Ivermectin-functionalized multiwall carbon nanotube enhanced the locomotor activity and neuropathic pain by modulating M1/M2 macrophage and decrease oxidative stress in rat model of spinal cord injury

Summary : Since the inflammation and oxidative stress is the main pathophysiological pathway of neural damage in spinal cord injury (SCI), we tried to evaluate the role of ivermectin (IVM) combined with multi-walled carbon nanotube (MWCNT) in the treatment settings of SCI and its underlying mechanism.

Methods-Results: Wistar rats with T9 vertebra laminectomy in five groups of: sham-operated, vehicle, IVM (0.1 mg/kg), IVM-MWCNT (0.1 mg/kg), and minocycline (90 mg/kg) were used. We evaluated the locomotor scaling and other behavioral tests for neuropathic pain. Also, tissue samples were obtained to evaluate the expression of M1 and M2 macrophage marker, concentration of TNF-**α**, IL-1**β**, and IL-1, and oxidative stress level to assess neuroinflammatory changes.

Conclusions: Both IVM and IVM-MWCNT after induction of SCI significantly enhanced the experimental tasks' outcomes, including locomotion and neuropathic tests. Also, decreasing in pro-inflammatory cytokines including TNF-**α**, IL-1**β**, and IL-1 in the spinal cord and dorsal root ganglion tissues was also notable in both IVM and IVM-MWCNT-treated groups 28 days after induction of SCI in compared to the vehicle-treated SCI group. Both IVM and IVM-MWCNT significantly decreased oxidative stress, induced by

SCI, based on the results of ROS and NADPH activity. IVM-MWCNT-treated animals indicated better outcome in every previous experiment in comparison to IVM-treated animals. The effectiveness of IVM-MWCNT was similar to minocycline treatment in all experimental task (as positive control group). IVM-MWCNT might be a novel treatment in spinal cord injury, which could act through decreasing the oxidative stress and increase the polarization of M1 in comparison to M2 macrophages.