHODS

Following the approval of the study by the hospital's ethics committee and an explanation of the study's objectives and methods, each subject patient signed a written informed consent form the day before surgery. ASA class I-II members (age 60+) scheduled for elective surgery under general anaesthesia were included in this study, as were 40 older patients with physical status I-II (ASA). An individual who has suffered myocardial infarction or cerebral infarction, is currently treated for respiratory diseases, has a history of hypertension or diabetes, is currently being treated for respiratory diseases, has dementia or is psychiatrically ill, or is receiving dialysis treatment for renal failure, or cannot perform endotracheal intubation is excluded from participating in this study. No premedication was given to the subject patients before surgery. They had fasted for more than eight hours before the procedure. As soon as the patient entered the operating theatre, he or she received a non-invasive electrocardiogram (ECG), a pulse oximeter, and a bispectrality index (BIS) sensor.

A baseline measurement of mean blood pressure, heart rate, and pulse saturation was taken after the patient was stabilized. To preoxygenate the patients before the induction of anaesthesia, 0.2 mg of glycopyrrolate was infused intravenously and 8 minutes of deep breathing were required before anaesthesia induction [9]. When a patient is young and healthy, it is recommended to deep breathe 100% oxygen four times, for 30 seconds. However, when a patient is elderly, where desaturation occurs rapidly, a longer period of time was required for desaturation to fill the tissues and veins as well as the pulmonary alveolus and arteries. All patients were able to maintain an oxygen saturation of more than 99% during the operation, using the aforementioned procedure to maximize oxygenation in the shortest possible time.

In order to initiate anaesthesia, 10 mg/kg/hr of remifentanil was administered through a drug infusion pump. Randomly selected groups of 20 subjects were allocated to the test (MP) and control (P) groups. Each group was administered midazolam and propofol simultaneously. A test group and a control group were divided into two groups. The MP test group received 0.03 mg/kg of midazolam.

Within 60 seconds of propofol administration, rocuronium 0.8 mg/kg was intravenously injected, followed by bag-valve ventilation for one minute and thirty seconds. It was necessary to administer rocuronium at 0.6 mg/kg as a muscle relaxant for endotracheal intubation in order to induce anaesthesia; however, an increased dose of 0.8 mg/kg was used in order to ensure sufficient muscle relaxation in clinical conditions where measuring TOF for assessing muscle relaxation was difficult.

A resident with over three years' experience performed the endotracheal intubation after confirming sufficient muscle relaxation. Remifentanil was administered at a reduced dose of 2 mg/kg/hour 5 minutes after the initial intubation to maintain anaesthesia using sevoflurane 1.5%, oxygen at 1.5 L/min, and air at 2.5 L/min. In addition, $PETCO_2$ was maintained at 30 to 35 mmHg by mechanical ventilation.

Anaesthesia was induced by measuring mean blood pressure (MBP) and heart rate. Three minutes after endotracheal intubation, immediately afterwards (PI0), and three minutes afterward (PI3), blood pressure and heart rate were measured. It was prescribed to administer intravenously atropine 0.5 mg when the patient's heart rate dropped to 45 beats per minute, while ephedrine was administered intravenously with an increase of 5 mg after endotracheal intubation when the patient's systolic blood pressure fell to 80 mmHg. In order to compare the changes in MBP and HR between groups, an unpaired T-test was performed, and repeated ANOVA measures were used to analyse the variations within groups. It was considered statistically significant if the P value was less than 0.05.

Table 1: Characteristics of Patients

	Group MP	Group P
	(n = 20)	(n = 20)
Gender (M/F)	9/11	12/8
Age (yr)	72.5 ± 6.4	70.5 ± 5.5

Height (cm)	165.7 ± 11.6	164.6± 9.1
Weight (kg)	64.8 ± 11.3	62.1±10.11
BMI (kg/m^2)	25.6 ± 4.5	25.0 ± 4.6

RESULTS

A significant difference in gender, age, weight, height, BMI, and ASA grading classification between groups is not observed. At baseline, neither BP nor HR differed significantly between groups. For the time taken until the loss of consciousness after intravenous administration of propofol, the MP group (40 ± 12.1) showed a significantly shorter time compared to the P group (55 ± 14.3), but there was no inter-group significant difference in BIS value at the time of loss of consciousness.

