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The Effects of Ketamine and Propofol Sedation on Patients Undergoing Curettage with General Anesthesia Based on the Bispectral Index Score

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ABSTRACT

Sedation is the reduction of irritability or agitation by administration of sedative drugs. Curettage is invasive procedure in women that requires procedural sedation. Ketamine-Propofol is a combination of sedative drugs which is expected to achieve effective and safe sedation. The aim of this research is to understand the sedation effect of using ketamine propofol in curettage patients with general anesthesia based on the Bispectral index score at Margono Soekarjo Hospital. This research design uses descriptive observational. The sampling technique used in this research was random sampling of 38 respondents with instruments of informed consent, patient data sheets and patient observation sheets, then the mean of the patient data was analyzed. The results of the study showed that the depth of sedation was good, namely 100% of patients experienced optimal sedation within 6 minutes after administering the drug, 100% of the patient's mean arterial pressure was optimal, the patient's pulse rate was 100% normal, and the respiratory rate was normal. in 100% of patients, and normal saturation in 100% of patients.

Keywords: Sedation Depth, BIS, Curettage, Ketamine-Propofol

1. INTRODUCTION

Sedation is a state of altered consciousness caused by the use of sedative drugs to reduce the effects of stress, anxiety, impatience, and stimulation. In 2019, The American Society of Anesthesiologists (ASA) provided an explanation regarding the levels of sedation and analgesia (Aldiar et al. 2021). Sedation procedures are performed on patients who experience anxiety and have the potential for pain. Curettage is one of the invasive procedures in women that requires sedation. This leads women to experience anxiety and pain (Cooper and Menefee 2022). Inadequate administration of sedatives during curettage can lead to restlessness. Poor management of pain and anxiety has an impact on the psychological trauma of women (Millizia 2018).

A good sedative drug is needed to achieve maximum sedation. Ketamine is the drug of choice for sedation procedures in curettage because it has a high level of safety and provides good analgesia. Propofol is also a preferred drug for curettage due to its strong sedative effect. Ketamine-Propofol is a drug combination expected to achieve effective and safe sedation and analgesia (Dal et al. 2014). The Bispectral Index Score (BIS) monitor is a

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tool used to measure the depth of sedation in patients during anesthesia and surgery.

The study by Aldiar dkk tahun 2021 compared the sedation effects with BIS monitoring on patients undergoing Bone Marrow Puncture (BMP) using sedative agents, namely Ketamine-Propofol and Ketamine-Midazolam. The research results indicate that both have a positive effect on pediatric BMP patients, and there is no significant difference between the use of Ketamine-Propofol and Ketamine-Midazolam in terms of the depth of sedation for pediatric BMP patients.

The study by Singarimbun, Indriasari, and Maskoen 2018 investigated the depth of sedation using the BIS monitor with sedative agents, namely Dexmedetomidine, and the combination of Fentanyl-Propofol on patients undergoing curettage. The research results indicate that both have a positive effect on the depth of sedation in these patients, and there is no significant difference between the use of Dexmedetomidine and the Fentanyl-Propofol combination.

Data from RSUD Prof. Margono Soekarjo shows that there are 60 curettage patients per month, while there are 70 patients per month for cesarean section cases and 50 patients per month for hysterectomy. The percentage of curettage cases reaches 30% per month, indicating that curettage is one of the commonly performed procedures at RSUD Prof. Margono Soekarjo. One of the sedative agents used in these procedures is Ketamine-Propofol.

Based on the above description, the researchers are interested in conducting their research on the effects of using Ketamine-Propofol sedation on patients undergoing curettage with general anesthesia, based on the Bispectral Index Score (BIS).

2. RESEARCH METHODS

This type of research is descriptive in nature. The purpose of this study is to measure and analyze data and provide an overview of the sedation effects of using Ketamine-Propofol on patients undergoing curettage based on the Bispectral Index Score (BIS). The research was conducted at the Central Surgery Unit (IBS) of Margono Soekarjo Hospital in Purwokerto (RSMS). The research took place from January to October 2022, with data collection occurring from August 1st to August 25th, 2022.

