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Research Article

Effect of Hypoxia on Severity Outcome of Early Onset Acute Ischemic Stroke: A Correlative Study and Review

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Abstract

Background And Objective

Stroke is the leading cause of long-term disability. One of the factors that play a role in exacerbating stroke is hypoxia. Hypoxia in the early onset of acute stroke can cause significant side effects in ischemic brain areas and may cause different neurological consequences depending on multiple factors. We hypothesized that the oxygen saturation level in the early days of acute onset would correlate with the outcome of patients with acute ischemic stroke. This study investigated the association between oxygen saturation in early onset acute ischemic stroke and the National Institutes of Health Stroke Scale (NIHSS) score.

Materials and methods

We conducted a cross-sectional study at Siloam Hospital, Lippo Village, between January and April 2021. Research data were collected from the medical records of patients with the first onset of acute ischemic stroke who met the inclusion and exclusion criteria. Data were processed using a chi-square test with IBM SPSS 26.0.

Results

95 Subjects (mean age 59.20 ± 1.254) were collected. The study showed significant association between hypoxia and higher NIHSS scores (p = 0.001, odds ratio [OR] = 0.099, confidence interval [CI] 95% = 0.021–0.461).

Heart diseases such as congenital heart disease, coronary heart disease, and heart failure showed a significant association with higher NIHSS scores and lowered oxygen saturation levels (p = 0.023, OR (95%CI) 0.265 (0.080–0.880).

Conclusion

Our study indicates that a lower oxygen saturation level at early onset correlates with a higher NIHSS score and is associated with a poor prognosis. Oxygen supplementation in patients with ischemic stroke is crucial for better outcomes.

Keywords: acute ischemic stroke; hypoxia; prognostic factor; nihss score

Introduction

Stroke is the second leading cause of death worldwide, with a mortality rate of 5.5 million deaths per year. [1,2] The mortality rate is worse in developing countries, where the management of stroke is not well established. Interrupted blood flow can lead to a lack of oxygenation of the brain cells, causing apoptosis and necrosis of the brain, which manifests as neurological deficits [3–5]. In addition, stroke causes a high disability rate in surviving patients, creating not only short-but also long-term permanent problems. Thus, acute management of stroke is pivotal [1,2]

These neurological deficits vary in symptoms and severity depending on the location and extent of the lesion in the brain [3]

Many scales are currently used to assess the progression of stroke, including the National Institutes of Health Stroke Scale (NIHSS) [6]

The severity of stroke is highly dependent on establishing the correct diagnosis and treatment, especially regarding the onset of events, arrival at the hospital, and other predisposing factors that occur at the time of

stroke. One of the important factors that play a role in exacerbating stroke is hypoxia [7].

Hypoxia is commonly found in stroke patients in the early days of hospitalization and is associated with higher mortality and morbidity rates. However, hypoxic conditions are often underdiagnosed and untreated, which may be attributed to conditions complicated by stroke, such as aspiration and respiratory dysfunction. Hypoxia that occurs in the first few hours can cause significant side effects in ischemic brain areas and, if left untreated, may cause different neurological consequences depending on multiple factors such as onset, the severity of hypoxia, and level of tissue perfusion [7,8]

The American Heart Association/American Stroke Association guidelines recommend administering oxygen supplementation to maintain oxygen saturation > 94% in stroke patients [9]

Comprehensive management of stroke is essential for better patient outcomes. Therefore, the present study was conducted based on the hypothesis that the oxygen saturation level at acute onset would correlate with the outcome of patients with acute ischemic stroke.

Materials and Methods

We conducted a single-center cross-sectional study at Siloam Hospital, Lippo Village, between January and April 2021. Research data were collected from the medical records of patients treated in the stroke unit with the first onset of acute ischemic stroke. Data were collected using consecutive sampling, and the patients with their first acute ischemic stroke with an onset of < 48 hours were included. Patients with incomplete medical record data, lung infection, recurrent stroke, altered consciousness level, and intubation were excluded from this study [9].

Oxygen saturation was measured by pulse oximetry for 2 min, and the NIHSS score was obtained at admission. Neurologists confirmed the diagnosis of ischemic stroke based on the physical and neurological examination in combination with the results of computerized tomography (CT) [9]

Other patient information, such as a history of hypertension, diabetes mellitus (DM), heart disease, dyslipidemia, and smoking, was also collected for demographic data. Results with a p-value < 0.05 were considered statistically significant.

Data were processed using IBM SPSS 26.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA) and analyzed using the chi-square statistical test method and Logistic Regression model The Pelita Harapan University Ethics Committee approved our study (ethical review number 041/K-LKJ/ETIK/I/2021).