When comparing the MP group to the P group, the MP group showed significant small decreases in mean blood pressure at BI, PI0, and PI3. In both MP and P groups, BP decreased significantly during BI (23.0%) and PI3 (17.5%), compared to baseline, while BP decreased prominently during PI3 (25.4%) in both groups.

There was no statistically significant difference between MP and P on the basis of the intergroup comparison. MP and P groups did not differ significantly in HR at any time point.

In spite of the fact that both groups had not experienced bradycardia, three patients in the group that received 1.2 mg/kg propofol had experienced a decrease in their systolic blood pressure; these patients were subsequently excluded from the study.

DISCUSSION

A comparison of the mean blood pressure after intubation at 1 minute and 1 minute after co-induction did not show a significant increase. Midazolam is therefore used in conjunction with propofol to induce anaesthesia in elderly patients, preventing sudden BP decreases immediately prior to and following endotracheal intubation. There is also a significant difference in blood pressure between three minutes after intubation versus immediately after intubation with midazolam.

In older people, this variation is more pronounced due to an increase in sympathetic tone during surgery [10]. According to Paterniti et al [11], an analysis of physiologic characteristics of older patients found that physical organic dysfunction and disease progression increased with age. Additionally, they showed reduced functions of the central nervous system, cardiovascular system, liver system, renal system, and pulmonary system, leading to an increased mortality rate. According to Ryu [1,] organic functions decreased with age, while cardiovascular function increased, as well as the emergence of pharmacodynamic and pharmacokinetic diseases, such as diabetes and renal dysfunction. The increased drug sensitivity, as well as increased side effects, would result in increased drug effects, even with the same dose of drug agent.

Even small variations in venous return impacted ventricular preload and cardiac output in aged patients with non-compliant hearts. Because Ryu had indicated that aged patients do not compensate well for the decrease in blood volume because of significant reductions in diastolic myocardial function, baroreceptor-controlled HR, adrenergic receptor responsiveness and vascular compliance [1], he suggested that age-related patients have no ability to compensate adequately. In terms of its effects on myocardial and cardiovascular inhibition, propofol plays the role of an alkylphenol group drug with direct inotropic effects on myocardium [8] and vasodilative effects on systemic vascular resistance [12]. By inhibiting the baroreflex mechanism, an appropriate dose for induction of anesthesia prevents the decrease of arterial pressure from accelerating heart rate. Factors such as large dosages, rapid infusion rates, and old age can further exacerbate these results.

The low clearance rate for propofol and the small capacity of the central compartment can cause propofol to maintain a high blood concentration in elderly patients [13]. These conditions allow a more prominent cardiovascular inhibition effect to be observed. A preemptive expectation is that patients who are elderly or who have unstable cardiovascular systems need to be prepared before anesthesia with propofol, with serious blood pressure decreasing in proportion to IV doses and speeds compared to young patients [3,14]. It is believed that the blood pressure did not reach the lowest level at the endotracheal intubation due to stimulation caused by the endotracheal intubation, five minutes after propofol administration in this study [1]. An endotracheal intubation might have resulted in a severe decrease in blood pressure in the absence of stimulation. According to the results, the elderly patient can be adversely affected by severe or prolonged BP decreases, and it is plausible to wait idly for 5 minutes before performing an invasive procedure or surgery after endotracheal intubation under these conditions. Since BP variation trends differed significantly between groups after endotracheal intubation, BP was measured only up to 3 minutes after intubation. The intraoperative blood pressure of 20% of patients with myocardial infractions decreased by more than 30% after induction of anesthesia, according to Charlson et al. [15]; furthermore,

when a mean myocardial drop of over 20 mmHg was sustained for 5 to 59 minutes, postoperative complications such as ischemic heart disease were extremely prevalent. The elderly should be prepared for a severe fall in blood pressure within five minutes of endotracheal intubation when induced anesthesia, and position changes or inotropics should be used if such a fall occurs so that the low blood pressure state can be maintained faster.

CONCLUSION

It is therefore possible to reduce prominent variations in blood pressure during and after endotracheal intubation when administering anesthesia to patients using remifentanil and propofol as a combination with co-induction with reduced propofol at 0.8 mg/kg combined with midazolam at 0.3 mg/kg.

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