2.1 Population and Sample

The population of this study consists of 60 curettage patients at RSMS. The sample size was determined using the Slovin formula with a margin of error of 10% (Umar 2013). Given that the population size is 60 curettage patients, the sample can be calculated as follows

n = N / 1+Ne2

n = 60 / 1+0,6

n = 60 / 1,6

n = 37,5 = 38 (rounded)

Patients between the ages of 18 and 60 who meet the American Society of Anesthesiologists (ASA) physical status criteria for Class I or Class II are included in the sample. Class I patients are "healthy" individuals who do not smoke or consume alcohol. Class II patients encompass those with mild systemic disorders to those with no functional limitations. This includes patients with uncontrolled diabetes or hypertension, smokers, pregnant women, or those with a body mass index (BMI) between 30 and 40 (ASA 2019). Exclusion criteria involve a history of heavy bleeding (more than 750 cc) during and after curettage, curettage followed by additional procedures, significant blood pressure increases, preeclampsia, and hypersensitivity (Pionas 2015).

2.2 Data Collection Methods and Techniques

Data were collected from August 1st to August 25th, 2022, involving 38 curettage patients as respondents. The research data were obtained through observations of curettage patients who had provided informed consent. This study utilized both primary and secondary data.

The data collection technique involved observations. Patients were randomly administered Ketamine-Propofol, and then crystalloid fluid infusions, oxygen cannulas, electrocardiography, non-invasive blood pressure measurement, oxygen saturation

monitoring, and BIS sensors were placed on the patient's forehead, temple, and the front of the left ear. Initial conditions such as Mean Arterial Pressure (MAP), respiratory rate, heart rate, oxygen saturation, and BIS values were recorded.

BIS values, MAP, heart rate, respiratory rate, and oxygen saturation during the curettage procedure were documented as primary data. Secondary data included the patients' medical records, including their name, age, weight, diagnosis, and ASA status.

Patients were administered a dose of 1 mg/kg body weight of Ketamine and 1.5 mg/kg of Propofol. Blood pressure, MAP, heart rate, respiratory rate, oxygen saturation, and BIS values were measured before drug administration (referred to as t0). After patients received sedation according to their respective groups, measurements and monitoring were conducted every 3 minutes during the procedure until the curettage was completed.

2.3 Data Analysis

The first step taken by the researcher was to gather the necessary information and data about the sedation effects of using Ketamine-Propofol on patients undergoing curettage with general anesthesia based on the Bispectral Index Score at Margono Soekarjo Hospital in Purwokerto. The data was then categorized according to predefined classifications.

BIS values were classified into flatline, general anesthesia sedation, sedation, and full consciousness. MAP values were grouped into optimal, normal, and high-normal. Heart rate values were categorized as normal or abnormal. Respiratory rate values were divided into normal and abnormal. Oxygen saturation values were grouped as normal or abnormal. Subsequently, data were coded and the percentage of data was analyzed using SPSS descriptive-exploratory analysis.

Finally, the mean ± standard deviation (SD), range (minimum to maximum) for each variable tested were analyzed, and the data was classified accordingly.

3. RESULT AND DISCUSSION

This research has obtained ethical clearance from the Research Ethics Commission of Universitas Harapan Bangsa with reference number B.I.PPM-UHB/1183/08/2022. The researcher documented patients who had provided informed consent according to the inclusion criteria for the study. Patients were administered a dose of 1 mg/kg body weight of Ketamine and 1.5 mg/kg of Propofol. Measurements conducted included heart rate assessment, oxygen levels, blood pressure, and pulse rate.

