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Propofol and Dexmedetomidine potentially maintain BIS, MAP, and BGA in Brain Tumor Patients

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Abstract

Introduction: Brain tumors have a high morbidity and mortality rate in Indonesia. According to data from the Ministry of Health, in 2020 the incidence of brain tumors was around 1.5 percent of all tumor cases. Anesthesia for brain tumor removal surgery has a high risk of postoperative complications such as hypotension, bleeding and intracranial infection. Propofol and dexmedetomidine are often used as anesthetic agents in neurosurgery that affect hemodynamics, depth of anesthesia and blood gas analysis. This study aims to determine the comparative effectiveness of propofol compared to dexmedetomidine on Bispectral Index (BIS), mean arterial pressure (MAP), and blood gas analysis (BGA) in patients undergoing intracranial tumor removal surgery.
Subject and Method: This study is an unpaired numerical comparative analytical observational study. A total of 42 participants who met the inclusion and exclusion criteria were randomly assigned into 2 groups, namely the propofol and dexmedetomidine groups. Furthermore, an assessment of mean arterial pressure, BIS, and BGA was carried out.
Results: Based on statistical tests using the unpaired T test, it was found that intraoperative MAP was significantly different between the two groups ($p<0.05$), where dexmedetomidine had a more stable MAP. While in BIS and BGA there was no significant difference in the two groups ($p>0.05$) statistically using the Mann Whitney test.
Conclusion: Dexmedetomidine has an effect that is not much different compared to propofol in maintaining changes in MAP, BIS and BGA in patients with intracranial tumor removal surgery.

Keywords: Bispectral, blood gas analysis index, mean arterial pressure, dexmedetomidine, intracranial tumor removal surgery, propofol

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Introduction

Propofol is an anaesthetic agent that is often used in neuro-anaesthetic procedures, Propofol has a rapid induction and can reduce ischemic brain damage. In addition, propofol does not increase intracranial pressure (ICP) and has a neuroprotective effect. Propofol also has a sedative effect that is useful in handling traumatic cases because of its relatively rapid onset and offset of action, thus facilitating neurological evaluation.[1] In addition to the use of propofol, another anesthetic agent that can be used in general anesthesia procedures is dexmedetomidine. Dexmedetomidine is a sedative and analgesic agent from the selective α2-adrenergic receptor (α2-AR) agonist group that acts as anxiolysis, perioperative sympatholytic and has a cardiovascular stabilization effect. The hypnotic effect caused by this agent is like natural sleep (Non-Rapid Eye Movement/NREM) so that it can maintain cognitive and immunological functions. In addition, this agent has the advantage of adequate sedation without causing respiratory

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depression and with a wide safety margin.[2] Brain tumors have a high incidence, according to statistics from the Central Brain Tumor Registry of the United State (CBTRUS) in 2011–2015, the highest number is occupied by meningioma from all cases of brain tumors, which is around 37%,[3] and women have twice the prevalence than men.

Diagnosis of brain tumors can be confirmed by imaging through Head Computed Tomography (CT) scans or Magnetic Resonance Imaging (MRI). However, CT scans have limitations and are a challenge when imaging the posterior fossa of the brain.[4] Patients undergoing neurosurgical operations can pose many challenges to anesthesiologists because neurosurgical events are common in all walks of life. Neurosurgical operations include cases of trauma, vascular disorders and tumors.[5] Mortality and morbidity of brain tumors are quite high, although the occurrence is very rare, but this is a serious health problem. Glioma ranks first in the type of brain tumor in adult patients; its prevalence is around 80% of all malignant brain tumors and 30% of all brain tumors. Although in the last few decades there has been treatment and diagnosis of brain tumors, it has not shown an increase in the 5-year survival rate <5% in cases of severe glioblastoma.[3,5,6]

Previously, many publications have reported cases of postoperative death occurring immediately after anesthesia and central nervous system surgery. These deaths can be prevented with special care after surgery. Recovery from anesthesia for neurosurgical patients is a life-threatening condition. A study stated that 24% of 18,473 patients experienced complications that occurred during recovery from anesthesia. The process of patient adaptation after neurosurgical procedures is counted from the time the operation is completed, monitoring in the resuscitation room, and close observation in the intensive care unit (ICU).[7,8] Nowadays, there are more discoveries of general anesthetic pharmacotherapy with different modes of action and chemical characteristics. Since its introduction in 1986, propofol has been increasingly used in anesthesia induction and sedation in neuro-intensive care with a protective effect on brain cells. The potential of dexmedetomidine as an α2-adrenergic receptor agonist in anesthesia has been widely recognized. The time to extubating in patients who have been given dexmedetomidine is also known to be short. The structure of each general anesthetic agent will affect the duration of action and the patient's ability to adapt, especially in the respiratory system.[7]