Variable (n = 95)	Frequency	Percentage	Means±SD
Gender			
Man	58	61.1	
Woman	37	38.9	
Age			
<50 years	26	27.4	59.08±12.27
≥50 years	69	72.6	
Work			
Doesn't work	31	32.6	
Work	64	67.4	
Risk Factors			
Hypertension	77	81.1	
Diabetes Mellitus	39	41.1	
Dyslipidemia	25	26.3	
History of Heart Disease	15	15.8	
History of Smoking Habits	47	49.5	
NIHSS Score (0-42)			
NIHSS Lightweight (<5)	36	37.89	8.05±6.33
Nihss Medium – Very heavy (5-42)	59	62.11	
Oxygen Saturation			
Normal (95-100%)	77	81.05	95.52±6,991
Hypoxia (<95%)	18	18.94	
Hb Level			
Normal (11.70-15.50)	69	72.6	13.89±1.62
Abnormal (<11.70 / >15.50)	25	27.4	
Blood Glucose Levels During			
Normal (<100 mg/dL)	18	18.9	176.75±101.19
High (≥100 mg/dL)	77	81.05	

Table 1: Baseline Characteristics of the patients

Results

Ninety-five subjects were included in this study, with male predominance (61%). Most patients were between 51 and 60 years old (34.2%, n: 25).

The mean age was 59.20 ± 1.254 years. The data distribution showed 81.05% of subjects with normal saturation levels (95%–100%) and 18.94% with hypoxia (< 95%). Moderate to severe NIHSS scores (NIHSS ≥5) were observed in 62.1% of subjects. Most of the patients had a history of hypertension (81.1%), followed by smoking habits (49.5%), diabetes mellitus (41.1%), dyslipidemia (26.3%), and heart disease (15.8%). High levels of non-fasting blood glucose were found in 81.05% of the subjects.

The study showed significant correlation between hypoxia and higher NIHSS scores (p = 0.001, odds ratio [OR] = 0.099, confidence interval [CI] 95% = 0.021–0.461).

Risk factors such as sex, hypertension, diabetes mellitus, dyslipidemia, and smoking habits were not significantly correlated with higher NIHSS scores. However, heart diseases such as congenital heart disease, coronary heart disease, and heart failure significantly correlate with higher NIHSS scores and lowered oxygen saturation levels (p = 0.023, OR 0.265, 95% CI = 0.080–0.880).

Multivariate logistic regression data showed that, among other independent variables, only heart disease and oxygen saturation levels influenced the NIHSS score (p = 0.043, p = 0.003, respectively).

A negative Pearson correlation test indicated that this study's lower oxygen saturation level correlated with a higher NIHSS score and vice versa (p = -0.318).

Variable (n = 95)	Its O2 <95%	SaO2 ≥95%	OR (95%CI)	P-value
Age				
<50 years	6	18	1.639 (0.538-5.988)	0.381
≥50 years	12	59		
Gender				
Man	10	48	1.324 (0.469-3.738)	0.595
Woman	8	29		
Hypertension				
Already	15	62	0.827 (0.212-3.227)	0.784
Don't	3	15		
Diabetes Mellitus				
Already	6	33	1.500 (0.510-4.412)	0.460
Don't	12	44		
Dyslipidemia				
Already	4	21	1.313 (0.388-4.442)	0.661
Don't	14	56		
History of Heart Disease				
Already	6	9	0.265 (0.080-0.880)	**0.023***
Don't	12	68		
History of Smoking Habits				
Already	9	38	0.974 (0.349-2.719)	0.960
Don't	9	39		
NIHSS Score				
<5	2	43	0.099 (0.021-0.460)	**0.001***
5-42	16	34		
Hb Level				
Normal (11.70-15.50)	12	57	0.702 (0.233-2.118)	0.528
Abnormal (<11.70 / >15.50)	6	20		
Blood Glucose Levels During				
Normal (<100 mg/dL)	2	16	0.477 (0.099-2.290)	0.346
High (≥100 mg/dL)	16	61		

***Significant P Value<0.05

Table 2. Chi- Square Univariate data

	Variable (n = 95)	Exp(B)	95% CI	P-value
Step 1	Age	1.119	0.263-4.760	0.879
	Gender	2.082	0.458-9.473	0.343
	Hypertension	1.971	0.329-11.769	0.457
	Diabetes Mellitus	**2.316**	**0.590-9.092**	**0.229***
	Dyslipidemia	1.092	0.252-4.732	0.906
	Heart Disorders	**0.234**	**0.053-1.022**	**0.054***
	Smoke	0.886	0.207-3.786	0.870
	NIHSS	**0.063**	**0.011-0.368**	**0.002***
	Hb Level	0.653	0.152-2.806	0.567
	Glucose Levels	**0.204**	**0.030-1.403**	**0.106***
Step 2	Diabetes Mellitus	2.544	0.704-9.190	0.154
	Heart Disorders	**0.228**	**0.055-0.946**	**0.042****
	NIHSS	**0.071**	**0.014-0.373**	**0.02****
	Glucose Levels	0.317	0.059-1.704	0.181
Step 3	**Heart Disorders**	**0.043**	**0.065-0.955**	**0.043****
	NIHSS	**0.003**	**0.20-0.460**	**0.003****

