Short Communication

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Macrophage Migration Inhibitory Factor (MIF) Protects the Brain in a Mouse Model of Ischemic Stroke

Joe Kong*

Department of Translational medicine, University of Aberdeen, Aberdeen, UK

*Author for correspondence: kong2@uk.ac.in

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Abstract

It is not clear how the macrophage Migration Inhibitory Factor (MIF) *in vivo* protects neurons. An *in vivo* ischemic stroke mouse model was used to see if the MIF helped the brain recover. In order to create an ischemic stroke mouse model, transient Middle Cerebral Artery Occlusion (MCAO) surgery was carried out. A sham vehicle, a sham MIF, a Middle Cerebral Artery Occlusion (MCAO) vehicle and an MCAO+MIF group were assigned to male mice. The vehicle and MIF were administered intra cerebroventricularly in the MCAO groups during transient MCAO (tMCAO). The rotarod test, the neurological functional scale, and T_2 weighted magnetic resonance imaging were examined. The expression levels of Bcl2, Brain Derived Neurotrophic Factor (BDNF) and Microtubule Associated Protein 2 (MAP2) were also measured using eastern blot assay. In comparison to the MCAO+vehicle group, the Garcia test was significantly higher in the MCAO+MIF group. In addition to having a significantly smaller total infarct volume on T_2 weighted MRI imaging than the MCAO vehicle group, the MCAO+MIF group performed on patients.

Keywords: Macrophage migration inhibitory factor • Stroke • *In Vivo* • Neurogenesis • Microtubule

Introduction

Worldwide, stroke is the leading cause of death and disability and has a significant direct and indirect economic impact. In 2020, the overall pervasiveness of stroke counting ischemic stroke was 68.16 million [1]. Eighty percent of stroke cases are ischemic, or when there is insufficient blood supply to the brain. Even though stroke is becoming more common, there are still no effective treatments. The majority of neuroprotective medications target the peripheral reversible infarction area known as a penumbra in order to prevent the development of damaged tissue [2]. Ischemic stroke causes the formation of a brain tissue necrosis core. The penumbra is damaged when inflammatory responses, apoptotic pathways and the production of reactive oxygen species are triggered by brain ischemia. As a result, recent breakthroughs in stroke treatment have aimed to control inflammation and suppress the apoptotic response [3].

In response to ischemia, the pro inflammatory cytokine macrophage Migration Inhibitory Factor (MIF) is activated. The MIF is tracked down in many sorts of cells, like lymphocytes, neutrophils, endothelial cells and neuronal cells. The MIF is implicated in a wide range of neurological conditions, but previous studies have produced contradictory findings. There is some debate regarding the MIF's role in ischemic stroke; the MIF may have a, according to some studies [4].

Description

MIF administration improved the infarction volume, neurological scale and motor function of MCAO model mice, according to our findings. In addition, the administration of MIF to MCAO mice resulted in an increase in the expression of MAP2, Bcl2, BDNF and IL-6, as well as a decrease in the Bax/Bcl2 ratio in the ischemic area.

Exercise induced MIF has been shown to help motor and neurological recovery in previous studies [4]. Chang and co. higher levels of MIF and BDNF were linked to better motor

and neurology recovery in MCAO mice, and neurologic scale and motor strength improved in the early treadmill exercise MCAO group.

Li and co. further found that MCAO rats with an increase in the MIF score had a lower neurologic severity score, indicating that the MIF helped the rats recover their neurologic function. The present study demonstrated that MCAO mice receiving an intracerebro ventricular MIF injection had improved motor recovery and neurologic function in accordance with these findings [5].

In addition, the MCAO mice treated with an MIF intracerebroventricular injection had a smaller infarction volume than the MCAO controls. In the past, Zhang, et al., was discovered that MIF knockout mice had a NF-B dependent increase in infarction volume in comparison to wild type mice [6]. However, our findings are in opposition to those of a previous study that found that the MIF causes a disruption in the blood brain barrier, thereby increasing permeability and the size of the infarction. In this review, the MIF was regulated intravenously, furthermore, the focus was very high: 3.3 µg/kg. There was no significant increase in infarction volume when the MIF was administered at a concentration that was ten times lower. This outcome may thusly have shown a poisonous impact of MIF glut. In the current study, we controlled 120 ng/mL MIF by means of the ventricle, as in a past report [7,8].

Under ischemic conditions, the MIF may also play a neuroprotective role, as evidenced by the increase in BDNF expression Jung, et al., conducted a prior study. Found that mice given the MIF had higher levels of BDNF expression than controls during oxygen and glucose deprivation/reperfusion. Neuronal survival is aided by BDNF, which also facilitates synaptic repair and growth. MIF treated MCAO mice had significantly higher levels of BDNF expression than the vehicle group. Synaptic plasticity may be facilitated by BDNF, enhancing neurologic performance. The MIF participates in and regulates immunological responses as a cytokine [9].

It is necessary to conduct additional research into how the MIF affects lacunar infarction. Fifth, ELISA might be a more delicate method for determining the expression level of the inflammatory marker and the apoptosis marker. Future research using a more delicate method for determining expression levels is necessary. Sixth, MIF injections were administered intracerebroventricularly, a technique that is extremely restricted to humans. In order to administer the agent in a clinical setting, additional research is required. Seventh, we employed the recommended MIF dose from an *in vitro* study on a human nueroblastoma cell. It might not be the best dose because humans and mice have different physiologies. However, significant advancements were made in imaging, neuroscience, and behavior. Last but not least, the effects of MIF over time were not examined in this study, so additional research is required to better understand pro-inflammatory processes following an ischemic stroke [10].

Conclusion

This study showed the way that the MIF could apply a neuroprotective capability later ischemic cerebral dead tissue. The MIF treated MCAO model mice had smaller ischemic volumes and better results on neurological and motor function tests. This suggests that the MIF may promote neurogenesis while simultaneously promoting apoptosis protection for neuronal cells.

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