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Correlation Between Blood Gas Indicators and Outcome of Status Epilepticus Patients in Prof. Dr. I.G.N.G. Ngoerah General Hospital 2019-2020

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ABSTRACT

Background: Status epilepticus (SE) is an emergency in which immediate and effective care is needed. Metabolic acidosis often occurs after SE. Peripheral vasoconstriction will enhance perfusion and adequacy of oxygenation to the most active metabolic organs which are the brain and muscles, so hypoventilation and hypoxia will occur.
Aim: This study aims to present the general description of SE patients in Prof. Dr. I.G.N.G. Ngoerah General Hospital and to analyze the correlation between blood gas indicators and SE patient outcomes.
Method: This is a cross-sectional study of SE patients that were admitted at Prof. Dr. I.G.N.G. Ngoerah General Hospital from January 2019 to December 2020 with a consecutive sampling method. The patient's data were acquired from the medical record and the hospital's information system. Statistical tests were done by the SPSS program.
Results: Hundred eight SE patients are enrolled in this study. The types of seizure are focal seizure (N=55) and general seizure (N=53). There are 51 (47.2%) patients who survived and 57 (52.8%) patients who died during medical care. Thirty-four patients needed intensive care. The duration of care is between 2 to 37 days. Factors related to mortality are comorbidity (p=0.00), renal failure (p=0.05), pneumonia (p=0.00), sepsis (p=0.00), intensive care (p=0.01), longer duration of care (p=0.008), and blood gas analysis abnormality (p=0.011) with 2.7 OR.

Conclusion: Blood gas analysis is correlated with worse outcomes in patients with SE.

Keywords: blood gas, status epilepticus, outcome

INTRODUCTION

Status Epilepticus (SE) is an emergency in which urgent and effective care is needed. In patients with SE, time is crucial. Faster care will decrease the damage to the nerves, systemic complications, substantial morbidity, and mortality depending on the type of status, duration, age, and etiology.[1] SE is a neurological emergency in which someone continuously or repeatedly suffers from a seizure, with each episode happening for five minutes or more without the return of consciousness in between the seizure episodes.[2] In SE, the severity depends on the type of seizure, underlying pathology, comorbidity, and medical management that is appropriate and on time. SE generally can be categorized as convulsive or nonconvulsive depending on if there is any motoric activity or not in the clinical presentation. Subtypes of SE further are marked by semiology, etiology, the pattern of electroencephalogram, duration, and the response from the drugs.[3] The outcome of SE is influenced by many factors, such as age, gender, etiology, duration, type of seizures, level of consciousness, and complication. SE can have acute complications such as respiratory failure and hypoxia, acid-base disturbances, glucose metabolism disturbances, infection and inflammatory response, thermal dysregulation, heart dysfunction, rhabdomyolysis, renal disturbances, physical trauma, and gastrointestinal disturbances.[4]

Prolonged SE can disturb acid-base homeostasis. Metabolic (lactic) acidosis often happens after SE. Over-contracting muscles produce glycogen and anaerobic glycolysis, that further augment the production of lactic acid from pyruvic acid. Lactic acidosis is usually defined by a pH of less than 7.35 and a concentration of more than 5 $mmol^{-1}$. The most important cause is sepsis, cardiogenic shock, severe hypoxemia, liver failure, and intoxication.[5]

For the first 20 to 40 minutes of SE, the homeostatic mechanism works to compensate for extreme metabolic demand from the brain area where the seizure happens and from the contracting muscles. There is an early enhancement of the brain's blood flow with tachycardia, increased blood pressure, and dilation of the brain's blood vessels. Peripheral vasoconstriction will enhance perfusion and adequacy of oxygenation to the most active metabolic organs which are the brain and muscles, so hypoventilation and hypoxia will occur and respiratory acidosis will happen and worsen the existing lactic acidosis.[6]

For all those reasons, this study was made to present the general description of SE patients of Prof. Dr. I.G.N.G. Ngoerah General Hospital and to analyze the relationship between blood gas indicators with the SE patients' outcome of Prof. Dr. I.G.N.G. Ngoerah General Hospital.

MATERIALS AND METHODS

This is a cross-sectional study and was done by collecting the data of SE patients who were admitted at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar, Bali, Indonesia from January 2019 to December 2020. The inclusion criteria were the age of 18 years and over and meeting the SE criteria according to the 2017 ILAE definition. Exclusion criteria were patients who are pregnant and have incomplete data.

