Study on Oxidative Stress and Cerebral Ischemia-reperfusion Injury

Yun Jie

Xi'an Peihua University, Xi'an, China

Keywords: oxidative stress; cerebral ischemia-reperfusion; injury

Abstract: The phenomenon of cerebral ischemia-reperfusion is a cascade reaction process, and it is relatively complicated because the process can involve multiple mechanisms. In this process, the existence of oxidative stress is of great significance. According to related research, protein denaturation and lipid peroxidation can be used as the pathway for oxidative stress to induce necrosis of nerve cells. Moreover, oxidative stress can also promote neuronal apoptosis in mitochondria, death receptors, endoplasmic reticulum and the possibility of application. In this paper, the author mainly studied oxidative stress and cerebral ischemia-reperfusion injury.

1. Introduction

In ischemic cerebrovascular disease, cerebral ischemia-reperfusion injury is a relatively common phenomenon. Specifically, it refers to the patient's spontaneous recovery of perfusion after a period of cerebral ischemia, which can increase the area of cerebral infarction, leading to more severe brain dysfunction [1]. According to relevant data and clinical research, the clinical symptoms of most patients significantly become more severe when blood supply restores, and the incidence of cerebral hemorrhage and cerebral edema also tends to increase. In general, patients may suffer from cerebral ischemia-reperfusion injury after thrombolysis and embolectomy, and there are no effective preventive and therapeutic measures for this situation. Cerebral ischemia-reperfusion can be involved in a variety of mechanisms, such as excitotoxicity, inflammatory injury, etc., but what plays the dominant role is oxidative stress [2].

The so-called "oxidative stress" is the oxidative damage of tissue cells caused by the imbalance of oxidation and antioxidant substances and it is mediated by activated oxygen produced by the body. During the process of oxidative stress, the expression and activity of various enzymes can change and lead to the accumulation of ROS. In addition to the above factors, the emergence of oxidative stress can directly cause cell necrosis [3].

2. Oxidative stress and neuronal cell necrosis

2.1 Lipid peroxidation

In the case of cerebral ischemia-reperfusion injury, phospholipase A2 can be activated to hydrolyze membrane phospholipids, followed by arachidonic acid and can generate a large amount of ROS by-products. During this process, the formation of biofilms is extremely susceptible to destruction, leading to cell collapse and death. At the same time, ROS can further react with lipids and form peroxidized lipids, which can then form toxic aldehyde products.

2.2 Protein denaturation and DNA modification

The emergence of ROS can lead to the inactivation of enzymes and the degeneration of proteins, leading to multiple blocking of cells in the process of vital activities. For example, if the mitochondrial respiratory chain is interrupted, it can lead to energy disorders, and then the cells will die due to energy failure. In this process, ROS can still achieve DNA fragmentation through oxidative modification and endonuclease, which effectively causes DNA damage and leads to the death of cells [4].

  DOI: 10.25236/ibmc.2019.007

3. Oxidative stress and neuronal cell apoptosis

If ROS are abundantly present, they can directly lead to the appearance of oxidative damage in cells and effectively cause cell death. When a patient is in the case of mild cerebral ischemia, moderate dose of ROS can cause neuronal apoptosis through multiple pathways such as mitochondria and endoplasmic reticulum, and it may involve several protein including caspase, apoptosis-inducing factors, etc.

3.1 Mitochondrial pathway

Under normal circumstances, it is believed that, when mitochondria cause cerebral ischemia-reperfusion in patients, the factors resulting in ROS mainly include glutamate excitotoxicity and hypoxia after ischemia. In the early stage of the patient's perfusion, there is a case where the neuronal cells initiate the mitochondrial apoptotic pathway, and the protein translation initiation also changes at this time; hydrolase activation occurs in the cell, and the endonuclease can also be activated at this time.

According to the results of cerebral ischemia-reperfusion test in mice, hyperbaric oxygen preconditioning can effectively reduce brain damage and apoptosis rate; and while the activity of caspase enzymes is reduced, hyperbaric oxygen preconditioning can effectively protect against cerebral ischemia-reperfusion and inhibit the mitochondrial apoptotic pathway, which has been confirmed [5].

Mitochondria have their own unique genetic system and their genes do not bind to histones. On this basis, because mitochondria are adjacent to the ROS production site, they are relatively less protected and less susceptible to free radical attack, resulting in ischemia and hypoxia; and thereby large-scale apoptosis occurs in the cells with the break of DNA strand and base disappearance [6].

In addition, in the case of cerebral ischemia-reperfusion, a large number of oxygen free radicals can be produced by the respiratory chain complex, and they can directly attack the respiratory chain; after being attacked and damaged, the respiratory chain can release a certain amount of Cyt-C and further cause apoptosis of brain cells [7].

3.2 Endoplasmic reticulum pathway

The endoplasmic reticulum belongs to an important organelle, and it is an indispensable medium for cells to realize synthesis and protein processing at the same time, the calcium balance of cells and the biosynthesis of lipids are all related to the endoplasmic reticulum pathway. When a patient is in the case of cerebral ischemia-reperfusion, a large amount of protein inevitably gather in the endoplasmic reticulum of nerve cells, and the protein are presented in an unfolded or misfolded manner, that is, endoplasmic reticulum stress occurs.

3.3 Death receptor pathway

The death receptor pathway is an important mechanism for cerebral ischemia-reperfusion in patients, and it is an external pathway compared with the pathway of mitochondrial apoptosis.

