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Effects of phosphate glass fiber–collagen scaffolds on functional recovery of completely transected rat spinal cords

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ABSTRACT

Phosphate-based glass fibers (PGFs), due to characteristics such as biodegradability and directionality, could be effective as spatial cues for axonal outgrowth following nerve injury. In the present study, PGF-containing cylindrical scaffolds of 1.8 mm diameter and 3 mm length were developed and implanted into the gap between the proximal and distal stumps following complete transection of rat spinal cords at T9. The PGF-free collagen scaffolds were implanted into the transected spinal cords of the control group. The open-field Basso, Beattie and Bresnahan locomotor scale revealed that the locomotor function of the experimental group was better than in the control group from 8 to 12 weeks after implantation, and urodynamic analysis revealed additional improvements in the experimental group in some parameters. Twelve weeks after implantation, some axon growth from the proximal and distal stumps to the scaffold was observed in the experimental group but not in the control group. Macrophages surrounded the injured thoracic spinal cord at 1 and 4 weeks after implantation; however, 6 h after implantation, the pro-inflammatory cytokines did not differ between the control and experimental groups. Anterograde corticospinal tract (CST) tracing with biotinylated dextran amine showed that, in the experimental group, some CST outgrowths could reach the lumbar enlargement. By 12 weeks, the mRNA levels of brain-derived neurotrophic factor in the bladder had increased more in the experimental group than in the controls. We conclude that PGFs can have a beneficial effect on functional recovery following complete transection of the thoracic spinal cord in rats.

1. Introduction

Spinal cord injury (SCI) results in somatic sensory and motor dysfunction, autonomic dysfunction, complications such as spasticity, decubitus ulcer and deep vein thrombosis, and, eventually, a significant decline in quality of life. The central nervous system is notoriously difficult to regenerate, and there is as yet no proven restorative therapy in the clinical setting [1].

Several research groups have pursued in vitro and in vivo studies to improve post-SCI somatic and autonomic functionality using stem cells, neurotrophic factors and suppressors of growth-inhibitory factors, though successes in the form of functional restoration have been rather limited in scope [2]. More optimistically, however, there are certain new treatment modalities that are expected to improve the potential for post-SCI regeneration. For example, recently developed adult-cell-derived stem cells such as induced pluripotent stem cells have exhibited pluripotency without graft rejection [3], and in animal studies, inhibition of the phosphatase and tensin homolog has elicited substantial axonal regeneration [4].

Biocompatible and biodegradable biomaterials could be an important delivery system for such stem cells and drugs, and have indeed reduced acute-stage inflammation [5] or promoted axonal outgrowth in chronic injury [6]. The outer structure of a scaffold used in treatment of SCI is usually tubular in order to connect disconnected spinal cords, while its inner structures should be designed such that injured axons can migrate into it from both proximal and distal stumps following transection. In previous animal-model studies, synthetic hydrogel or poly(lactic-co-glycolic

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