Review Article

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Stroke Models in Animals

Abstract

The disease of stroke is devastating and has a high mortality rate. Animal models are essential for investigating mechanisms and developing novel therapeutic regimens because they can replicate stroke processes. It is impossible to replicate every aspect of a human stroke in an animal model because stroke is a heterogeneous disease with complex pathophysiology. Each model has distinct advantages and disadvantages. The most common models used to simulate human ischemic stroke are transient or permanent Intraluminal Thread Occlusion (ITO) models, thromboembolic models, and Middle Cerebral Artery occlusion (MCAo) models. The endovascular filament occlusion model is good for studying the pathogenesis of focal ischemic stroke and reperfusion injury because it is easy to manipulate and can accurately control reperfusion. The embolic model is more convenient for investigating thrombolysis, despite its poor reproducibility. The most common animal model for stroke is the rat. The stroke models used in rats are mainly described in this review, along with their advantages and disadvantages.

Keywords: Animal Models • Cerebral Hemorrhage • Ischemia • Stroke

Kim Su*

Department of Cardiology, University of South Seoul, South Korea

*Author for correspondence:

suxi56@yahoo.com

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Introduction

Worldwide stroke is the leading cause of morbidity and mortality. In 2017, stroke was the leading cause of death and disability-adjusted life years (DALYs) in China. Age standardized DALYs per 100,000 people fell by 33.1% for stroke. Up to 80% to 85% of all strokes are ischemic, which can be broken down according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification. Large vessel atherosclerosis of the cervical or proximal intracranial vessels is a major cause of acute stroke, accounting for between 30% and 43% of cases, while cardio embolism accounts for between 20% and 31%. Diabetes and high blood pressure are the primary causes of lacunar stroke, which accounts for between 10% and 23% of all strokes. 2 to 11 percent of cases are caused by other unusual factors like vasculopathy or extra cranial artery dissection. Hypertension and vascular malformations are the most common causes of hemorrhagic strokes, which account for between 5% and 21% of all strokes. Because strokes are diverse diseases, in vivo models are essential tools for imitating these processes in order to investigate pathophysiology and treatment options. The best one for an investigation can only be chosen once we are aware of their significance; the term "best" refers to the one that most closely resembles one of the many aspects of strokes [1].

Discussion

What is global ischemic stroke?

Global brain damage caused by cardiac arrest and resuscitation also includes global cerebral ischemia, despite its rarity. A global model of reversible ischemia may also be useful in determining how potential neuroprotective agents work.The global ischemia model, which can be either incomplete or complete and is characterized by a significant reduction in cerebral blood flow throughout the entire brain, is typically simpler to implement. It can be induced in a variety of ways. The most regularly utilized ones are the deficient worldwide ischemic models of the four-vessel occlusion model (4-VO model) and two-vessel impediment model (2-Global brain damage caused by cardiac arrest and resuscitation also includes global cerebral ischemia, despite its rarity). A global model of reversible ischemia may also be useful in determining how potential neuroprotective

agents work. The global ischemia model, which can be either incomplete or complete and is characterized by a significant reduction in cerebral blood flow throughout the entire brain, is typically simpler to implement. It can be induced in a variety of ways. The most regularly utilized ones are the deficient worldwide ischemic models of the four-Vessel Occlusion model (4-VO model) and two-Vessel Impediment model (2-VO model) [2-4].

4-VO model

4-VO model for highly reproducible forebrain ischemia on the basis of the anatomical basis of the vertebral artery. The vertebral conduit at the second vertebra was electro cauterized under magnifying instrument to ensure complete impediment of course of both vertebral artery. This models shows biphasic changes in mind edema and searching action of superoxide following cerebral ischemia reperfusion. Mind water contents increments at 1-48 hours after distribution be that as it may, are practically equivalent to the ordinary cerebrum at 24 hours. The least also, most noteworthy superoxide searching exercises are found at 45 minutes and 12 hours after distribution, respectively. The model enjoys different benefits, for example, simplicity of readiness, a high pace of unsurprising ischemic neuronal harm, and a low occurrence of seizures. Furthermore, animals require better postoperative care due to the high mortality rate and frequent complications [5].

2-VO model

The fact that rats have a well developed circle of Willis is primarily to blame for the fact that ligament of the carotid arteries only results in a reduction in cerebral blood flow of approximately half that which is normal. However, it does not significantly alter the energy state of the tissue. As a result, a model for chronic cerebral hypoperfusion related euro degenerative diseases could be created by permanent occlusion of the bilateral carotid arteries. The changes in CBF can be broken down into three phases: the acute phase, which marks the beginning of occlusion and lasts no more than two to three days, the chronic hypoperfusion phase, which lasts from eight weeks to three months. On the other hand, the second phase is the closest to the condition of decreased CBF in dementia and aging humans. Other changes in pathophysiological processes, such as altered electrophysiological activity, neuro pathologic changes, and continuous oxidative stress, are seen even though the permanent 2-VO model does not show BBB destruction [6-8].

Whole blood injection model

Whole blood injection model is under the consideration of the intracerebral hemorrhage stroke. The model was altered by connecting the stereotactically inserted cannula in the caudate nucleus or lateral ventricle to the femoral artery in order to induce ICH in rats at arterial pressure. The principal drawback of this strategy is the uncontrollable size of hematomas caused by the fluctuation in blood pressure. Developed the model later, stereotaxically injecting 0.2 milliliters of autologous blood drawn from a femoral vein into the caudate nucleus. The using of a micro pump connected to a stereotactic syringe, injected autologous femoral artery blood continuously and slowly into the caudate nucleus. However, the aforementioned models always reflux the blood along the needle tract. The blood toxicity and hemostasis mass effect are best simulated by the whole blood injection model, which does not involve the rupture of cerebral vessels. As a result, the study of the bleeding mechanism and the treatment for hemostasis cannot be done using the blood injection model [9].

Collagenase model

The fundamental component of this model is the stereotactic injection of bacterial collagenase into specific brain regions, resulting in intraventricular hemorrhage or cerebral parenchyma. The model best resembles bleeding, and manipulation is simple. In addition, adjusting the amount of collagenase makes it simple to regulate the hemotoma's size. As a result, the model is frequently applied to rodents and large animals. However, the clinical incidence of ICH cannot be completely simulated by this model, particularly in the following ways: Due to the rupture of small vessels and capillary beds around the injection site, the model's bleeding is slow and diffuse [10].

Conclusion

The survival rate and prognosis of patients

following ischemic stroke and hemorrhagic stroke are currently limited by the available treatment options. The low translational rate of preclinical studies undoubtedly contributes to these. The most effective research strategy should be chosen based on the advantages and disadvantages of various animal models in order to accelerate the development of effective agents. Additionally, despite the constant development of models' technologies over the past few decades the current stroke models still require additional testing. Moreover, taking into account that the physiological elements of nonhuman primates and other huge creatures are more like those of people, we ought to progressively confirm the restorative impact on these creatures in the wake of confirming the treatment adequacy in different models of little creatures.

Acknowledgement

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Conflict of Interest

None

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