Before and during the surgery, patients' heart rate, respiratory rate, and oxygen saturation levels were monitored, as well as blood pressure (MAP), pulse rate, and BIS values. After patients were anesthetized, MAP, HR, RR, and SpO2 values were measured and monitored every 3 minutes until the curettage was completed. The curettage procedure took approximately 10 minutes, so the researcher collected BIS data at t0 (before sedative administration), t1 (3 minutes after sedative administration), t2 (6 minutes after sedative administration), and t3 (9 minutes after sedative administration). This procedure was performed on 38 patients.

After obtaining results for all parameters, the researcher processed the data by calculating the mean ± standard deviation (SD) and range (minimum-maximum). Subsequently, the researcher analyzed whether the data fell into the categories of optimal/normal/high-normal/abnormal for MAP, pulse rate, respiratory rate, and oxygen saturation parameters. BIS values were analyzed to determine whether patients' data fell into the categories of Flatline EEG (patients with apnea), general anesthesia sedation (patients in a deep sleep), sedation (patients asleep), or full consciousness (patients fully awake).

3.1 Results

Here are the research findings that have been obtained:

Table 1. Characteristics *Mean Arterial Pressure* (MAP)

***Mean Arterial Pressure* (MAP)**	**Pre OP**		**Intra OP**	
	n	**(%)**	**n**	**(%)**
Optimal	38	100.0	38	100.0
Normal	0	0	0	0
High Normal	0	0	0	0
Total	**38**	**100.0**	**38**	**100.0**

Table 1 shows the Mean Arterial Pressure (MAP) with optimal results before the administration of Ketamine-Propofol to curettage patients, which is 100%, and optimal MAP during intra-OP, which is 100%.

Table 2. Characteristics of Heart Rate

Heart Rate	**Pre OP**		**Intra OP**	
	n	**(%)**	**n**	**(%)**
Normal	38	100.0	38	100.0
Abnormal	0	0	0	0
Total	**38**	**100.0**	**38**	**100.0**

Table 2 displays the heart rate of curettage patients before the operation (Pre-OP) with normal results, totaling 100%. The heart rate during the operation (Intra-OP) for curettage patients also had normal results, totaling 100%.

Table 3. Characteristics of Respiratory Rate

Respiratory Rate	**Pre OP**		**Intra OP**	
	n	**(%)**	**n**	**(%)**
Normal	38	100.0	38	100.0
Abnormal	0	0	0	0
Total	**38**	**100.0**	**38**	**100.0**

Table 3 shows the respiratory rate of curettage patients before the operation (Pre-OP) with normal results, totaling 100%. The respiratory rate during the operation (Intra-OP) for curettage patients also had normal results, totaling 100%.

Table 4. Characteristics of Oxygen Saturation

Oxygen Saturation	**Pre OP**		**Intra OP**	
	n	**(%)**	**n**	**(%)**
Normal	38	100.0	38	100.0
Abnormal	0	0	0	0
Total	**38**	**100.0**	**38**	**100.0**

Table 4 presents the oxygen saturation levels of curettage patients before the operation (Pre-OP) with normal results, totaling 100%. The oxygen saturation levels during the operation (Intra-OP) for curettage patients also had normal results, totaling 100%.

Table 5. Characteristics of Sedation Depth

Research Variable	**Time**	**Mean**	**n**	**(%)**	**Classification**
Bispectral index	t0 (0 menit)	0	0	0	Flatline EEG
		0	0	0	Sedation General Anesthesia
		0	0	0	Sedation
		93	38	100	Full consciousness
	t1 (3 menit)	0	0	0	Flatline EEG
		55	28	74	Sedation General Anesthesia
		66	10	26	Sedation
		0	0	0	Full consciousness
	t2 (6 menit)	0	0	0	Flatline EEG
		46	38	100	Sedation General Anesthesia
		0	0	0	Sedation
		0	0	0	Full consciousness
	t3 (9 menit)	0	0	0	Flatline EEG
		58	27	71	Sedation General Anesthesia
		65	11	29	Sedation
		0	0	0	Full consciousness

