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Short Communication

Oxygen saturation profile in traumatic brain injury animal model after propofol administration

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Abstract

Traumatic brain injury (TBI) is a traumatic that often leads to death due to untreatable cerebral hypoxia, indicated by oxygen saturation of <90%. Cerebral hypoxia is rarely monitored and thereby often overlooked as a cause of mortality and monitoring oxygen saturation is an accurate method to detect the condition. Propofol, an anesthetic agent, is commonly used in the management of TBI; however, its effect on brain tissue and cerebral hypoxia in TBI cases is not well understood. The aim of this study was to evaluate the profile of oxygen saturation in TBI animal model after propofol administration. A laboratory experimental study was conducted, involving 18 male *Rattus novergicus* rats (aged 4–8 weeks with weight between 150–200 grams) divided into three different treatment groups (non-TBI, TBI without propofol, and TBI with propofol). Oxygen saturation was measured regularly from day 1 to day 8 using pulse oximetry. The oxygen saturation percentages were compared between the TBI rats with and without propofol administration using independent Student t-rest. The results revealed significant reductions of oxygen saturation levels of animals within propofol-treated TBI group compared to that of the untreated-TBI group (p<0.05), with the average oxygen saturation ranging from 80.8%±6.96% vs 86.8%±5.48%. This finding suggests a reducing effect of propofol administration on oxygen saturation levels in rats with TBI and this potentially causes cerebral hypoxia.

Keywords: Traumatic brain injury, oxygen saturation, propofol, animal model, cerebral hypoxic

Introduction

Traumatic brain injury (TBI) is a form of head injury that commonly occurs worldwide. Approximately 69 million people are estimated to experience TBI each year with the highest proportion of TBI associated with traffic accidents occurred in Southeast Asia and the lowest in North America [1]. The incidence of TBI was also reportedly higher in Southeast Asia compared to Europe (1.5% vs 1.2% of the total population per year, respectively) [1]. TBI is caused by external mechanical forces, resulting in the alteration of brain function and providing evidence of brain pathology. Clinical signs of changes in brain function include gradual loss of consciousness, anterograde and retrograde amnesia, neurological deficit disorders such as

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balance disturbances, changes in vision, sensory disturbances, aphasia, muscle paralysis, and altered mental status such as disorientation and bradyphemia [2, 3]. These disorders can either be permanent or temporary [2, 3].

TBI often leads to death as a result of uncurable cerebral hypoxia [4, 5]. This condition occurs due to the presence of sudden apnea associated with abnormal breathing patterns, or the presence of airway obstruction owing to the head or neck injury. Cerebral hypoxia is rarely monitored and thus often unnoticed as a cause of death [6]. Monitoring oxygen saturation is considered an accurate method to identify cerebral hypoxia [6, 7]. Oxygen saturation is one of the determining indicators of oxygen levels in the blood that is supplied to all body tissues including the brain. Its level of <90% is considered hypoxic [8, 9]. TBI causes cerebral hypoxia since it causes damage to the brain tissue and disrupts the regulation of cerebral blood flow and metabolism. A decrease in oxygen saturation, which can trigger ischemic processes in brain tissue, is the main characteristic of cerebral hypoxia [9].

The main management of TBI is maintaining hemodynamic stability and oxygen saturation level of >95% [8]. Propofol, an anesthetic agent, is often used for the treatment of TBI. It has minimal adverse effects and a short onset of drug activation and duration, as well as provides greater ease of anesthetic depth control [10]. Propofol possesses neuroprotective effects attributed to its antioxidant activity and ability to decrease brain metabolic rate and it helps redistribute cerebral blood flow, suppress glutamate during ischemic events, and regulate apoptosis-associated proteins [10]. However, its effects on brain tissue following TBI, either neuroprotective or neurotoxic, are not fully understood [11-15]. In addition, apart from its neuroprotective effect, propofol can also cause respiratory depression, bronchospasm, laryngospasm, and apnea [16, 17]. To investigate the double effects of propofol, conducting study on its effects on cerebral hypoxia is of significant importance. The aim of this study was to determine the profile of oxygen saturation in traumatic brain-injured animal model after propofol administration.

