

Borax Partially Prevents Neurologic Disability and Oxidative Stress in Experimental Spinal Cord Ischemia/Reperfusion Injury

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Objectives: The aim of this study is to investigate the potential effects of borax on ischemia/reperfusion injury of the rat spinal cord. **Methods:** Twenty-one Wistar albino rats were divided into 3 groups: sham (no ischemia/reperfusion), ischemia/reperfusion, and borax (ischemia/reperfusion + borax); each group was consist of 7 animals. Infra renal aortic cross clamp was applied for 30 minutes to generate spinal cord ischemia. Animals were evaluated functionally with the Basso, Beattie, and Bresnahan scoring system and inclined-plane test. The spinal cord tissue samples were harvested to analyze tissue concentrations of nitric oxide, nitric oxide synthase activity, xanthine oxidase activity, total antioxidant capacity, and total oxidant status and to perform histopathological examination. **Results:** At the 72nd hour after ischemia, the borax group had significantly higher Basso, Beattie, and Bresnahan and inclined-plane scores than those of ischemia/reperfusion group. Histopathological examination of spinal cord tissues in borax group showed that treatment with borax significantly reduced the degree of spinal cord edema, inflammation, and tissue injury disclosed by light microscopy. Xanthine oxidase activity and total oxidant status levels of the ischemia/reperfusion group were significantly higher than those of the sham and borax groups ($P < .05$), and total antioxidant capacity levels of borax group were significantly higher than those of the ischemia/reperfusion group ($P < .05$). There was not a significantly difference between the sham and borax groups in terms of total antioxidant capacity levels ($P > .05$). The nitric oxide levels and nitric oxide synthase activity of all groups were similar ($P > .05$). **Conclusions:** Borax treatment seems to protect the spinal cord against injury in a rat ischemia/reperfusion model and improve neurological outcome. **Key Words:** Borax—spinal cord—ischemia—reperfusion injury—neuroprotection—oxidative stress.

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Paraplegia from neuronal injury after ischemia/reperfusion (I/R) of the spinal cord may occur in patients undergoing thoracoabdominal aortic surgery for different reasons.^{1,2} Ischemia is the initiating factor in spinal cord injury after thoracoabdominal aortic clamping. Paradoxically, reperfusion of ischemic tissue leads to a much more serious damage than the effect of ischemia only.³ Many factors (postoperative hypotension, apoptosis, proinflammatory cytokines, and an increase in the production of leukocyte adhesion molecules), mainly free oxygen radicals formed by rapid entry of molecular oxygen into the cell play a role in the injury observed during the reperfusion period.⁴ Increased free oxygen radicals in particular leads to membrane and organelle damage of the cell, lipid peroxidation, and inactivation of some critical enzyme systems.⁵

Various treatment methods have been used after aortic surgery to reduce ischemic injury of the spinal cord and induce distal aortic perfusion.⁶⁻⁸ However, none of the methods can prevent spinal cord ischemia and neurological complications.

Boron (B) is an essential element known to influence several metabolic actions and physiological systems of the organism. In nature, B combines to form boric acid and inorganic salts called borates and does not exist by itself. Borax is a B compound, a mineral, and a salt of boric acid. It affects the activity of approximately 26 different enzymes of animal, plant, cultured, and chemical systems.⁹ B interacts with several micronutrients (calcium, magnesium, vitamin D), steroid hormones, and plasma lipid metabolism.^{10,11} Study results have also demonstrated that B is able to scavenge free oxygen radicals.^{12,13} In this context, we investigated the protective effects of borax on histopathological and neurological outcomes of spinal cord I/R injury after aortic occlusion in rats.

Materials and Methods

Twenty-one adult male Sprague-Dawley rats weighing 350 to 450 g were used in the study. All of the rats were maintained in a 12-hour light/dark cycle environment (lights on 7:00-19:00 hours) at a temperature of $22 \pm 1^\circ\text{C}$ and 50% humidity. Rats had access to food and water ad libitum. Animals were randomly assigned into 3 groups as follows:

1. Control (sham) group ($n = 7$): the animals underwent a surgical procedure, but the aorta was not occluded.
2. I/R group ($n = 7$): the animals received 100 mg/kg sterile saline solution through a gastric tube for 7 days before spinal cord I/R injury and for 3 days before the animals were killed.
3. Borax group (ischemia + borax) ($n = 7$): the borax-treated group received a daily dose of 100 mg/kg

borax ($\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$, Sigma-Aldrich) dissolved in normal saline through a gastric tube for 7 days before spinal cord I/R injury and for 3 days before the animals were killed.

All experimental procedures and protocols used in this investigation were reviewed and approved by the Animal Research Committee of Ankara Education and Research Hospital.

Anesthesia and Surgical Procedure

Anesthesia was induced by intramuscular administration of 50 mg/kg ketamine hydrochloride (Ketalar, Pfizer, Istanbul, Turkey) and 10 mg/kg xylazine (Rompun, Bayer, Istanbul, Turkey). Body temperatures were maintained at approximately 37°C with a heat lamp and a heating pad during the surgical procedure until the animals' recovery from anesthesia.

Spinal cord I/R was performed using a previously described method.¹⁴ The rats were placed in the supine position. Using a transperitoneal approach, the aorta was isolated from the beginning of the left renal artery down to the aortic bifurcation. A total of 200 IU/kg heparin was administered intravenously 5 minutes before occlusion. The aorta was then cross-clamped from a point just inferior to the left renal artery to the aortic bifurcation using 2 aneurysm clips (Yasargil FE 721; Aesculap, Tuttlingen, Germany) with a closing force of 70 g. After the occlusion, the pulsation of the femoral artery disappeared. The clips were removed after 30 minutes and return of the aortic pulse was verified. The wound was closed in layers after the operation. After the injury, bladder massage was performed twice a day to stimulate autonomic urinary reflex. Rats were sacrificed 72 hours after the surgery.

Neurological Evaluation

The rats were assessed blindly by neurologist for hindlimb motor function 72 hours after I/R injury. Locomotor performance after spinal cord I/R injury was graded for each animal through an open field test according to an efficient and accurate Basso, Beattie, and Bresnahan (BBB) scoring system described by Basso et al. The 21-point BBB locomotor rating scale is used to analyze the animal's activity in limb joints, coordination in forelimb/hindlimb movement, weight support, and trunk position, which standardizes locomotor outcome measures between laboratories.¹⁵ The animal's ability to maintain postural stability was assessed by the inclined-plane test. The rats were placed on the inclined plane, and the maximum inclination at which the rat could maintain its position for 5 seconds was recorded as the final angle.¹⁶

Biochemical Analyses

Spinal cord segments were excised between L2 and S1 and divided into 2 equal parts. For biochemical analysis,

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