Table 5 shows the results of sedation depth at t0, t1, t2, and t3. The results at t0, which is before administering Ketamine-Propofol, indicate that all patients were fully conscious, with an average BIS score of 93, involving 38 patients or 100%. Three minutes later at t1, the sedation depth ranged from 55 to 66, with 10 patients classified as sedation (26%) and 28 patients as general anesthesia sedation (74%). At the second 3-minute interval (t2), all patients, a total of 38 (100%), fell into the group of general anesthesia sedation with an average score of 46%. In the third 3-minute interval (t3), there were 11 patients classified as sedation (29%) and 27 patients as general anesthesia sedation (71%) with average scores ranging from 58 to 65.

3.2 Discussion

The administration of sedative drugs during medical care serves several purposes, including alleviating patient discomfort, inducing temporary amnesia, reducing the risk of adverse drug reactions, maintaining control, and ensuring the stability of respiration and heart rate. The desired level of sedation varies depending on the specific procedure being performed, making the assessment of sedation depth an integral aspect of the sedation process. Both subjective and objective measurements can be used to evaluate the level of sedation or anesthesia. An objective measurement for assessing the level of anesthesia and sedation is the bispectral index (BIS), which has been developed (Anggorotomo et al. 2015).

The increase in heart rate, blood pressure, and cardiac output caused by ketamine is largely mediated through the sympathetic nervous system. Ketamine relaxes the airway by acting on various receptors and bronchial smooth muscles, with minimal effect on the respiratory center. Ketamine enhances muscle strength and salivary production. The significant anesthetic, cataleptic, amnestic, and analgesic effects of ketamine are all dose-dependent. Cataleptic states are characterized by immobility and an absence of consciousness-altering effects, such as the loss of the orthostatic reflex. Ketamine's dissociative effects are unique compared to other drugs because users appear alert but detached from their surroundings while keeping their eyes open. Its mechanism of action is primarily through noncompetitive antagonism of N-methyl-D-aspartate (NMDA) receptors. It also interacts with opioid, monoamine, cholinergic, purinergic, adrenoreceptor systems, and has local anesthetic effects (Kurdi, Theerth, and Deva 2014).

Propofol is an intravenous anesthetic agent used for sedation during medical procedures, anesthesia maintenance, or as an induction agent for general anesthesia. Propofol can be administered as a bolus or infusion, or a combination of both. Propofol is formulated in a lipid emulsion, giving it a characteristic milky appearance. Strict aseptic techniques must be employed during the production of propofol as the emulsion can support microbial growth. Like most general anesthetic agents, the exact mechanism of action of propofol is not fully understood, but it is believed to be related to its effects on the GABA-mediated chloride channel in the brain. Propofol may work by reducing the dissociation of GABA from GABA receptors in the brain, potentiating the inhibitory effects of neurotransmitters (Folino et al. 2022)

The BIS (Bispectral Index) is an objective method for measuring the hypnotic effects by analyzing the EEG (Electroencephalogram) wave characteristics of patients. The results of this study indicate that 100% of the patients were fully conscious before receiving ketamine-propofol, with an average BIS score of 93. At 3 minutes afterward, 10 patients (27%) experienced sedation with an average BIS score of 65, and 28 patients (74%) experienced sedation allowing for general anesthesia with an average BIS score of 55. In the following 3 minutes (t2), all patients (100%) experienced sedation with general anesthesia, with an average BIS score of 46. In the final 3 minutes (t3), 11 patients (28.9%) experienced sedation with an average BIS score of 58, and 27 (71.1%) patients experienced sedation with general anesthesia, with an average BIS score of 65. The researchers observed a decrease at the 3-minute mark, and the best results were seen at 6 minutes (t2), indicating that at t2, or 6 minutes, the patients were in a deep state of sedation, making it safe and comfortable for the administration of general anesthesia. BIS values in the range of 41-60 should be maintained because values higher than that may lead to the patient awakening, while values lower than 41 might result in the patient being in a very deep state of sedation or even reaching a flatline EEG, which could be extremely dangerous. The research conducted by Singarimbun dkk in 2018 stated that BIS values between 41-60 indicate a state of sedation that allows for the administration of general anesthesia. This aligns with the results of this study, which indicate that the sedation levels at t1-t3 ranged between 46-60. This means that the sedation effects on curettage patients at Margono Hospital, with the administration of the predetermined dose of ketamine-propofol, were satisfactory. The study by Singarimbun et