There were 108 samples obtained by consecutive sampling. Patient gender, age, etiology, type of seizure, comorbidities, intensive care, length of stay, outcome, blood glucose, hematological values, and blood gas results were obtained from medical records and the hospital's information system. The patient's blood gas analysis result was divided into acidosis and alkalosis, which would be compared with normal patient blood gas results and the patient's outcome would be observed. Laboratory data standards used were: pCO2 (35-45 mmHg), pO2 (80-100 mmHg), HCO3 (22-26 mEg/lt), and pH (7.35-7.45). A PaCO2 level > 45 mmHg was defined as hypercapnia and a PaO2 level <70 mmHg was defined as respiratory failure, and an arterial pH <7.35 was defined as acidosis.

STATISTICAL METHODS

The data collected for each variable was presented in the form of a table of frequency and size of data concentration according to variable types. All variables were tested for normality by the Kolmogorov-Smirnov test. If the data was normally distributed, a comparative parametric test (Chi-Square and unpaired T-test) would be performed for nominal data and a correlative test (Pearson) for numerical data. If the data was not normally distributed, a comparative non-parametric test (Mann-Whitney) would be performed for nominal data and a correlative test (Spearman) for numerical data. The results were declared significant if the p-value <0.05. Statistical tests were carried out using the SPSS program.

RESULTS

This study involved 108 SE patients, consisting of 58 men and 50 women aged 18-95 years (mean age 49.9 years). The types of seizures included focal (n=55) and general (n=53) seizures. A total of 51 patients survived and 57 patients died while being treated. Several patients requiring intensive care 34 (31,5%). The length of stay ranged from 2 to 37 days.

Table 1. Characteristics of SE patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital, 2019-2020

Characteristics	**Frequency (%)**	**Average (Min-Max)**
Gender		
Male	58 (53.7)	
Female	50 (46.3)	
Age		49.9 (18-95)
Etiology		
Stroke/Vascular	33 (30.6)	
Tumor	12 (11.1)	
Trauma	2 (1.9)	
Metabolic	33 (30.6)	
Infections	20 (18.5)	
Idiopathic	8 (7.4)	
Seizure types		
Focal aware	3 (2.8)	
Focal impaired awareness	15 (13.9)	
Focal to bilateral	27 (25)	
General	63 (58.3)	
Comorbid		
Present	79 (73.1)	
Absent	29 (26.9)	
Comorbid types		
Diabetes	22 (20.4)	
Hypertension	43 (39.8)	
Kidney failure	42 (38.9)	
Pneumonia	30 (27.8)	
Cardiovascular	32 (29.6)	
Sepsis	36 (33.3)	
Malignancy	6 (5.6)	
Intensive care		
Yes	34 (31.5)	
No	74 (68.5)	
Outcome		
Survived	51 (47.2)	
Dead	57 (52.8)	
Length of stay (LOS)		8.8 (1-37) days
pH		7.36 (6.83-7.64)
pO2		130 (47.2-246.6) mmHg
pCO2		42.56 (14.60-88.50) mmHg
HCO3-		22.6 (4.90-128.50) mmol/L

The mean pH of 108 patients was 7.36, with the lowest pH level of 6.83, lowest patient's pO2 was 47.2 mmHg. The average pCO2 was 42.5 mmHg with the highest level being 88.5 mmHg. The lowest HCO3- level in the patient was 4.90 mmol/L with an average of 22.6 mmol/L. The comparative test results are shown in Table 2 with each variable based on the outcome. Patients were grouped into patients who experienced disturbances in the form of acidosis or alkalosis with metabolic or respiratory, which were included in the category of blood gas disorders. Patients with type 1 and 2 respiratory failure and mixed types were also included in the comparative analysis with the category of patients with respiratory failure with nominal variables.

Table 2. Comparative analysis of research variables on patient outcomes

Factors	**Outcome**		**p-value**	**Statistical Analysis**
	Survived (n=51)	**Dead (n=57)**		
Gender				
Male	27 (52.9%)	31 (54.4%)	0.881	Chi-Square
Female	24 (47.1%)	26 (45.6%)		
Age	49.8 (18-95)	50.0 (18-78)	0.212	Non-paired T-test
Comorbid				
Present	28 (54.9%)	51 (89.5%)	0.000*	Chi-Square
Absent	23 (45.1%)	6 (10.5%)		
Comorbid type				
Diabetes	13 (25.5%)	9 (15.8%)	0.211	Chi-Square
Hypertension	18 (35.3%)	25 (43.9%)	0.364	

Kidney failure	15 (29.4%)	27 (47.4%)	0.050*	
Pneumonia	4 (7.8%)	26 (45.6%)	0.000*	
Cardiovascular	14 (27.5%)	18 (31.6%)	0.639	
Sepsis	4 (7.8%)	32 (56.1%)	0.000*	
Malignancy	2 (3.9%)	4 (7.0%)	0.483	
Intensive Care				
Yes	8 (15.8%)	26 (45.6%)	0.001*	Chi-Square
No	43 (84.3%)	31 (54.4%)		
LOS	10 (2-37) days	6 (1-25) days	0.008*	Non-paired T-test
Blood Gas Problem				
Yes	17 (15,7%)	33 (30.6%)	0.011*	Chi-Square
No	34 (31.5%)	24 (22.2%)		
Breathing failure				
Yes	15 (13.9%)	18 (16,7%)	0.87	Chi-Square
No	36 (33.3%)	39 (36,1%)		