*p<0.25 value; **p Value<0.05

Table 3. Multivariate Data Logistic Regression

Discussion

Oxygen saturation (SpO_2) measurement using pulse oximetry is one of the blood oxygen level measurement methods that is widely available and cost-effective[7]. This method has been proven reliable in assessing oxygen saturation, especially > 90%. Hypoxia is a condition where the oxygen saturation is < 95%, which can worsen brain ischemia and lead to an unfavorable prognosis8. A study by Rauniyar et al. revealed that pulse oximetry measurement could be used as an alternative to arterial blood gas to detect hypoxia up to SpO_2 > 90%. The present study showed that 18.94% of subjects had low oxygen saturation < 95% [10]

Another study reported that the oxygen extraction fraction (OEF) increases during acute stroke. OEF, defined as the ratio of blood oxygen tissue from the blood flow, acts as one of the two compensatory mechanisms when cerebral perfusion pressure (CPP) falls, highlighting the importance of adequate oxygen delivery in stroke [11].

Hypoxia during the first few days after a stroke may adversely affect cells in the ischemic penumbra, worsening neurological deficits and clinical outcomes.

The condition of neurological deficits can be assessed using the NIHSS score. The current study presented 62.1% of subjects with a moderate to severe NIHSS score (NIHSS ≥ 5) and showed significant correlation with oxygen saturation < 95% (p =0.001), OR = 0.099, 95% CI = 0.021–0.461). These data prove that hypoxia plays a major role in higher NIHSS scores.

One of the most important findings of this study is the negative Pearson correlation test, which indicates that a lower oxygen saturation level correlates with a higher NIHSS score and vice versa (p = -0.318). This result showed that even a slight decrease in the normal oxygen saturation range (95%–99%) would also give rise to higher NIHSS scores. These findings indicate that a disproportion in cerebral tissue supply and oxygen demand promotes a sequence of biochemical and molecular events that lead to neuronal cell death.

Oxygen is essential for the survival of aerobic organisms and is crucial for the survival of the penumbra during ischemic stroke. Therefore, oxygen saturation is essential to maintaining the penumbra 12]. Severe and prolonged reductions in cerebral blood flow following low oxygen saturation levels lead to more deprivations in oxygen and glucose delivery, leading to the build-up of potentially toxic substances.

The pathophysiology of ischemic stroke at the cellular level is composed of numerous processes, including increased intracellular calcium levels, excitotoxicity, free radical-mediated toxicity, cytokine-mediated toxicity, activation of glial cells, and infiltration of leukocytes, which can later lead to ischemic necrosis. Cerebral ischemia results in a dramatic reduction in blood flow and subsequent necrotic cell death [15]. These hemodynamic changes can reduce ATP, causing metabolic stress, energy failure, ionic perturbations, and ischemic injury. This incidence is highly threatening for neurons, as the brain is vulnerable to oxidative stress due to its high rate of oxidative metabolic activity [14,16].

Oxidative stress may lead to calcium accumulation, mitochondrial dysfunction, and production of reactive oxygen radicals, which are essential cell death mechanisms following ischemic insults [15,16]

To summarize, hypoxia at the early onset can lead to significant side effects in ischemic brain areas, which are associated with poor prognosis, higher NIHSS score, and higher mortality rate [6,9.17,18].

Further, our study found that heart diseases such as congenital heart disease, coronary heart disease, and heart failure showed a significant correlation with higher NIHSS scores and lowered oxygen saturation levels. Moreover, multivariate logistic regression data showed that, among other independent variables, only heart disease and oxygen saturation levels influenced the NIHSS score. The results of this study indicate that cardiovascular disease can induce hypoxia during the early onset of acute stroke and lead to the worsening of the stroke condition.

This is because the heart is a circulatory system that distributes blood flow to each tissue and transports oxygen and nutrients. Disturbance in the circulatory system would decrease oxygen delivery, leading to tissue hypoxia, which occurs in several cardiovascular disorders, including atherosclerosis, pulmonary arterial hypertension, and heart failure. This would also explain how cardiovascular disease worsens the prognosis of patients with stroke [19,20].

Limitations

The accuracy of the criteria for early stroke onset needs to be emphasized so that each sample has the same range of onset

Conclusion

Our study indicates that a lower oxygen saturation level at early onset correlates with a higher NIHSS score and is thus associated with a poor prognosis. Oxygen supplementation is crucial for better outcomes in patients with ischemic stroke.

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