al. added an additional dose of propofol to achieve deeper sedation, specifically 22 mg. However, in this study, no additional propofol was necessary, as the sedation effects achieved were already optimal (Singarimbun, Indriasari, and Maskoen 2018).

In this study, the BIS value was maintained between 41-60 because within this range, patients achieve sedation that allows for the administration of general anesthesia with a dose of 1.5 mg/kg BW IV of propofol and 1 mg/kg BW IV of ketamine. Hal tersebut sejalan dengan penelitian Silalahi, Frw dan Suryono tahun 2014, which demonstrated the effectiveness of a combination dose of 1.5 mg/kg BW IV of propofol and 1 mg/kg BW IV of ketamine in achieving a BIS score of 41-60 (Silalahi, Frw, and Suryono 2014).

Throughout the research process, BIS values, MAP, heart rate, respiratory rate, and oxygen saturation were monitored before and during the surgery. This was done to assess the risks that might occur, as the risk of postoperative heart and kidney problems increases with intraoperative hemodynamic changes and variations in saturation. Therefore, this information is of utmost importance. Hemodynamic disturbances during surgery often occur due to the effects of anesthetic agents and techniques, surgical manipulation, and the patient's medical comorbidities.

As one of the vital signs, MAP must be monitored in patients undergoing anesthesia and surgery. Monitoring MAP during perioperative care is based on the following arguments: blood pressure can be highly fluctuating, abnormal MAP and unfavorable patient conditions are interrelated, and abnormal MAP can be promptly treated (Meng et al. 2018)

In this study, the MAP values for all patients undergoing curettage, both pre-OP and intra-OP, fell within the optimal range. This means that none of the patients undergoing curettage experienced hypotension or hypertension. The MAP values slightly decreased after the administration of ketamine-propofol, which the researchers observed to be due to adequate sedation of the patients. The decrease in MAP is caused by a reduction in systemic vascular resistance, heart contractility, and venous return. In this research, there were no abnormal hemodynamic values and intraoperative saturations, with the pre-OP MAP at 83 and intra-OP MAP at 80. This aligns with the results of a study by Laurent (2012), which reported a 4.6% decrease in MAP during the administration of ketamine-propofol (Laurent ius Sandhie Praset ya, Anestesiologi dan Terapi Intensif UGM, and Sardjito 2012)

Heart rate is essential to monitor during the process of general anesthesia sedation. Heart rate serves as a predictor that the heart rate is well-maintained when the patient is under sedation. The results of this study indicated that the heart rate remained normal both pre-OP and intra-OP for all 38 patients, representing 100% of the cases. This suggests that patients were in good condition during general anesthesia sedation. The researchers assessed that the decrease in heart rate in patients was due to a reduction in the level of patient anxiety. Changes in heart rate during sedation are attributed to shifts in the balance between the sympathetic and parasympathetic nervous systems. During sedation, the sympathetic nervous system does not exhibit significant fluctuations, but there are changes in parasympathetic nervous system activity. The balance between the sympathetic and parasympathetic nervous systems shifts toward the parasympathetic side as the level of sedation increases, and the heart rate gradually slows down (Kang et al. 2019).

Checking the patient's pulse rate is a common way to record any changes in their health status. The average heart rate for adults is typically between 60 and 100 beats per minute. Similarly, a normal pulse rate falls within the range of 60 to 100 beats per minute (Sarotama and Melyana 2019). In this study, the pre-OP pulse rate was 85, and the intra-OP pulse rate was 82. Despite a decrease in the pulse rate, these values still fall within the normal range because there were no concerning symptoms, and the change was only brief. Previous research also reported a 2.63% decrease in the pulse rate during the intraoperative period (Laurent ius Sandhie Praset ya, Anestesiologi dan Terapi Intensif UGM, and Sardjito 2012).

