Use of Chitosan Conduit for Bridging Small-Gap Peripheral Nerve Defect in Sciatic Nerve Transection Model of Rat

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Abstract

Objective-To evaluate effect of chitosan conduit for peripheral nerve regeneration using sciatic nerve transection model in rat  
Design- Experimental in vivo study.  
Animals- Sixty healthy male Wistar rats.  
Procedures- The rats were divided into four experimental groups (n=15) randomly. In sham group the left sciatic nerve was exposed through a gluteal muscle incision and after careful homeostasis the wound was sutured. In transected control group the left sciatic nerve was exposed the same way, transected proximal to the tibio-peroneal bifurcation leaving a 10 mm gap and the nerve ends were sutured to the adjacent muscles. In silicone or chitosan groups the left sciatic nerve was transected the same way and proximal and distal stumps were each inserted into a silicone or chitosan tube. Each group was further subdivided into three subgroups of five animals each and were studied 4, 8, 12 weeks post operatively.  
Results- Functional and electrophysiological analyses showed significant improvement of nerve function in chitosan than in silicone group ($P < 0.05$). Morphometric indices and immuohistochemistry indicated that there were significant differences ($P < 0.05$) between chitosan and silicone with transected control groups 12 weeks after surgery.

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Conclusion and Clinical Relevance - Chitosan conduit could be considered clinically as an effective biodegradable tube for peripheral nerve regeneration in the least harmful way that is available, easily performed and affordable. It also averts the need for foreign materials that are likely to provoke a foreign body reaction.

Key words - peripheral nerve regeneration, chitosan conduit, rat.

Introduction

Peripheral nerve injuries are common in clinical practice due to trauma or deliberate surgical resection. Several methods as direct neurorrhaphy, nerve grafting, neurotisation, end-to-side neurorrhaphy and tissue engineering have been used in order to bridge peripheral nerve gaps. The gaps which are not suitable to the neurorrhaphy can be bridged with autologous, heterologous (allografts) grafts or synthetic biomaterials. Autologous nerve graft is widely accepted, however, it has several disadvantages and donor graft nerves are limited. Therefore, studies on nerve conduits as an alternative method in nerve regeneration have been focused on using a non-bioabsorbable material such as silicone or natural bioabsorbable grafts such as artery and vein.

Biodegradable nerve guides as a temporary scaffold are better than non-degradable biomaterials because latter remain in situ as a foreign body and ultimately result in limiting recovery of nerve function. Silicone has been extensively tested in the form of a prototype nerve tube. Nevertheless, its resistance to biodegradation can be a cause of chronic nerve compression in the long run. A second surgery may therefore be required for its removal. Recent studies show a benefit of using chitosan as scaffold in promoting wound healing, cartilage repair and nerve regeneration. It seems chitosan as a natural polymer has excellent properties including biocompatibility, biodegradability, non-toxicity and adsorption properties might be a suitable functional material for peripheral nerve regeneration. The objective of this study was to evaluate the efficacy of chitosan as a conduit on peripheral nerve regeneration using a rat sciatic nerve transection model. Assessment of the nerve regeneration was based on functional (walking track analysis), electrophysiological study, muscle mass measurement, histomorphometric, and immunohistochemical (Schwann cell detection by S-100 expression) criteria 4, 8, and 12 weeks after surgery.

Materials and Methods

Experimental Design

Sixty male Wistar rats weighing approximately 210 g were divided into four experimental groups (n = 15), randomly: Sham-operation (Sham), transected control (TC), silicone conduit positive control (SIL) and chitosan conduit (Chit). Each group was further subdivided into three subgroups of five animals each. Two weeks before and during the entire experiments, the animals were housed in individual plastic cages (50 × 40 × 20 cm) with an ambient temperature of 23 ± 3 °C, stable air humidity, and a natural day/night cycle. The animals were handled on a regular daily basis for 2 weeks prior to the study in order to acclimatize them with testing area and experiments. The rats had free access to standard rodent laboratory food and tap water. All procedures were carried out in accordance with the guidelines of the Ethics Committee and the University Research Council approved all experiments.

Preparation of chitosan conduit