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IN SITU IMPLANTATION OF MICROPARTICLES OF PLGA WITH GALANTAMINE REDUCES LESION SIZE AND IMPROVES MOTOR RECOVERY AFTER SPINAL CORD INJURY

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Introduction: 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 incorporation in nanoparticles, which sustain the release of encapsulated drugs. Aim: The present study investigates the effects of microparticles containing galantamine in vitro on astrocytes and in vivo in a rat contusion model of SCI. Methodology: Galantamine microparticles were produced by electrospraying of 4% PLGA polymer solutions 5% Galantamine. The morphology of the particles was evaluated by Scanning Electron Microscopy and the diameter and zeta potential of the particles was measured by the Zetasizer. Astrocytes isolated from rat pups were treated with the microparticles and the cell viability and cytotoxicity were analyzed by the WST8 and LDH assay. The effects of galantamine (gal) on functional recovery and histological outcome in a rat contusion model of SCI were analyzed. Male Wistar rats were submitted to SCI with an impactor and received either an implant of PLGA particles or PLGA/Gal particles. The BBB scale was used to evaluate locomotor activity. The size of lesion was evaluated and the expression of beta3-tubulin, NFM, GFAP was analyzed by flow-cytometry. Results and discussion: The particle morphology changed as Galantamine was added, as can be seen by the MEV analysis. The zeta potential of the particles was of -41.5 ± 4.9 mV for 4% PLGA and 33 ± 0.15 mV for the PLGA/Gal, respectively. The average particle diameter was 434.73 ± 49.67 nm for particles with 4% PLGA alone, 762 ± 338.03 nm for the PLGA/Gal, respectively. The WST8 assay showed that 4% PLGA increased astrocyte viability on day 1 as well as day 7 as compared to the controls (cells with no treatment) on days 1 and 7, respectively. However, cell viability was lower in the 4% PLGA/gal groups on both day 1 and day 7 when compared to the groups treated with Gal. The LDH assay showed that the particles are not cytotoxic for the cells when compared to the control. The animals that received the implant of PLGA/Gal particles showed better motor recovery than the animals that received the PLGA particles only. The PLGA/Gal group presented a smaller lesion size (2.16 mm3) compared to PLGA group (2.89 mm3). The analysis of neural and glial markers by flow-cytometry showed no significant differences between the two animal groups. Conclusions: The PLGA microparticles present good biological activity with astrocytes and are non-cytotoxic. The PLGA/Gal particles promote locomotor recovery after spinal cord injury and reduce the scaring at the injury site.