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# COMMUNIST CAROTIC ARTERY CLOSURE DURATION EFFECT ON WISTAR WHITE RATS MOTORIC

## *(PENGARUH LAMANYA PENYUMBATAN PEMBULUH DARAH ARTERI KAROTIS KOMUNIS TERHADAP MOTORIK TIKUS PUTIH WISTAR)*

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**ABSTRACT**

The carotid artery consists of two carotid arteries, namely the dextra communist artery and the sinistra, the main blood vessels in the neck that supply blood to the brain, the basal ganglia, which have the function of regulating the motor functions of the body. The communal carotid arteries blocked flow can cause brain ischemia. It is due to hypoxia due to a lack of oxygen supply carried by the brain, resulting in motor body function disorders, incredible blockages in the carotid arteries that supply blood to the brain, and neurons as regulators of motor functions. The research is a literature study that has relevance to the formulation of the problem meets the criteria and research objectives to determine the effect of the length of the blockage of the arteries of the carotid artery of the communist to the motor function of the Wistar strain rats. The results of a literature review or literature studies in some previous scientific research journals indicate if the blockage of the arteries of the

communal carotid arteries affects the disruption of motor function caused by hypoxia and damage to neurons and brain tissue in motor neurons. The conclusion is that the blockage and the duration of blockage of the communal carotid arteries affect motor function.
**Keywords:** carotid artery; blockage; ischemic stroke

***ABSTRAK***

*Arteri karotis comunis merupakan pembuluh darah utama di leher yang mensuplai darah ke otak dan ganglia basalis, yang salah satu fungsinya mengatur fungsi motorik tubuh. Tersumbatnya aliran pembuluh darah arteri karotis komunis dapat menyebabkan terjadinya iskemia otak akibat hipoksia karena kekurangan jumlah pasukan oksigen yang dibawa oleh darah ke otak sehingga terjadi gangguan fungsi motorik tubuh. Penelitian ini merupakan penelitian studi kepustakaan atau literature review yaitu jenis penelitian yang mengumpulkan, mengelola, menggunakan dan mengkaji data penelitian bersumber dari jurnal penelitian ilmiah, naskah penelitian terdahulu dan buku teks yang memiliki relevansi dengan rumusan masalah yang memenuhi kriteria dan tujuan penelitian untuk mengetahui pengaruh lamanya penyumbatan pembuluh darah arteri karotis komunis terhadap fungsi motorik tikus putih galur wistar. Hasil literature review atau studi kepustakaan menunjukan jika penyumbatan pembuluh darah arteri karotis komunis dapat berpengaruh terhadap terganggunya fungsi motorik yang diakibatkan karena hipoksia dan kerusakan neuron serta jaringan otak pada motor neuron. Kesimpulannya adalah penyumbatan dan durasi lamanya penyumbatan pembuluh darah arteri karotis komunis berpengaruh terhadap fungsi motorik*.
***Kata Kunci:*** *arteri karotis; penyumbatan; stroke iskemia*

## INTRODUCTION

The carotid arteries are the main blood vessels in the neck that supply blood to the brain, neck, and face. The carotid artery is a branch of the aortic arch that consists of two arteries, namely the right common carotid

artery and the left common carotid artery. Each common carotid artery divides into the internal carotid artery and the external carotid artery. The internal carotid artery is a blood vessel that supplies blood to the brain. These arteries supply the brain, which has a vital role in regulating the body's motor function.[1]