Methods

Study design and setting

An experimental analytical study was conducted, involving 30 male *Rattus novergicus* rats (4–8 weeks old; 150–200 grams body weight) obtained from the Faculty of Veterinary Medicine, University of Syiah Kuala, Banda Aceh, Indonesia. The samples were selected using the Federer formula. The rats were divided into three treatment groups consisting of six rats each: (1) rats without TBI (Group 1); (2) rats with TBI but without propofol administration (Group 2); and (3) TBI with propofol 10 mg/kg body weight intramuscular (IM) (Group 3).

Preparation of animal model

All the 30 healthy male *R. novergicus* were maintained in a room-temperature cage and acclimatized for ten days before the experiment. The animals were fed with BR I daily *ad libitum*. Each animal was given a number on its fur for simple randomization process.

Treatment of traumatic brain injury

A modified Feeney's weight drop model was carried out by shaving and incising the right fronto-parietal (4 mm) of *R. novergicus* rats to enable bone exposure. The center of the skin opening was 1.5 mm posterior to the bregma and 2.5 mm lateral to the midline. The rats were dropped from a height of 1 meter with a load of diameter 2.5 mm. Feeney TBI model also has been used a previous study which indicated that the model could increase the levels of tumor necrosis factor alpha (TNF-α), interleukin (IL)-1β and IL-6 [18].

Oxygen saturation measurement

The level of oxygen saturation was measured one time in the morning for eight days (day 1 to day 8) by pinching the fingertips of rats with or without TBI using a pulse oximetry (Mixio, China).

Statistical analysis

A Shapiro-Wilk normality test was used to assess the normality of data distribution and independent sample Student t-rest was performed to compared the oxygen saturation between propofol and non-propofol groups each day. A *p*-value of <0.05 was considered statistically significant. All the statistical analyses were carried out using SPSS (IBM, New York, US).

Results

The profiles of the rats' oxygen saturation in each treatment group are presented in **Table 1**. Rats with TBI (Group 2) experienced decreased oxygen saturation levels (mean 86.88%) compared to the healthy group (Group1) (mean 88.31%) throughout the entire study period. However, TBI group without propofol treatment possessed better oxygen saturation profiles compared to that receiving propofol therapy (mean 80.83%).

Table 1. Oxygen saturation profile in all experiment groups

Group	Rats	Oxygen saturation (%)								
		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Mean ± SD
Non-TBI (G1)	1	88	94	87	93	90	86	90	85	88.31 ± 3.38
	2	92	86	93	88	85	94	85	91	
	3	87	91	86	86	91	83	91	85	
	4	94	90	85	94	85	87	90	85	
	5	87	87	90	83	90	93	85	90	
	6	86	90	82	90	82	86	91	90	
TBI (G2)	1	70	93	82	94	86	91	87	92	86.88 ± 5.48
	2	84	85	90	86	91	85	93	90	
	3	88	83	85	91	90	88	86	94	
	4	74	88	91	90	85	92	85	83	
	5	72	85	85	87	91	90	90	91	
	6	73	90	88	90	89	85	82	90	
TBI with propofol (G3)	1	89	85	90	84	82	81	73	73	80.83 ± 6.96
	2	74	88	73	87	79	75	89	89	
	3	65	91	78	88	72	76	84	81	
	4	83	79	84	77	85	82	87	73	
	5	90	74	95	82	91	79	88	78	
	6	84	81	66	73	74	72	77	80	

*Oxygen saturation of <90% indicates moderate hypoxia

The independent Student t-test analysis, as presented in **Table 2**, revealed significant lower in oxygen saturation after 4–8 days of propofol administration compared with non-propofol group, with the average oxygen saturation levels ranging between 77.5%–83.0%. These findings suggest a reducing effect of propofol administration on oxygen saturation levels in the rats with TBI.