Respiratory rate serves as a predictor of good airway patency while a patient is undergoing sedation. Monitoring the respiratory rate during sedation is important to assess whether the respiratory rate remains adequate during the sedation. In this study, the respiratory rate of all patients was normal both pre-OP and intra-OP, representing 100% normal values. The normal range for respiratory rate is typically 10-25 breaths per minute. The pre-OP respiratory rate was 19, and the intra-OP respiratory rate was 18. When a patient is relaxed, the respiratory rate tends to be normal. The decrease in respiratory rate is also influenced by propofol's action in inhibiting GABA, which can reduce the respiratory rate, leading to hypoventilation. Besides the reduction in breathing frequency, an increase in frequency can occur due to a reduction in the depth of anesthesia. This may require corrective action, as an increased rate and depth of respiration can also occur if carbon dioxide accumulates in the respiratory system. This situation may arise during anesthesia or due to gas supply system failures (Pangolins 2020)

The saturation levels in this study were observed to be normal. The pre-OP saturation was 98, and the intra-OP saturation was 100. The slight increase in these values was due to the administration of oxygen through a nasal cannula. Saturation during sedation needs to be monitored because, during sedation, it is crucial to ensure the patient's oxygen supply. Saturation is inversely related to the respiratory rate, with saturation increasing from pre-OP to intra-OP, while the respiratory rate decreases from pre-OP to intra-OP. This aligns with a study by Ristanto et al., which states that the respiratory rate has a significant correlation with SpO2 levels in a negative direction. (Ristanto and Zakaria 2018)

Despite some fluctuations, the data indicate that the hemodynamic values and saturation fall within the normal classification. Therefore, sedation anesthesia for surgery provided by the combination of ketamine and propofol has a rapid onset, rapid offset, optimal sedation, stable hemodynamics, and potential analgesic effects. In this study, ketamine-propofol provided good analgesic and sedative effects without increasing myocardial depression, affecting the respiratory system, and demonstrated good hemodynamic stability.

CONCLUSSION

Based on the research results to determine the overview of the sedative effects of ketamine-propofol in patients undergoing curettage at Margono Soekarjo Hospital in Purwokerto, several key findings can be summarized as follows:

The BIS values at t0 showed that 100% of the patients were fully conscious, while at t1, 26.3% of the patients exhibited sedation, and 73.7% experienced general anesthesia sedation. At t2, 100% of the patients reached a state of sedation with general anesthesia, and at t3, 28.9% of the patients were in a sedated state, while 71.1% were under sedation with general anesthesia. The depth of sedation measured by the Bispectral index at t1-t3 had an average result ranging from 46 to 60. This indicates that these values fall within the classification of 40-60, meaning that the patients were in a state of sedation suitable for the general anesthesia procedure.

Mean Artery Pressure (MAP) in all 38 patients (100%) showed optimal values. The heart rate in all 38 patients (100%) indicated normal values. The respiratory rate in all 38 patients (100%) showed normal values. Oxygen saturation in all 38 patients (100%) displayed normal values.

RECOMMENDATION

1. For the Hospital

Implement a Standard Operating Procedure (SOP) for the use of BIS in patients undergoing curettage surgery.

2. For Healthcare Professionals

Healthcare professionals, especially anesthesia nurses at Margono Soekarjo Hospital in Purwokerto, should consider using BIS to monitor the depth of patient sedation.

3. For Patients

Patients need not worry or fear when undergoing surgical procedures because BIS will monitor the depth of sedation, ensuring their safety and comfort.

4. For Future Researchers

Future research endeavors should aim to expand on this study by conducting further analyses, especially regarding post-operative effects.

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