In 2022, a study was conducted using propofol and dexmedetomidine in craniotomy patients, showed that the administration of Dexmedetomidine was effective in maintaining stress responses in the form of decreased random blood sugar (RBS) in emergency craniotomy patients compared to propofol. However, the hemodynamic values in the administration of dexmedetomidine and propofol did not have significant differences.[8] Other studies have shown that propofol was comparable to dexmedetomidine as a maintenance anesthetic agent and could produce better control of BIS values and hemodynamic variables.[9]

Method

Study Design and Setting

This study is an unpaired numerical comparative analytical observational study. The sample used in this study were all patients undergoing intracranial tumor removal with general anesthesia at Zainoel Abidin Hospital (ZAH) who met the inclusion and exclusion criteria. The inclusion criteria of this study were patients who underwent neurosurgery tumor removal with Glasgow Coma Scale (GCS) ≥ 9, patients aged 18–60 years, American Society of Anesthesiologist (ASA) criteria 2–3, and patients without heart disorders (Congestive heart failure (CHF), ST elevated myocardial infarct (STEMI), Valve disorders, and congenital disorders). The exclusion criteria were patients with epilepsy history, pregnancy, patients using vasopressors reaching 0.5 mcg/kg.BW, MAP <50 mmHg or >150 mmHg, patients with stroke problems, and patients with lung problems (Chronic Obstructive Pulmonary Disease (COPD), and Asthma). Patients who experienced allergic reactions and drug side effects, and patients who experienced bleeding >2,000 cc at the time of treatment were dropped out of this study.

Study Subjects

The study subjects used were 42 patients who were divided into 2 groups, namely the propofol group and the dexmedetomidine group. In each group, MAP, BIS, and BGA were assessed. Furthermore, the results of the examination will be compared and analyzed using statistical analysis.

Data Analysis

Statistical test processing determines the comparison of the effectiveness of each treatment group on MAP, BIS, and BGA uses an unpaired t-test on the data that was normally distributed, in the data is not normally distributed then the Mann Whitney test was used. The decision making of this data analysis is based on the p-value, for data that has a p value < 0.05, it is stated as significant.

Ethical Approval

The study protocol of this study was approved by the Ethical Committee of Health Research, Dr Zainoel Abidin Hospital (Approval No.: 035 / ETIK-RSUDZA / 2023).

Results

This study involved 42 study subjects that met the inclusion criteria. No data was excluded. The overall characteristics of the study subjects are presented in table 1. The overall characteristics of the study subjects presented in table 1 did not have significant differences (p-value > 0.05). Male gender dominated both the propofol group and the dexmedetomidine group. The sample was aged 18–30 years, there were 2 people (9.5%) in both groups, aged 31–45-year 8 people (38.1%) in the propofol group, as many as 9 people (42.9%) in the dexmedetomidine group, at the age of 46-90 there were 11 (52.4%) in the propofol group and 10 (47.6%) in the dexmedetomidine group. Based on the duration of surgery, the median in the propofol and dexmedetomidine groups was 262 minutes and 275 minutes respectively in each research group. In addition, the total bleeding was also not much different between the two groups, namely with a median of 720 ml and 750 ml respectively.

In table 2, the administration of propofol to brain tumor patients has the effect of changing the BIS value, namely with a mean of 49 and MAP with an average of 81.1 ± 6.5 mmHg. Furthermore, table 2 shows that the administration of dexmedetomidine to brain tumor patients has the effect of changing the BIS and MAP values, respectively, with a mean of 47 and 76.5 ± 5.7 mmHg.