One of the blood vessel disorders is the blockage of blood vessels that can cause ischemia. Prolonged blockage of the carotid arteries can cause several abnormalities. Blocking blood vessels for more than 3 minutes can cause irreversible cerebral ischemia in the cerebral cortex and basal cell nucleus. In contrast, if the blood vessels are blocked for 5 minutes to 10 minutes, it can cause loss of consciousness because the oxygen supply carried by blood flow to the brain is reduced. And cause hypoxia which results in ischemic stroke.[2] Cerebral Blood Flow (CBF) varies by 3-4% (2cc/100g/min), everyone mmHg changes in partial pressure of carbon dioxide (PaCO2) between 28 -80 mmHg and response changes occur within 20-30 seconds, this is called carbon dioxide (CO2) reactivity. Symptoms that arise are caused by damage to motor neurons in the pyramidal pathway. Disorders of blood vasculature in the brain can result in lesions of the upper motor neurons (UMN) and loss of control over motor movements.[3-4] Auto-regulatory mechanisms in which cerebral blood flow is maintained constant within the mean arterial pressure range of 50-150 mmHg with the following mechanism: rapid vascular response.[3-4] The occurrence of disturbances in motor function depends on the duration of blood vessel blockage and neurological damage or neurological deficits, especially neurons in the precentral gyrus area of the frontal area of the brain or motor cortex. Each event has a different impact. Symptoms that arise are caused by damage to motor neurons in the pyramidal pathway. Disorders of blood vasculature in the brain can result in lesions of the upper motor neurons (UMN) and loss of control over motor movements.[3-4]Auto-regulatory mechanisms in which cerebral blood flow is maintained constant within the mean arterial pressure range of 50-150 mmHg with the following tool: rapid vascular response.[3-4] The occurrence of disturbances in motor function depends on the duration of blood vessel blockage and neurological damage or neurological deficits, especially neurons in the precentral gyrus area of the frontal area of the brain or motor cortex. Each event has a different impact. Symptoms that arise are caused by damage to motor neurons in the pyramidal pathway. Disorders of blood vasculature in the brain can result in lesions of the upper motor neurons (UMN) and loss of control over

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Loss of blood supply to the brain causes damage to the integrity of neuron cell membranes caused by an imbalance between electrolytes, glutamate-mediated excitotoxicity, oxidative stress, mitochondrial dysfunction, and apoptosis. They resulted in a decrease in neurological function.[5] WHO data in 2015 states that 15 million people in the world experience a stroke each year. Of these 15 million, at least 2.5 million men and 3 million women die from stroke.[5] The prevalence of stroke in Indonesia based on Riskesdas 2013 at 7/mile. North Sulawesi is the area with the highest stroke prevalence in Indonesia, which is 10.8%. West Java has a stroke prevalence of 6.6%.[5]

Research involving experimental animals has begun to be carried out for research on stroke and motor function.44 Research on stroke has been successfully carried out on experimental rats by making ischemic stroke models. One of the animal models of ischemic stroke was carried out in Lukito's study in 2016 by performing ligation on the common carotid artery of a unilateral Wistar strain white rat for 45 minutes and found a significant decrease in motor function after reperfusion.[6]

Based on the description above, the author is interested in taking the title because it can determine the effect of the

duration of clogging of the common carotid artery on the motor function of Wistar rats.

## METHOD

The design of this research is a literature review research. Literature review research design is a research method used to collect data related to the formulation of the problem in research papers obtained from various literature sources such as scientific research journals, previous research manuscripts, related textbooks. The research can answer the number of samples of scientific research journals used to respond to the problem formulation. The exclusion criteria in this study were scientific journals that had no relevance and could not answer the problem formulation in the formulated research paper. There are procedures in managing the data sources of this research; the first was to organize, which is to organize the literature that will be reviewed. The next step was screening literature and eligibility included in the systematic review that will be reviewed.

## RESULT

Duration of the blockage of the carotid arteries of the white Wistar rat affects the motor function that occurs on an average 45 minutes after the blockage of the blood vessel.

Improves motor function in ischemic stroke model Wistar rats assess motor function in white Wistar rats after treatment for clogging of the common carotid arteries for 45 minutes. The motor function can be evaluated using the ladder rung walking test method. The assessment was carried out with rats walking on cylindrical iron arranged regularly with a distance of 1 meter, observing the left and right leg movements, and observing the rat's steps. When the rat slips, it is a sign of weakness in the rat's motor function. The score on motor function is assessed based on the assessment that has been determined according to the ladder rung walking test scoring table, and observations are also made on the volume of infarcted areas of the brain by microscopic examination.

**Table 1.** Pearson correlation test results research on grape skin and seed extract (*Vitis vinifera*) reduces the number of damaged neuron cells in infarction volume and improves motor function in ischemic stroke model Wistar mice

| | | Ladder_rung | Damage_neuron | Volume_infarction |
|---|---|---|---|---|
| Ladder_rung | Pearson Correlation | 1 | ,306 | ,346 |
| | Sig. (2-tailed) | | ,189 | ,136 |
| | N | 20 | 20 | 20 |
| Damage_neuron | Pearson Correlation | ,306 | 1 | ,645* |
| | Sig. (2-tailed) | ,189 | | ,002 |
| | N | 20 | 20 | 20 |
| Volume_infarction | Pearson Correlation | ,346 | ,645* | 1 |
| | Sig. (2-tailed) | ,136 | ,002 | |
| | N | 20 | 20 | 20 |

Note: * shows a significant correlation on

the results of P< 0.05 (2-tailed)

Based on the journals, the blockage of the common carotid artery causes cytotoxicity edema. And also result in increased expression of NMDA, Ca2+. The results can lead to apoptosis, and hypoxia could cause ischemia, neuronal damage, and neuronal death due to the lack of oxygen supply carried by the blood flow to the rat brain.

