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Research Report

Supplement zinc as an effective treatment for spinal cord ischemia/reperfusion injury in rats

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ABSTRACT

Objective: Brain-derived neurotrophic factor (BDNF) plays a key role in the pathophysiology process and therapy of spinal cord injury (SCI). Accordingly, zinc regulates the expression of BDNF and its receptor in the central nervous system, the mechanism of which is still unknown. The present study investigates whether supplement zinc could reduce neurological damage in a rat model, with spinal cord ischemia–reperfusion (I/R) injury and how the effect of zinc transporter 1(ZnT-1) was involved. *Methods:* 100 Sprague–Dawley male rats were randomly and evenly divided into four groups. They were subjected to spinal cord ischemia by clamping the abdominal aorta for 45 min. Rats in the zinc-deficient dietary model group (ZD), zinc-adequate dietary model group (ZA), and zinc-high dietary model group (ZH) were given free access to purified diet, containing 5, 30, or 180 mg Zn/kg. Sham operation rats were subjected to laparotomy without clamping of the aorta and were fed by ZA diet (30 mg Zn/kg). Neurological function was scored by Tarlov's score. The spinal cord segments (L5) were harvested for histological examination, auto-metallographic (AMG) analysis, myeloperoxidase (MPO) activity analysis, expression of ZnT-1 and BDNF. *Results:* The rats in the ZH group have shown the higher neurological scores, slighter histological changes and the attenuated MPO activity, compared with those in the ZD and ZA groups at the four observation time points ($p<0.05$). The AMG staining density in the ZH group was significantly higher than that of ZD group in 14 days later after the operation. Compared with other groups, ZH group's expression of Zn-T1 and BDNF were significantly increased, and was positively correlated with the same time points after surgery (Spearman rho=0.403, $p=0.0152$.) *Conclusion:* These findings suggest that zinc supplement can significantly reduce the spinal cord I/R injury in rats. The mechanism may be related with restraining the MPO activity and increasing of ZnT-1, which promoted the synthesis and release of BDNF.

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1. Introduction

I/R injury of the spinal cord causes paraplegia, which is a serious complication after thoracic or thoracoabdominal aortic surgery. The specific mechanism of spinal cord I/R injury is not clear now, while it has been recognized that oxygen free radical mediated lipid peroxidation, calcium overload, excitability amino acids, and prostaglandins play important roles in SCI mechanism. A few studies have taken measures to protect against I/R injury, and achieved some good results (Deniro and Al-Mohanna, 2012; Jiang et al., 2009; Yang et al., 2011).

As an essential trace element, zinc plays a key role in multiple metabolic and signaling pathways, which can resist ischemia reperfusion injuries (Bulbuloglu et al., 2011). Supplemental zinc can be used during recovery to improve cognitive and behavioral deficits associated with brain injury (Cope et al., 2012). It is recently demonstrated in the study that zinc supplement could reduce neurological damage after acute SCI, and promote the recovery of spinal cord function. Related with increasing of Zn-T1, the mechanism may promote the synthesis and release of BDNF and play an essential role in modulating spinal zinc homeostasis (Su et al., 2012; Wang et al., 2011a, b; Wang et al., 2011). However, few studies have described the protective effect of dietary zinc on spinal cord I/R. The current study, therefore, was designed to test the neuroprotective effects of zinc supplement in a spinal cord I/R model in rats, and furthermore to preliminarily verify the possible mechanisms of this neuroprotection.

2. Results

2.1. Neurological function assessment

The four groups (1, 3, 7, and 14 days after the operation) of the individual Tarlov's score are shown in Fig. 1. The sham-operated rats had a normal motor function of hind limbs throughout the observation period. A 45-min aortic occlusion resulted in severe lower extremity neurologic deficits in ZD and ZA groups, and the neurologic status of ZH group were significantly superior to ZD and ZA groups at the four observation time points ($p<0.05$). The Tarlov score of ZD group was significantly lower than that of ZA group 14 days later after the operation ($p<0.05$).

2.2. Histologic assessment

Paraffin-embedded sections of lumbar spinal cords stained with hematoxylin and eosin for light microscopic examination are shown in Fig. 2 A–D, and the results of counting viable motor neurons are summarized in Fig. 2 E. No sign of spinal cord damage was observed in sections in the sham-operated rats, and many large motor neurons were presented in the anterior horn.

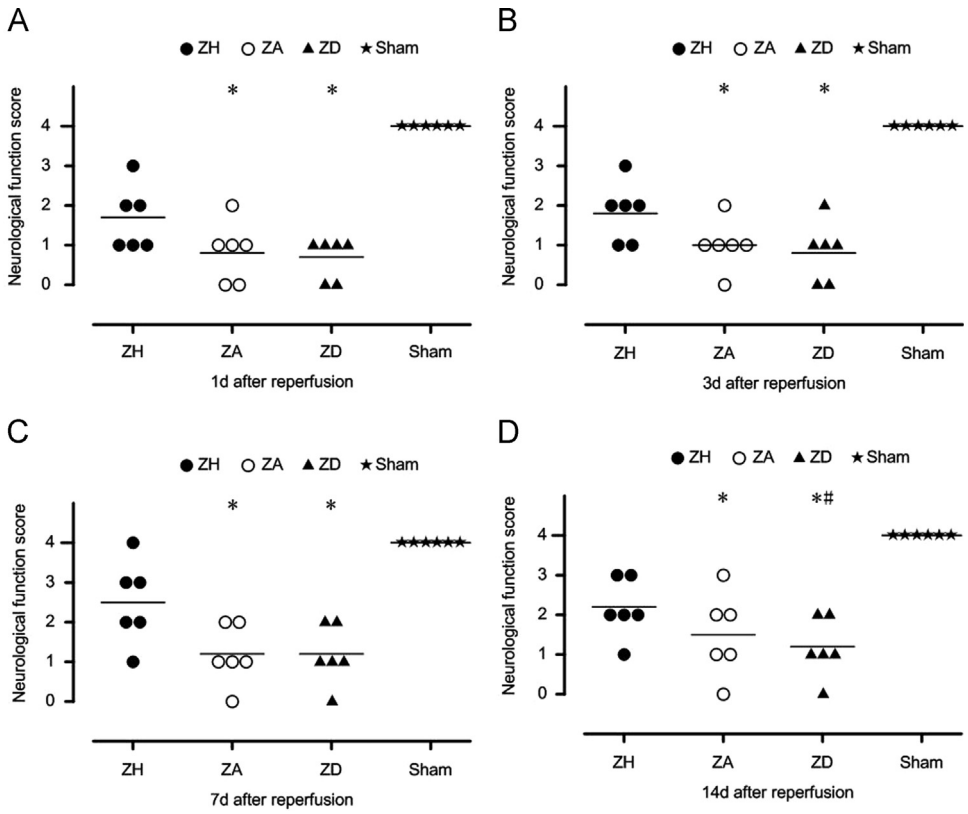

Fig. 1 – Motor functions of the hind limbs assessed with Tarlov's score on day 1, 3, 7, and 14 after spinal cord ischemia/reperfusion injury in rats. ZH=zinc-high dietary model group (180 mg Zn/kg); ZA=zinc-adequate dietary model group (30 mg Zn/kg); ZD=zinc-deficient dietary model group (5 mg Zn/kg); and Sham=sham-operated group (30 mg Zn/kg). $^{*}p<0.05$ versus ZH group. $^{\#}p<0.05$ versus ZA group.