Table 2 shows a comparison of the effects of dexmedetomidine and propofol administration on BIS and MAP variables. The table shows that only intraoperative MAP differs significantly between the two groups, where the dexmedetomidine group is lower than the propofol group. While in the BIS variable there is no significant difference between the Dexmedetomidine and Propofol groups at each assessment time. Table 3 shows

Table 1. Characteristics of Research Subjects (n=42)

Variables	Propofol		Dexmedetomidine		p-value
	n	%	n	%	
Sex					0.50
Male	11	52.4	12	57.1	
Female	10	47.6	9	42.9	
Age (Years)					
18-30	2	9.5	2	9.5	
31-45	8	38.1	9	42.9	
46-60	11	52.4	10	47.6	
Duration of anesthesia (minute)	262	83	275	62	0.59
Total Bleeding (ml)	720	375	750	260	0.56

Table 2. Average MAP and BIS during Intraoperative in Both Groups

Anesthetic Agent	Variables	Mean ± SD	Median	Min-Max
Propofol	BIS	48.1	49	45-50
	MAP	81.1±6,5	79.0	72-100
Dexmedetomidine	BIS	47.3	47	45-50
	MAP	76.5±5.7	76.0	64-86

Table 3. Intraoperative BGA in Both Groups

Anesthetic Agent	Variables	Mean ± SD	Median	Min-Max
Propofol	pH	7.44±0.04	7.45	7.37-7.53
	pCO_2	34.1±2.4	33.9	27-39
	HCO_3	23.3±2.7	22.5	20-30
	BE	(-)0.52±3.3	0	(-)6-7
	pO_2	121±24.9	118	88-186
Dexmedetomidine	pH	7.45	7.45	7.40-7.53
	pCO_2	33.7±2.1	33.7	29-39
	HCO3	24.5±2.9	24.3	20-30
	BE	(-)0.38	0	(-6)-4
	pO_2	111±35	107	88-183

Table 4. Differences in BGA in Both Groups

Variable	Propofol	Dexmedetomidine	p-value
pH	7.45(0.04)	7.45(0.05)	0.520
pCO_2	34.1±2.4	33.7±2.1	0.510
HCO_3	23.3±2.7	24.5±2.9	0.210
BE	0(4)	0(3)	0.820
pO_2	121±24.9	111±35	0.370

that the administration of propofol to brain tumor patients causes changes in BGA to: pH 7.45 (0.004), pCO_2 34.1 ± 2.4, HCO_3 23.3 ± 2.7, BE 0 (4), PO_2 121 ± 24.9. Meanwhile, the changes in BGA when dexmedetomidine is given to brain tumor patients, where the pH is 7.45 (0.005), pCO_2 33.1±2.1, HCO_3 24.7±2.1, BE 0(3), PO_2 111±35. Table 4 shows the difference in BGA variable values in the propofol and dexmedetomidine groups. Of the four BGA assessments, namely pH, PO_2, pCO_2, HCO and BE, there is no significant difference in both groups, either propofol or dexmedetomidine intraoperatively.

Discussion

This study compared the effects of two groups of propofol administration with dexmedetomidine in patients undergoing intracranial tumor removal at ZAH. The first group was the group that received propofol. The second group was the group that received dexmedetomidine. Based on table 1, it was found that there was no significant difference in gender between the two test groups. This is in line with research published in 2015, which stated that there was no difference in the demographic status of patients with respect to the treatment group.[10]

However, the table 1 also shows that most patients overall were male, which is in accordance with research published in 2020, which stated that malignant brain tumors are more common in men, namely 58%. However, on the other hand, women more often experience benign brain tumors.[11] In terms of age, there was also no significant difference in the two groups where the average age of patients was below 45 years in both groups, namely 44.7 years in the propofol group and 43.5 years in the dexmedetomidine group. This is in line with research published in 2015, where both the dexmedetomidine and propofol groups had similar age ranges.[10]

Based on table 2, it shows that the BIS in propofol administration has a median value of 49. This is because propofol has hypnotic and sedative effects. A 2021 meta-analysis published in research demonstrated that the closed-loop group reduced propofol doses, thereby reducing the incidence of intraoperative hypertension, hypotension, and postoperative cognitive dysfunction. The optimal BIS value is 40–60 to maintain anesthesia, with evidence suggesting a greater than 80% reduction in intraoperative awareness.[12] While intraoperative MAP in propofol administration was obtained an average of 81.1 ± 6.5 mmHg. Based on research published in 2018, where propofol administration can suppress hemodynamic responses, especially diastolic only in the early minutes, while there is no difference in MAP and pulse.[13]