Edema can occur so that with damage to neurons, even neuronal death in the precentral gyrus area of the brain's frontal area or motor cortex can cause impaired motor function in Wistar rats.

Unilateral Cerebral Artery Occlusion (UCAO) Method Increases MMP-9 Levels in Brain Tissue in Ischemic Stroke Rat Model. In the scientific journal research above, the research paper used the research subject of the Wistar *Rattus norvegicus* strain rats induced by stroke using the Unilateral Carotid Artery Occlusion method. UCAO (Unilateral Cerebral Artery Occlusion) is a stroke induction method by tying the carotid artery, which directs blood to the brain for 45 minutes. This method aims to produce hypoxic conditions in brain tissue to prepare experimental animals for further research. With this method, the blood supply to the brain will be obstructed, and an ischemic stroke will occur due to blockage in the blood vessels, and then the MMP-9 marker level is measured. MMP-9 is an early marker of stroke that can be detected using ELISA through the blood serum of experimental animals. MMP-9 coexists with neutrophil infiltration in ischemic brain neurons. MMP-9 expression also increased along with the increasing ischemic process in neuronal cells.[7]

**Table 2.** Average results of MMP-9 measurements in the UCAO method research increases MMP-9 levels in brain tissue in ischemic stroke rat models

| Group | Number of Samples | Mean | Standard Deviation |
|---|---|---|---|
| Control | 4 | 0.582 | 0.124 |
| Treatment | 4 | 0.747 | 0.028 |

Based on the data contained in table 2 of the scientific journal research above, it can be concluded that if there is an increase in MMP-9 marker levels in the blood of white Wistar rats, the growth can indicate or signal damage to brain tissue caused by an ischemic stroke. Brain tissue affected by stroke will experience hypoxia and not the oxygen supply needed in the homeostasis process. The UCAO (Unilateral Cerebral Artery Occlusion) blockage method can increase rat serum MMP-9 levels based on the data. Blockage of the carotid artery

affects the motor function of Wistar white rats, which is concluded based on research data on MMP marker levels.

The effect of systemic hypoxia on Glutathione (GSH) levels in the heart and blood of *Sprague Dawley* Rats showed that using experimental methods in vivo hypoxia models in *Sprague Dawley* male rats, which were grouped into seven groups. Group 1 is the control group without treatment. The other six groups were the treatment group exposed to hypoxia.[8] Examination samples were obtained from the heart of *Sprague Dawley* rats in the control group and the systemic hypoxia-induced group in various time groups, namely 1 hour, 3 hours, 6 hours, 12 hours, 24 hours. Hours, and 72 hours. Six treatment groups from groups 2 to 7 were sequentially exposed to hypoxia according to the time of each group in an airtight hypoxic hood connected to a gas tank containing a gas mixture of 8% oxygen and 92% nitrogen.[8]

Parameters examined and observed in this study were glutathione levels in the heart and blood of Sprague Dawley rats. [8] Glutathione levels were examined by the Ellman method. The study's overall results can be seen in Table 3, which showed a significant decrease in pO2, pCO2, pH, HCO3, and O2 saturation between hypoxia and normoxia treatment. This change in blood gas parameters indicates that the given treatment causes systemic hypoxia in Sprague Dawley rats.

