ABSTRACT INTRODUCTION
Nerve allografts with immunosuppressants may be an alternative to conventional nerve autografts for the treatment of multiple nerve injuries
with a long interstump gap. General use of immunosuppressants is associated with increased risks of infection, generation of neoplasm, and other toxic complications, some of which are lethal. It is therefore controversial to use peripheral nerve allografts with immunosuppressants when repairing peripheral nerve injuries.

Green tea polyphenol protects tissues from ischemia, has antineoplastic and anti-inflammatory effects, and suppresses immune responses. We have previously demonstrated successful nerve regeneration within peripheral nerve allografts that were immersed in a polyphenol solution at 4 °C and does not require any specialized equipment. Moreover, our method simply improve the survival of donor neural cells.

RESULTS

The CD4:CD8 ratios in the polyphenol-0.2 allograft, polyphenol-2 allograft, and isograft groups were 2.79 ± 0.19, 2.75 ± 0.22 and 2.70 ± 0.14, respectively. There were no significant differences between the groups (P = 0.5978, 0.7927, 0.4311, respectively). Electrophysiological studies were performed at 12 weeks. The amplitudes of action potentials evoked in the pedal adductor muscle and the motor nerve conduction velocity (MNCV) in the operated limbs were expressed as percentages of measurements taken from the contralateral nonoperated limb in each rat. The mean pedal adductor muscle amplitude of the polyphenol-0.2 allograft group (39.4 ± 6.4%) was similar to that of the polyphenol-2 allograft group (42.1 ± 11.1%, P = 0.5403) and that of the isograft group (37.1 ± 10.3%, P = 0.5841). The mean pedal adductor muscle amplitude of the polyphenol-2 allograft group was not significantly greater than that of the isograft group (P = 0.2506). The mean MNCVs (%) of the polyphenol-0.2 allograft group, the polyphenol-2 allograft group and the isograft group were 67.5 ± 9.2%, 67.9 ± 7.7% and 67.5 ± 12.3%, respectively (P = 0.9381, 0.9978, 0.9360, respectively).

Morphological studies were subsequently performed at 12 weeks. There were significantly more myelinated axons in the polyphenol-0.2 allograft group (9,096 ± 1,583) and the polyphenol-2 allograft group (9,549 ± 1,147) than in the isograft group (6,411 ± 1,631, P = 0.0004, < 0.0001, respectively). There was no significant difference between the polyphenol-0.2 allograft group and the polyphenol-2 allograft group (P = 0.4964). There were no significant differences between the axon diameters in either the polyphenol-0.2 allograft group (1.57 ± 0.09) and the polyphenol-2 allograft group (1.57 ± 0.11) or the isograft group (1.56 ± 0.09, P = 0.9456, 0.9095, 0.8557, respectively).

The mean ratios of Sry to β-actin in the polyphenol-0.2 allograft, polyphenol-2 allograft, and isograft groups were 0.317 ± 0.075, 0.331 ± 0.09, and 0.622 ± 0.074, respectively, with no significant difference between the polyphenol-0.2 allograft group and in the polyphenol-2 allograft group (P = 0.6955).

DISCUSSION

There were no significant decreases in either the numbers of the CD4:CD8 ratio in the polyphenol-0.2 allograft group or the polyphenol-2 allograft group in this study. Davenport et al.16 reported a significant decrease in the CD4:CD8 ratio of T-cell subsets in peripheral blood from days 2–3 to day 7 following transplantation in recipients with rejection episodes. Here we confirm, from the assessments of posttransplant blood lymphocyte phenotype subsets, that polyphenols combined with very low doses of FK506 reduce the donor–host immune reaction following nerve allotransplantation.

The PCR studies showed that about 30% of the nerve cells in the graft were derived from polyphenol-treated nerve allografts plus 0.2 mg/kg per day FK506. Our previous study showed that 12 weeks following transplantation, 29% of the nerve cells in isografts and 14% of the cells in allografts originated from donor nerve segments treated by polyphenol without immunosuppressant. The current study has demonstrated successful peripheral nerve allograft and preservation using a combination of a subclinical dose of FK506 and green tea polyphenol pretreatment.

Although our electrophysiological and morphohistological analyses found no significant differences in nerve regeneration between polyphenol-treated nerve allografts plus 0.2 mg/kg per day FK506 and those given 2 mg/kg per day FK506, nerve regeneration in the nerve segments treated with the FK506 administration was better than in nerve isografts without FK506. We believe that these results demonstrate a neuroregenerative property for FK506.

Our current study indicates a potential improvement in peripheral nerve allotransplantation in patients with peripheral nerve injuries with the use of low-dose immunosuppressants combined with polyphenol storage of the transplant segment. Moreover, our method simply immerses the peripheral nerve segments in a 1 mg/ml polyphenol solution at 4 °C and does not require any specialized equipment. However, further studies are necessary to investigate further and improve the survival of donor neural cells.

REFERENCES


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