Table. 2. Comparison of oxygen saturation after traumatic brain injury in animals without or with propofol administration

Time	Group	Oxygen saturation					*p*-value*
		Mean	Median	SD	Minimal	Maximum	
Day 1	Non-propofol	76.83	73.50	7.33	70.00	88.00	0.437
	Propofol	80.83	83.50	9.62	65.00	90.00	
Day 2	Non-propofol	87.33	86.50	3.72	83.00	93.00	0.174
	Propofol	83.00	83.00	6.23	74.00	91.00	
Day 3	Non-propofol	86.83	86.50	3.43	82.00	91.00	0.254
	Propofol	81.00	81.00	10.81	66.00	95.00	
Day 4	Non-propofol	89.67	90.00	2.88	86.00	94.00	0.015
	Propofol	81.83	83.00	5.85	73.00	88.00	
Day 5	Non-propofol	88.67	89.50	2.58	85.00	91.00	0.024
	Propofol	80.50	80.50	7.06	72.00	91.00	
Day 6	Non-propofol	88.50	89.00	3.02	85.00	92.00	<0.001
	Propofol	77.50	77.50	3.83	72.00	82.00	
Day 7	Non-propofol	87.17	86.50	3.87	82.00	93.00	0.209
	Propofol	83.00	85.50	6.54	73.00	89.00	
Day 8	Non-propofol	90.00	90.50	3.74	83.00	94.00	0.003
	Propofol	79.00	79.00	5.97	73.00	89.00	

* Analyzed using independent sample Student t-test

Discussion

In the present study, administration of propofol significantly reduced oxygen saturation of the animals compared to those within untreated TBI group. The animals experienced moderate cerebral hypoxia after 4–8 days being treated with 10 mg/kg of propofol, with average oxygen saturation levels ranging between 72–89% (**Table 2**). This finding suggests that administration of propofol has a risk of reducing oxygen saturation in rats with TBI, which is assumingly associated with its adverse effects on respiratory system such as causing respiratory depression.

Induction of propofol as an anesthetic agent has exhibited adverse effects such as pain during injection. Its induction in the respiratory system can lead to respiratory depression, bronchospasm, laryngospasm, and apnea. In the cardiovascular system, propofol injection can result in hypotension, bradycardia, tachycardia, and arrhythmias, whereas its effects on the central nerve include dizziness, headache, euphoria, confusion, seizures, myoclonic clonic movements, opisthotonus, nausea, and vomiting [19-22].

Since propofol has been widely used in the management of TBI, anticipating decreased oxygen saturation postoperatively is of significant importance. To evaluate the patient's oxygenation status, oxygen saturation can be used as it only requires a non-invasive pulse oximetry [23]. A study found that hypoxemia often occurred postoperatively with respiratory complications, where 35% of patients experienced hypoxemia with oxygen saturation of <90% and 12% of them experienced severe hypoxia with oxygen saturation of <85% [24].

TBI often leads to death as a result of untreatable cerebral hypoxia [4, 5]. There are several ways to determine the prognosis of TBI, including by monitoring cerebral perfusion, in which a decrease in cerebral perfusion can worsen cerebral hypoxia [25]. A study suggested a significant correlation between decreased oxygen saturation and mortality among head-injured patients [26]. Another study reported that oxygen saturation is inversely related to the risk of death, where an increase in oxygen saturation reduces the risk of death [27]. One percent (1%) increase in oxygen saturation has resulted in an 8% decrease in the risk of death [28].

To anticipate the occurrence of cerebral hypoxia in the management of TBI, especially in the administration of propofol, oxygen therapy should be considerate. A study suggested that postoperative oxygen therapy could prevent hypoxemia because there were 19% of patients who were transferred without oxygen experiencing a decrease in oxygen saturation while only 0.8% those who were given oxygen experiencing a decrease in oxygen saturation [29].

Conclusion

Administration of propofol has the risk of decreasing oxygen saturation in TBI rats. To anticipate the occurrence of cerebral hypoxia during the management of TBI, especially in the administration of propofol, providing oxygen therapy should be considered in daily medical practice.

Ethics approval

This study was approved by the Veterinary Research Ethics Committee of the Faculty of Veterinary, Universitas Syiah Kuala, Banda Aceh, Indonesia, No. 208/KEPH/III/2023.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

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