The usefulness of a novel poly-lactide film as a nerve protector after nerve surgery

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ABSTRACT

INTRODUCTION

Perineurium constitutes an important component in the mechanisms regulating the internal milieu of the endoneurial space for functional maintenance and recovery from nerve damage. There is no doubt as to the value of external neurolysis. Conversely, internal neurolysis involves exposure by epineurotomy or epineurectomy, and separation of the individual fascicles, if necessary, by the removal of interfascicular scar tissue. Opening the perineurium is a dangerous procedure that should not be performed except in cases of interfascicular invasion by lepromatous bacilli in leprosy. However, in situations such as recurrent carpal tunnel syndrome and severe nerve injuries, postoperative epi- and intraneural fibrosis and adhesions represent major factors contributing to chronic neuropathy. At that time, secondary neurolysis is often worthless, since perineural adhesions recur in most patients. Fukuhira et al. have developed a novel biodegradable poly-lactide (PLA) film (honeycomb film) with a honeycomb-patterned structure on one side. The honeycomb surface adheres to the tissue immediately, functioning as a diffusion barrier. The purpose of this experimental study was to investigate effects of the honeycomb film in preventing postoperative adhesions and as an artificial perineurium in a rat extensive neurolysis model.

MATERIALS AND METHODS

All experimental protocols and animal maintenance procedures used in this study were approved by the Animal Ethics Research Committee at Nagoya University. We used two types of thin PLA film of 7 µm in thickness: a honeycomb film; and a cast film with smooth surfaces on both sides.

Procedure 1: Thirty male Lewis rats were used for the experiment. The sciatic nerves were exposed bilaterally. Under an operative microscope, the sciatic nerves were dissected from surrounding tissues. In the extensive internal neurolysis model, both epi- and perineurium were carefully removed from a 5-mm length of nerve at the mid-thigh level. To stimulate local fibrotic response around the nerve, the surface of the biceps femoris muscle-composing neural bed was repeatedly burned using an electrocoagulator. After neurolysis, the right nerve was wrapped with a 1-cm piece of honeycomb film (Group H), while the left nerve was left untreated as a control (Group C). For histological analysis, nerves with surrounding tissue were harvested weekly after surgery and stained with Masson trichrome stains. In addition, wet weights of tibialis anterior and gastrocnemius muscles were measured.

Procedure 2: For functional analysis, 24 rats were used. The 48 limbs were randomly assigned to four groups: Group H, application of honeycomb film; Group CA, application of cast film; Group C, operation, but no treatment; and Group N, sham operation. The same operations as in Procedure 1 were performed. For electrophysiological evaluations, all animals were anesthetized 6 weeks after surgery. We measured distal latency of compound muscle action potentials (CMAPs) from tibialis anterior muscle, and evaluated motor nerve conduction velocity (MCV). Wet weights of tibialis anterior and gastrocnemius muscles were subsequently measured.

Procedure 3: For functional analysis of the blood-nerve barrier (BNB), two rats were used. The same operations as in Procedure 1 were performed. At 2 days after surgery, the sciatic nerves were exposed again. Briefly, 400 mg of Evans blue and 1 g of bovine albumin were dissolved in 10 ml of phosphate-buffered saline, and 0.2 ml of Evans blue albumin was applied topically around the sciatic nerve to assess the perineural barrier. The rats were killed 2 h later, and the sciatic nerves were harvested and fixed.

For statistical analysis, Student’s t-test or the Tukey-Kramer test was used. Values of p<0.05 were considered statistically significant. All data are expressed as mean ± standard deviation.

RESULTS

Histological analysis (Procedure 1): At 1 week postoperatively, histological examination showed that the honeycomb film was closely attached to the nerve surface, with no adhesions or inflammation between the film and surrounding tissues in Group H. In contrast, nerves showed severe adhesion to the neural bed with intraneural scar formations(*) in Group C (Fig. 1).

**Figure 1:** A, Group H, ×400. B, Group C, ×100

Macroscopic findings (Procedure 2): At 6 weeks postoperatively, the honeycomb film remained in situ, and no adhesions were seen between the film and surrounding tissues in Group H. In contrast, sciatic nerves showed severe adhesion to the neural bed in Group C. In Group CA, cast film did not remain fixed in place in many specimens.

Functional analysis (Procedure 1 and 2): Mean percentage wet tibialis anterior and gastrocnemius muscle weight was significantly higher in Group H than in Group C at 4 and 6 weeks, although no significant differences were apparent at 2 weeks. Mean MCV was higher in the order of Group N, Group H, Group CA and Group C. MCV was significantly higher in Group H than in Group C at 6 weeks, whereas the difference between Group CA and Group C was not significant (Fig. 2).

**Figure 2:** MCV at 6 weeks after surgery. NS, not significant.

Functional analysis of the BNB (Procedure 3): In Group C, Evans blue albumin was widely distributed in the endoneurial spaces after internal neurolysis. In contrast, the honeycomb film was closely attached to the nerve and did not allow any Evans blue albumin molecules to enter the endoneurial spaces, as demonstrated by absence of Evans blue albumin within the endoneurial spaces on fluorescent microscopy.

DISCUSSION

The honeycomb film is a very thin PLA film, 7 µm thick. The honeycomb structure provides useful adhesion properties. Conversely, the honeycomb film has a smooth surface on the other side to prevent adhesion formation between the nerve and surrounding tissues.

Our results demonstrate that the honeycomb film has the potential to prevent adhesion even after internal neurolysis. The significantly better functional recovery seen in Group H thus suggests that the diffusion-barrier function and adhesion-prevention function provided by the honeycomb film enhances remyelination and axonal regeneration and inhibits progressive intraneural scarring by improving the endoneurial milieu after neurolysis.

The present findings clearly suggest that the honeycomb film is a useful substitute for perineurium and offers the potential to significantly expand the indications for neurolysis in peripheral nerve surgery. Taking the characteristics of materials such as adhesiveness, absorbability, and easy-handling into consideration, we believe honeycomb material has applications other than artificial perineurium.

DISCLOSURES

None of the authors have received any financial benefits as a result of this work.