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JNS JOURNAL OF
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J Neurosurg Spine. 2016 Jun;24(6):949-59. doi: 10.3171/2015.10.SPINE15612. Epub 2016 Feb 12.

Neuroprotective effects of thymoquinone against spinal cord ischemia-reperfusion injury by attenuation of inflammation, oxidative stress, and apoptosis

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PMID: 26871652 DOI: [10.3171/2015.10.SPINE15612](https://doi.org/10.3171/2015.10.SPINE15612)

Abstract

OBJECTIVE Ischemia-reperfusion (I/R) injury of the spinal cord following thoracoabdominal aortic surgery remains the most devastating complication, with a life-changing impact on the patient. Thymoquinone (TQ), the main constituent of the volatile oil from *Nigella sativa* seeds, is reported to possess strong antioxidant, antiinflammatory, and antiapoptotic properties. This study investigated the effects of TQ administration following I/R injury to the spinal cord. **METHODS** Thirty-two rats were randomly allocated into 4 groups. Group 1 underwent only laparotomy. For Group 2, aortic clip occlusion was introduced to produce I/R injury. Group 3 was given 30 mg/kg of methylprednisolone intraperitoneally immediately after the I/R injury. Group 4 was given 10 mg/kg of TQ intraperitoneally for 7 days before induction of spinal cord I/R injury, and administration was continued until the animal was euthanized. Locomotor function (Basso, Beattie, and Bresnahan scale and inclined plane test) was assessed at 24 hours postischemia. Spinal cord tissue samples were harvested to analyze tissue concentrations of malondialdehyde, nitric oxide, tumor necrosis factor- α , interleukin-1, superoxide dismutase, glutathione-peroxidase, catalase, and caspase-3. In addition, histological and ultrastructural evaluations were performed. **RESULTS** Thymoquinone treatment improved neurological outcome, which was supported by decreased levels of oxidative products (malondialdehyde and nitric oxide) and proinflammatory cytokines (tumor necrosis factor- α and interleukin-1), increased activities of antioxidant enzymes (superoxide dismutase, glutathione-peroxidase, and catalase), as well as reduction of motor neuron apoptosis. Light microscopy and electron microscopy results also showed

preservation of tissue structure in the treatment group. CONCLUSIONS As shown by functional, biochemical, histological, and ultrastructural analysis, TQ exhibits an important protective effect against I/R injury of the spinal cord.

Keywords: BBB = Basso, Beattie, and Bresnahan; CAT = catalase; ELISA = enzyme-linked immunosorbent assay; GSH-Px = glutathione-peroxidase; I/R = ischemia-reperfusion; IL-1 = interleukin-1; IP = inclined plane; IQR = interquartile range; MDA = malondialdehyde; MP = methylprednisolone; NO = nitric oxide; SOD = superoxide dismutase; TNF α = tumor necrosis factor- α ; TQ = thymoquinone; apoptosis; inflammation; methylprednisolone; neuroprotection; oxidative stress; rat; spinal cord injury; spinal cord ischemia-reperfusion injury; thymoquinone.

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