Delivery of Nitric Oxide-Releasing Silica Nanoparticles for In-vivo Revascularization and Functional Recovery after Nerve Autografting

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Introduction

NO is a unique bioregulatory molecule which not only enhances local blood flow, but also directly stimulates axonal regeneration.

Recently introduced nanoparticle-based scaffolds enable the controlled and sustained delivery of NO to targeted tissue.

The aim of this study was to determine whether exogenous NO-releasing silica nanoparticles (NO-sNP) promote new vessel formation, as well as motor functional recovery, after repair of short sciatic nerve defects in rats.

Methods

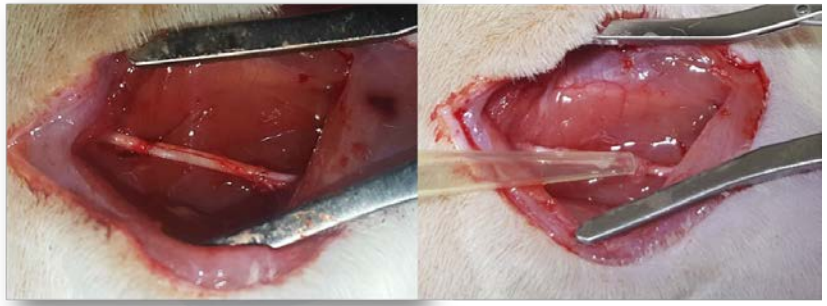
48 Lewis rats, 10-mm sciatic nerve defect was reconstructed with an ipsilateral reversed autologous nerve graft.

Group I (n = 24) control group.
Group II (n = 24) received NO-sNP in a fibrin gel carrier (Fig. 1).
6 in each group were sacrificed at day 7 for nerve microangiography.

Outcome assessment

- Every 2wks: ankle contracture angle and CMAP
- 4, 8 and 16 wks: maximum isometric tetanic force of the TA muscle, wet muscle weight and nerve histomorphometry.

Figure 1



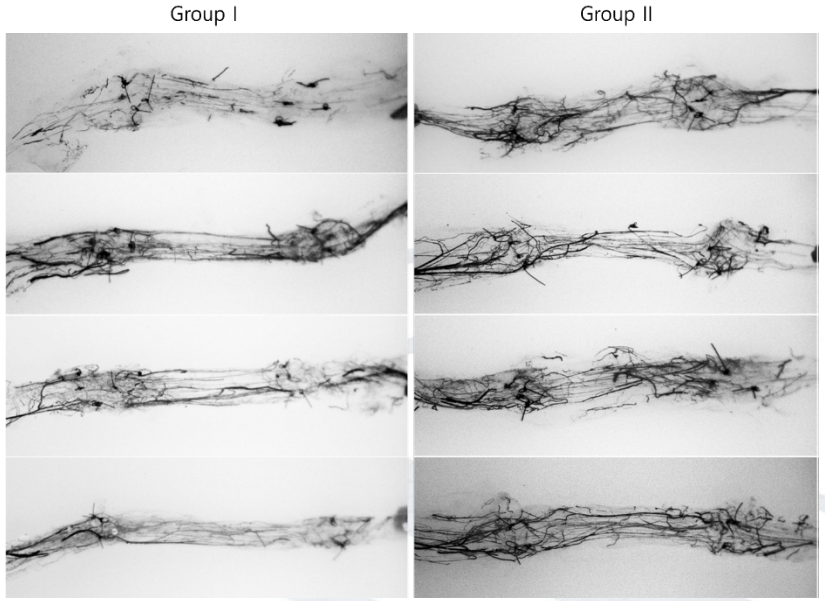
After nerve autografting, fibrin gel with or without NO-sNP was applied around the sciatic nerve graft site.

Results

Microangiography showed significantly greater vascular density in group II than in group I (group I, 17.1 ± 3.1%; group II, 23.7 ± 3.2%, P < 0.05) (Fig. 2).
Serial measurement of CMAP and ankle contracture angle showed no significant difference throughout the entire period (Fig. 3).

Maximum isometric tetanic force showed no significant difference at 4, 8, 16 wks. Wet muscle weight was not significantly different at 4, 8, 16wks.
Nerve histomorphometry showed no significant on imaging analysis (Fig. 4)

Figure 2



Microangiography pictures of nerve grafts for both groups.

Figure 3

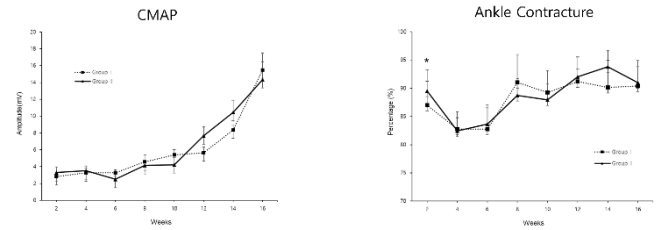
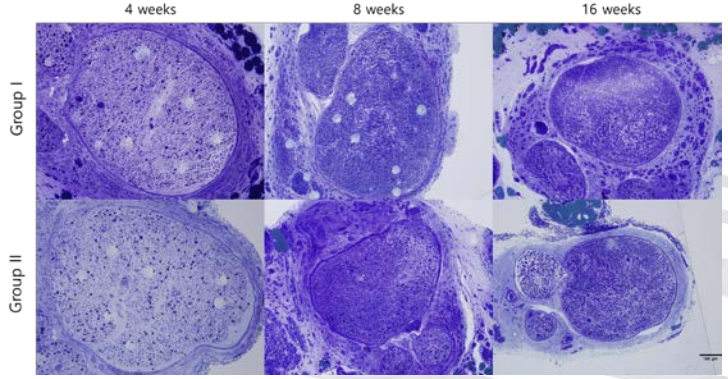


Figure 4



Histologic findings of the distal autograft stained with toluidine blue (magnification x100) at 4, 8, and 16 wks

Conclusions

- Exogenous delivery of NO using silica nanoparticles enhanced neo-angiogenesis in nerve autografts in the early recovery period; however, this effect did not translate into improved functional recovery.
- Early increase in vessel density around an injured nerve does not necessarily predict subsequent improvement in motor function.

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