**Table 3.** Blood gas and hematology values effect of systemic hypoxia on glutathione (GSH) levels in the heart and blood of *Sprague Dawley* rats

| Parameter | Normoxia | Hypoxia | | | | | |
|---|---|---|---|---|---|---|---|
| | | 1 hour | 3 hours | 6 Hours | 12 hours | 24 hours | 72 Hours |
| Ph | 7.43 ±0.02 | 7.43 ± 0.01 | 7.42 ± 0.01 | 7.41 ± 0.02 | 7.40 ± 0.01* | 7.40 ± 0.03 * | 7.39 ± 0.02* |
| pCO2 (mmHg) | 40.7 ±2.7 | 39.2 ± 2.2* | 38.3 ± 2.2* | 36.4 ± 3.3* | 35.7 ± 2.4* | 32.5 ± 3.6* | 30.2 ± 3.4* |
| pO2 (mmHg) | 97.8 ±4.8 | 87.2 ± 6.1* | 72.3 ± 5.2* | 68.6 ± 4* | 57.3 ± 3.1* | 53.1 ± 7.4* | 48.7 ± 2.6* |
| HCO3 (mmol/L) | 24.8 ±2.5 | 22.2 ± 2.3* | 20.4 ± 1.7* | 17.9 ± 1.2* | 21.4 ± 1.1* | 19.3 ± 2.8* | 18.2 ± 2.1* |
| SAT O2 (%) | 95.8 ±3.1 | 89.7 ± 6.2* | 80.2 ± 5.5* | 71.3 ± 5.4* | 65.7 ± 8.6* | 54.7 ± 8.6* | 58.2 ± 5.4* |
| Hemoglobin (g/L) | 120.1 ± 1.6 | 120.7 ± 3.1 | 123.2 ± 3.7* | 126.6 ± 5.5* | 133.4 ± 3.9* | 148.6 ± 4.4* | 162.5 ± 5.2* |
| Hematocrit (%) | 45.2 ±2.5 | 45.6 ± 3.6 | 47.1 ± 5.1* | 48.3 ± 2.7* | 51.2 ± 2.6* | 53.4 ± 5.4* | 55.8 ± 4.3* |
| red blood cells (µL/1000) | 6.7 ± 0.1 | 6.8 ± 0.2 | 7.0 ± 0.2 | 7.2 ± 0.5* | 7.8 ± 0.5* | 8.15 ± 0.4* | 8.3 ± 0.8* |

Based on the data above, it was found that there was a significant decrease in pO2, pCO2, pH, HCO3, and O2 saturation between hypoxia and normoxia treatments. This change in blood gas parameters indicates that the treatment given causes systemic hypoxia in Sprague Dawley rats.

*The* effect of prolonged hypoxia on erythrocyte numbers and hemoglobin levels of *Rattus Norvegicus* Animals were randomly grouped into four groups, namely, control group 1 and then the

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hypoxia-induced group for 12 hours, 24 hours, and 36 hours with each group consisting of 6 Rattus norvegicus. Hypoxia treatment to the treatment group, hypoxia induction was carried out by adjusting the volume of oxygen that entered the closed cage used as a substitute for the hypoxia chamber by 10% of the volume of the cage used, and sampling was carried out before and after hypoxia treatment.[9] Animals were randomly grouped into four groups, namely group 1 control and then the hypoxia-induced group for 12 hours, 24 hours, and 36 hours with each group consisting of 6 ***Rattus*** norvegicus. I. The research was carried out by giving hypoxia treatment to the treatment group, hypoxia induction was carried out by adjusting the volume of oxygen that entered the closed cage used as a substitute for the hypoxia chamber by 10% of the volume of the cage used, and sampling was carried out before and after hypoxia treatment.[9]

Data from the overall research results in scientific research journals can be seen in diagrams 1 and 2.

Diagram of Comparison of Hemoglobin Levels and Erythrocyte Levels Experimental Results Journal of Scientific Research Written by Uyun and Indriawati entitled "The Effect of Long Time Hypoxia on Erythrocyte Numbers and Hemoglobin Levels Rattus Norvegicus."

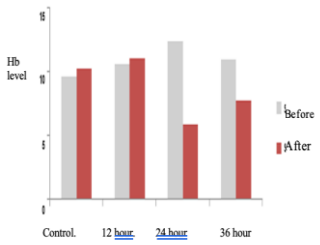


**Figure 1**. Diagram compares the average hemoglobin levels of *Rattus norvegicus* before and after hypoxia treatment for each treatment group.

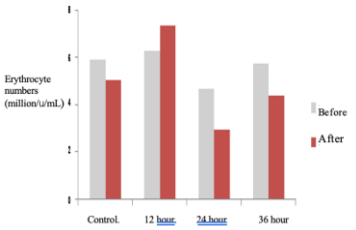


**Figure 2.** Diagram compares the average number of *Rattus norvegicus* erythrocytes before and after hypoxia treatment for each treatment group.