ICU= Intensive Care Unit, LOS= Length of Stay, p is significant if <0.05*

From the comparative analysis, it was found that the presence of comorbidities, kidney failure, pneumonia, sepsis, intensive care, length of stay, and blood gas conditions in patients with acidosis/alkalosis were related to the patient's outcome. It was found that 33 patients, 30.6% of the total population, had blood gas disorders and died, while only 17 patients lived, which accounted for 15.7% of the total population. There was a total of 33 patients with respiratory failure in the population with 18 (16.7%) patients dying, whereas in patients without respiratory failure, 39 (36.1%) patients died.

DISCUSSION

This study was conducted to see how blood gas disturbances could affect the outcome of patients with SE. Patients with blood gas changes in the form of acute acid-base disturbances were found to present with worse outcomes compared to patients who did not experience blood gas disorders. The literature emphasizes lactic acidosis as the most common disturbance of acid-base homeostasis in patients with seizures.[7] Metabolic disorders, deficiencies of substrates necessary for cell metabolism or cell membrane function, intracellular accumulation of toxic substances, and especially changes in plasma osmolality and electrolyte disturbances, increase nervous excitability and further increase the risk of seizures.[8] SE can disrupt blood gas exchange which plays an important role in causing mortality to patients with respiratory disorders and epileptic seizures if not treated promptly. The main etiological causes of symptomatic seizures are metabolic changes, the most important of which are a decrease in mean arterial PaO2 and pH value. Respiratory acidosis in patients with SE can be caused by the decreased respiratory drive as a result of previous seizure activity in central respiratory neurons, contraction of the diaphragm during spasms which is followed by peripheral respiratory muscle fatigue, or both.[9,10]

Respiratory failure is a complication of SE that can occur if it is not treated properly. This can be possibly caused by the prompt treatment that had been done beforehand, therefore adequate re-ventilation occurred which resulted in stable pO2 and pCO3- levels. Experimental studies have shown that prolonged episodes of hypoxia caused by decreased pO2 saturation can increase the severity of hypoxic-ischemic brain damage.[11] In addition, increased power output requirements can be imposed on the ventilation pump due to the amplified mechanical load. These loads reflect increased upper airway resistance and injury to the lungs from aspiration, which will result in respiratory compromise. Several studies have found a relationship between epileptic seizures and the severity of brain damage and acute death. Severe and prolonged postictal hypoxemia and hypercapnia in patients with partial onset seizures lead to impaired respiratory function and increase the risk of sudden death in epilepsy (SUDEP).[12]

Peri-ictal apnea is also associated with severe prolonged hypoxemia which is a potential predictor of SUDEP. This finding shows the correlation between death and hypoxemia, hypercapnia, and respiratory acidosis. These parameters can affect the prognosis of patients with respiratory diseases who experienced seizures and epilepsy. Abnormality of blood gas in patients with respiratory disorders can affect death because of a possible unknown mechanism in seizure pathophysiology, and a recent large-scale study is needed to unveil the possible mechanism.[13]

Patients with normal arterial blood gas analysis in admission have a good outcome so they can be recovered from SE. There is plenty of confounding factors that can cause respiratory acidosis and those factors cannot be excluded in a retrospective review. For example, central depression from respiratory control by benzodiazepine can cause respiratory acidosis from hypoventilation in some patients.[14]

The limitation of this research is the number of samples and the design which did not control the confounding factors that can affect outcomes. Therefore, only general descriptions are expected in this study. This limitation hinders the interpretation of the results. Nevertheless, as a pilot study, with a more specific design, some variables can be controlled to determine a closer relationship and multivariate analysis.

CONCLUSION

We discovered that the disturbance of blood gas was correlated with poor outcomes in patients with SE. It can result in various complications which might lead to patient death. Furthermore, as proven by the alteration of blood gas, hypoxemia, and respiratory acidosis are related to the development of symptomatic seizures. In this research, respiratory failure does not correlate with poor patient outcomes because of rapid initial management and appropriate re-ventilation. Therefore, it is important to carefully consider these factors if they are observed in patients with status epilepticus. We also found that comorbidity, such as kidney failure, pneumonia, sepsis, intensive care, and length of stay in the hospital have a meaningful correlation with the outcome (mortality). A more specific study design is needed to control the confounding factors to further determine the correlation between blood gas with SE' patient outcome at Prof. Dr. I.G.N.G. Ngoerah General Hospital.

Declaration by Authors

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