

**CENTELLA ASIATICA INDUCED MESENCHYMAL STEM CELLS PROMOTE FUNCTIONAL RECOVERY AND MYELINATION OF SCIATIC NERVE IN CRITICAL-SIZE DEFECT IN RATS**

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ARTICLE INFO

Published: 26th August
2018

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KEYWORDS

Centella asiatica;
Mesenchymal stem cells;
Nerve conduit;
Nerve defect

SUMMARY

Centella asiatica, a traditional herbal medicine, has been shown to have neuroprotective and neuroregenerative properties. However, no studies have been reported on the effects of *C. asiatica* induced mesenchymal stem cells (MSCs) on *in vivo* nerve regeneration. The aim of this study was to investigate the effect of natural conduit seeded with neural differentiated MSCs (ndMSCs) (using *C. asiatica*) on the functional recovery and myelination of critical-size defect sciatic nerve in rats. ndMSCs were differentiated using 400µg/ml of *C. asiatica*, and nerve conduit was constructed by seeding MSCs or ndMSCs into decellularized artery conduit. Then, 1.5 cm sciatic nerve gap in Sprague-Dawley rats was bridged either with reversed autograft (RA)(n=3) (positive control), MSCs seeded conduit (MC)(n=4) or ndMSCs seeded conduit (NC)(n=4). Functional studies (pinch test and nerve conduction studies) were performed every 2 weeks up to 12 weeks. Morphometric analysis of axonal regeneration was done at 12 weeks post-implantation. Immunocytochemistry analysis revealed that MSCs had differentiated into neural lineage cells. It was found that rat's sensory sensitivity was improved in NC similar to RA. At 12th week, nerve conduction velocity was found to be the highest in NC (1.167 ± 0.243) compared to RA (1.033 ± 0.136) and MC (0.778 ± 0.177) (cm/ms). The average number of myelinated axon was significantly higher in NC (66.5 ± 1.217) compared to MC (47.5 ± 1.815) but significantly lower than RA (78.5 ± 2.098). The myelin sheath thickness found to be higher in NC (0.603 ± 0.012) than MC (0.503 ± 0.021) but lower than RA (0.762 ± 0.069) (µm). The G-ratio of NC (0.718 ± 0.006) and RA (0.689 ± 0.011) found to be significantly lower (higher myelination) compared to MC (0.772 ± 0.011). In conclusion, NC showed promising effects on functional restoration and myelination in comparison to MC. These observations demonstrated the neuroregenerative properties of *C. asiatica* and its potential as an alternative strategy to the treatment of critical-size nerve defect.

Acknowledgement: This study was funded by the Ministry of Agriculture and Agro-based Industry Malaysia under NKEA Research Grant Scheme (NRGS) (Project code: NH 1014 D048) and Universiti Kebangsaan Malaysia (Project code: FF-2017-175).