Based on Figure 1, the hemoglobin level of the control group increased, and the group that was treated with 12 hours of hypoxia increased, and the group that was treated with hypoxia for 24 hours and 36 hours decreased. In Figure 2, it can be seen

that the change in erythrocyte numbers in the control group decreased. The group with 12 hours of hypoxia treatment experienced an increase. In contrast, the 24-hour and 36-hour hypoxic treatment groups decreased due to the formation of erythrocytes from the body. Anemia affects the work of the heart and an ischemic stroke due to iron deficiency. Anemia, resulting in a decrease in hemoglobin levels in the blood resulting in a low supply of oxygen to the tissues, can cause ischemic stroke due to blockage of blood vessels and cause motor disorders in rats. [9]

**DISCUSSION**

The brain gets its blood supply from two blood vessels, namely the internal carotid arteries and the vertebral arteries. The carotid arteries supply 70% of the blood from the brain. The internal carotid arteries branch from the common carotid, which provides the brain, and the external carotid arteries supply the face and neck. The internal carotid arteries branch to form the anterior cerebral arteries, which give the cerebral cortex's parietal, frontal, and temporal lobes. At the same time, the vertebral arteries drain 30% of blood from the whole brain blood. The vertebral arteries unite to form the bacillary arteries and then divide to create the two posterior cerebral arteries that supply the interior brain surface and the lateral part of the occipital lobe, cerebellum, and bulbar. The base of the internal carotid artery is the most common site for narrowing. This narrowing affects blood flow and can result in the formation of blood clots. A stroke can occur when a blood clot is released and carried into the internal carotid artery and then clogs the small arteries in the brain. When a disturbance in the blood vessels or their branches, an infarction can occur in an area it flows through it. Cerebral infarction is closely related to atherosclerosis. It can cause various clinical manifestations by constricting the lumen of blood vessels. Brain ischemia is the inability of brain perfusion to provide sufficient oxygen and nutrients necessary to maintain metabolic integrity and neuronal function. 35-38 Brain tissue ischemia is usually caused by sudden occlusion of an artery in the brain, usually the vertebrobasilar artery, when a plaque ruptures, then activate the clotting system. The interaction of the atheroma with the clot will fill the lumen of the artery, so that blood flow is suddenly blocked. The center of the brain area with reduced blood flow followed by cerebral ischemia is the core of brain ischemia. In this region, blood flow is decreased, and neurons die irreversibly within minutes. [10-13]

A model is an object that can match something (human) accurately. Model

animals are animals that can imitate humans to be used to study biological or pathobiological phenomena. The use of animals as models is based on the similarity of biological characteristics with humans. Rats have biological features that are almost the same as humans in several organs, for example, the brain. It's just that one significant difference between rats and humans is the smaller size, so it is necessary to calculate the dose with the correct scale. The ischemic animal model consists of global and local models. Unilateral common carotid artery tying is included in the transient local model commonly used to test anti-inflammatory, glutamate antagonists, and antioxidant activity.[16] The nervous system in all mammals is the same: the central nervous and peripheral nervous systems. Mice have the same brain structure as mammals but on a smaller scale. The mouse brain is in the skull, and the spinal cord is in the spine to the tail. The mouse brain also has bilaterally symmetrical characteristics, namely the right and left sides are exactly like the image in a mirror. The rat brain has three parts in common with mammals, namely the cerebrum, cerebellum, and brain stem. The rat's cerebrum has two hemispheres, namely the right and left hemispheres, separated by the sagittal fissure. The concept is the same as that in humans. Mice also have the same brain vasculature as humans. The rat's right hemisphere plays a role in the sensory and motor functions of the left side of the rat's body. The rat's left hemisphere plays a role in the sensory and motor function of the rat's right side, so it can be concluded that its brain has similarities in both anatomical characteristics and processes, making it suitable as a model for the human brain.[14-18]

## CONCLUSION

Based on a literature review or literature study, it can be concluded that there is an effect of blockage of the common carotid artery on the occurrence of motor function disorders in white Wistar rats. The longer the common carotid artery blockage, the more severe the disruption of motor function in white Wistar rats.

## CONFLICT OF INTEREST

The author affirms no conflict of interest in this study.


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