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EVALUATION OF ANTIOXIDANT EFFECT OF GALANTAMINE MICROPARTICLE TREATMENT AFTER SPINAL CORD INJURY IN RATS

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Spinal cord injury (SCI) is a serious condition that can lead to gross lost of body sensitivity, potentially leading to debilitating paralysis and other complications. Currently there is no effective treatment for SCI. Injury events secondary to the primary injury cause the damage to spread and include oxidative stress. Galantamine is an acetylcholinesterase inhibitor and it has been shown to have neuroprotective and antioxidant effects. Previous studies from our group have indicated that galantamine improves recovery after spinal cord injury (SCI). However, the need of repeated dosing and cholinergic side effects of galantamine are the major hurdles for the optimum usage of this drug. Drug release characteristics are improved with the use of biodegradable polymer carriers, which sustain the release of encapsulated drugs. Hence, the aim of this study was to produce galantamine microparticles and to evaluate its effects on oxidant parameters after implantation on the spinal cord after SCI. The microparticles were produced by electrospraying, with 2.5% of galantamine hydrobromide in a 4% PLGA solution (PG) or 4% PLGA alone (PLGA), used as a vehicle control. The solutions were electrosprayed with a flow rate of 0.1 ml/h, voltage of 26kV and 9 cm of distance from the needle to the collector plate. The morphology of the particles was evaluated by scanning electron microscopy (SEM) and the diameter, zeta potential and polydispersion index was measured by Zetasizer. For the SCI model, Wistar rats were submitted to a contusion injury at the thoracic spinal cord, using MASICS impactor (CEUA 35781). The animals were divided in 5 groups: (1) only laminectomy (sham); (2) only SCI (injury); (3) SCI with galantamine treatment (gal); (4) SCI with implant of PLGA particles (PLGA) and (5) SCI with implant of PLGA particles containing galantamine (PG). Three days after the injury, the animals were euthanized and the spinal cords were collected. Reactive oxygen species (ROS) production in the spinal cord was assessed by DCF analysis, and lipid peroxidation was analyzed by measuring thiobarbituric acid reactive substances (TBARS). The average particle diameter was 434.73±49.67 nm for the 4% PLGA particles and 568.3±172.5 nm for the PG. The zeta potential of the particles was -41.5 ± 4.95mV for the 4% PLGA particles and -23.6±4.6 mV for PG. The polydispersion index was 0.543±0.04 for the 4% PLGA particles and 0.6±0.09 for PG. The group treated with PG showed significantly decreased ROS production when compared to the injury and sham groups, as well as to the group treated with PLGA particles alone. Furthermore, all the treatment groups presented a decreased TBARS production when compared to the injury group. The present study showed that groups 3, 4, and 5 were able to decrease lipid peroxidation. However, the present work demonstrated that treatment with PG was able to reduce the oxidative stress at 72 h after spinal cord injury, decreasing ROS production.