According to relevant research, in the model of cerebral ischemia-reperfusion in rats, pretreatment with silymarin can effectively improve the situation of ischemia-reperfusion injury; this is mainly because ischemia-reperfusion can effectively inhibit the production of ROS [8].

4. Cerebral ischemia-reperfusion injury and anti-oxidation therapy

The generation and release of oxygen free radicals have a decisive influence on the death of neurons, and the removal of oxygen free radicals is the main way to treat patients with ischemia-reperfusion injury. Theoretically, if the pathway or key molecules generating ROS can be blocked and acted upon, the damage of patients can also reduce. In recent years, relevant personnel have been studying anti-oxidation treatment methods for cerebral ischemia-reperfusion injury. And so far, some progress has been made: from the treatment of cerebral ischemia-reperfusion injury in mice, it can be seen that the application of alfalfa can play a significant therapeutic role, and the area of cerebral infarction in mice is smaller. Moreover, as the activity of the oxidase decreased, it

was found that the neuroprotective effect of the alfalfa extract is mainly attributed to its own antioxidant properties. At the same time, resveratrol can also have a good therapeutic effect on cerebral ischemia-reperfusion injury in mice, and its protective effects on mice is also closely related to its own antioxidant specificity [9].

In addition to extracts from plants, it is also feasible to apply some clinically common cardiovascular drugs (such as simvastatin with lipid-lowering effects or trimetazidine with anti-angina) in the treatment of cerebral ischemia-perfusion injury; they all can play a protective role, and their effects are closely related to their antioxidant activity. It can be seen that the treatment of cerebral ischemia-reperfusion injury with drugs is very important to improve the permeability of the blood cerebrospinal fluid barrier [10].

5. Conclusion

For patients with cerebral ischemia-reperfusion injury, anti-oxidation therapy can achieve a certain therapeutic effect, but this method is currently not widely used in clinical practice. This is because the application effect is not very satisfactory; the oxidative stress mechanism is not completely clear, and the antioxidant lacks certain specificity. Based on the analysis above, the effective explanation of the molecular mechanism of oxidative stress and the search for new antioxidants with high specificity are of great significance.

Acknowledgement

In this paper, the research was sponsored by Project of Shaanxi Education Department: Extraction and purification of resveratrol from peanut buds and its protective effect on rats with ischemic stroke(16JK2134)and Xi'an Peihua University School-level topics:Study on the mechanism of hydroxytyrosol intervention on oxidative stress in cardiomyocytes(PHKT20150703)

References

[1] Xiao Jing, Wang Wenbo, Yao Yixun, et al. Effects of Calycosin on Neurological Function and Oxidative Stress in Rats with Cerebral Ischemia-reperfusion Injury [J]. Yiyao Qian, 2018, 8(24): 220-221.

[2] Hou Chen, Tang Peng, Liu Yue, et al. Regulation Effects of Lupeol on Oxidative Stress Injuries and Inflammatory Reaction in Rats with Cerebral Is-chemia-reperfusion and Its Mechanism [J]. Medical & Pharmaceutical Journal of Chinese People's Liberation Army, 2018, 30 (10): 6-10.

[3] Zhu Yaobin, Zhang Yazhen, Li Zhiqiang, et al. Effects of Cystic Fibrosis Transmembrane Conductance Regulator on Mitochondrial Function and Oxidative Stress in Mice with Cerebral Ischemia-reperfusion Injury [J]. Journal of Chinese Practical Diagnosis and Therapy, 2018, 32(11): 1047-1050.

[4] Hu Yueqiang, Tang Nong, Qin Hongling, et al. Mechanism of cerebral I/R injury based on oxidative stress signal pathway mediated by Keap1-Nrf2 [J]. Chinese Journal of Geriatric Heart Brain and Vessel Diseases, 2018, 20 (12): 1311-1314.

[5] Yu, Wei,Gao, Dapeng,Jin, Wen, et al. Propofol Prevents Oxidative Stress by Decreasing the Ischemic Accumulation of Succinate in Focal Cerebral Ischemia-Reperfusion Injury[J]. Neurochemical research, 2018, 43(2): 420-429.

[6] Qu Y, Zhang H-L, Zhang X-P, et al. Arachidonic acid attenuates brain damage in a rat model of ischemia/reperfusion by inhibiting inflammatory response and oxidative stress[J].Human & Experimental Toxicology, 2018, 37(2): 135-141..

[7] Qu, Y, Zhang, H-L, Zhang, X-P, et al. Arachidonic acid attenuates brain damage in a rat model of ischemia/reperfusion by inhibiting inflammatory response and oxidative stress[J]. Human and

Experimental Toxicology, 2018, 37(2): 135-141.

[8] Hou, Yanghao, Wang, Yueting, He, Qi, et al. Nrf2 inhibits NLRP3 inflammasome activation through regulating Trx1/TXNIP complex in cerebral ischemia reperfusion injury[J]. Behavioural Brain Research: An International Journal, 2018, 336: 32-39.

[9] Xia Li, Hao Guo, Lei Zhao, et al. Adiponectin attenuates NADPH oxidase-mediated oxidative stress and neuronal damage induced by cerebral ischemia-reperfusion injury [J]. Biochimica et biophysica acta. Molecular basis of disease: BBA, 2017, 1863(12): 3265-3276.

[10] Su, Jing, Liu, Jie, Yan, Xiao-Yu, et al. Cytoprotective Effect of the UCP2-SIRT3 Signaling Pathway by Decreasing Mitochondrial Oxidative Stress on Cerebral Ischemia-Reperfusion Injury[J]. Journal of Turbulence, 2017, 18(7).