Another study also stated that propofol administration reduces the incidence of postoperative hypertension, where postoperative hypertension can increase the risk of postoperative intracranial hemorrhage and cerebral hyperemia.[14] Hemodynamic stability is important for a fast and smooth recovery. In addition, acute hypertension after craniotomy can increase morbidity and mortality by worsening cerebral edema, increasing Intracranial pressure (ICP), or disrupting postoperative hemostatic conditions.[15] BIS on dexmedetomidine administration has a median value of 47. While intraoperative MAP on dexmedetomidine administration obtained an average of 76.5 ± 5.7 mmHg. Based on research published in 2022, where dexmedetomidine has a stable hemodynamic effect.[16] Hemodynamic stability caused by dexmedetomidine is the result of central and peripheral mechanisms. In addition to stable hemodynamics, the administration of dexmedetomidine can also suppress postoperative stress and inflammation and maintain patient immunity.[17,18]

Based on table 3 it shows that BGA on propofol administration causes BGA changes to: pH 7.45 (0.004), pCO_2 34.1 ± 2.4, HCO_3 23.3 ± 2.7, BE 0 (4), pO_2 121 ± 24.9. Changes in BGA in the administration of propofol to brain tumor patients, where pH 7.45 (0.005), pCO_2 33.1 ± 2.1, HCO_3 24.7 ± 2.1, BE 0 (3), pO_2 111 ± 35 were obtained. This is because dexmedetomidine is less likely to cause respiratory depression. Even in animal studies, it was found that dexmedetomidine does not have the potential to cause respiratory depression. This is because dexmedetomidine weakens the stress response during surgery due to reduced sympathetic tone mediated by alpha 2. Therefore, respiratory depression is less common in the use of dexmedetomidine.[19]

Comparison of the effects of using dexmedetomidine and propofol based on table 2 shows that the BIS value with the use of dexmedetomidine and propofol has an optimal anesthetic effect, where there is no significant difference between the two anesthetic agents in achieving optimal anesthesia levels based on the BIS Index. This is in line with a study where Dexmedetomidine and propofol have optimal effects as anesthetic regimens in maintaining the depth of anesthesia (good response to anesthesia).[20] However, research conducted in 2022 stated that the use of dexmedetomidine is better in providing the effect of anesthetic depth, especially in the first 75 minutes of surgery.[16] This is also seen in this study where in post-induction and 30 minutes of surgery, dexmedetomidine BIS tends to be lower and optimal although there is no significant difference between the two groups. The same thing was also stated in studies have shown that dexmedetomidine has a better effect of maintaining the depth of anesthesia than propofol.[9]

In intraoperative MAP there is a significant difference in intraoperative MAP when given dexmedetomidine. This is in line with some research, where dexmedetomidine has a stable hemodynamic effect even during the peak of surgical stress. Therefore, MAP in dexmedetomidine tends to be low which will later accelerate the patient's recovery period. This is because if there is an increase in MAP during the perioperative period, it can cause bleeding or swelling in the surgical area.[18-20] The more stable hemodynamic effect of dexmedetomidine is because it works on highly selective α2-adrenoceptors. By activating pre- and postsynaptic α2-adrenoceptors in the

central nervous system, dexmedetomidine will hyperpolarize noradrenergic neurons, induce inhibitory feedback loops, and reduce the release of norepinephrine, resulting in a sympatholytic effect. Dexmedetomidine has pharmacokinetic and pharmacodynamic advantages when compared to other similar α2-adrenoceptor agonists. The pharmacodynamic advantage has a significantly better affinity ratio than α2: α1-adrenoceptor, pharmacokinetically Dexmedetomidine has a shorter elimination period.[17-20]

Comparison of the effect of using dexmedetomidine and propofol on BGA shows that the administration of propofol and dexmedetomidine did not have a significant difference in both groups, both preoperatively and postoperatively, on BGA values (pH, PO_2, pCO_2, HCO_3, and BE). Other studies comparing dexmedetomidine and propofol in neurosurgery are still very limited.[16,20] The limitation in this study is that we did not adjust the controlled variables in the form of a history of hypertension and the use of anti-hypertension drugs that might affected intraoperative mean arterial pressure. In addition, sedation was not given singly, but with a combination of inhalation gas and opioids.

Conclusion

Dexmedetomidine has an effect that is not much different compared to propofol in maintaining changes in MAP, BIS and BGA in patients with intracranial tumor removal surgery.

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