Peran Implantasi Sel Punca Mesenkimal dalam Regenerasi Neuromuscular Junction pada Model Cedera Saraf Tepi Kronik Tikus Sprague Dawley = Effect of Mesenchymal Stem Cell Application on Neuromuscular Junction Regeneration in A Chronic Peripheral Nerve Injury Model Sprague Dawley Rat

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Abstrak

Pendahuluan: Cedera saraf tepi dapat menyebabkan cacat fungsional yang parah. Denervasi yang berkepanjangan menyebabkan perubahan permanen pada organ target sekalipun dilakukan operasi dengan teknik rekonstruksi saraf bedah mikro. Oleh karena itu, banyak penelitian regeneratif telah dilakukan untuk meningkatkan luaran fungsional setelah tindakan rekonstruksi saraf pada cedera saraf tepi.
Metode: Dilakukan transeksi komplet saraf iskiadikus tungkai belakang kanan pada 20 tikus Sprague-Dawley jantan. Setiap ujung saraf dijahit ke otot terdekat untuk mencegah pertumbuhan saraf spontan. Setelah 3 minggu denervasi, dilakukan penyambungan saraf dan implantasi sel punca mesenkimal (SPM) ke neuromuscular junction (NMJ) otot gastroknemius pada kelompok perlakuan (n=10). Sepuluh tikus lainnya (kelompok kontrol) menerima plasebo (NaCL). Delapan minggu setelah penyambungan saraf, seluruh sampel dinilai luaran fungsional dengan analisis walking track dan studi neurofisiologi yang dilakukan sebelum terminasi. Berat otot basah dievaluasi kemudian dilakukan pemeriksaan histomorfometri.
Hasil dan Diskusi: Denervasi saraf iskiadikus selama tiga minggu menghasilkan model cedera saraf perifer kronis yang secara klinis mengakibatkan gangguan berjalan dan secara histologis menyebabkan degenerasi otot gastroknemius. Tidak ada perbedaan analisis walking track, compound muscle action potential (CMAP) dan berat otot basah antara kedua kelompok. Namun, penyambungan saraf yang dikombinasikan dengan implantasi SPM memberikan gambaran preservasi NMJ dan regenerasi otot yang lebih baik sebagai organ target saraf yang terbukti secara histologis dengan fragmentasi reseptor asetilkolin (AChR) yang jauh lebih rendah, jumlah dan kepadatan AChR yang lebih besar, serta diameter serat otot yang lebih besar.
Kesimpulan: Implantasi SPM di NMJ berpotensi menunda degenerasi organ target dan meningkatkan regenerasi
.....Introduction: Peripheral nerve injury is a devastating condition that can lead to severe functional disabilities. Despite the use of advanced microsurgical nerve reconstruction techniques, prolonged denervation causes irreversible changes in target organs. Thus, many regenerative studies have been conducted to increase functional outcomes in animal models.
Methods: Complete sciatic nerve transection was performed on the right hind limb of 20 male Sprague-Dawley rats. Each nerve end was sutured to the approximate muscle at a distance to prevent spontaneous nerve regrowth. After 3 weeks of denervation, the nerve was repaired and mesenchymal stem cells was injected directly to the gastrocnemius neuromuscular junction (NMJ) in MSCs group (n=10) and the rest of the rats (control group) received placebo (normal saline). Clinically, all sample were observed by walking track analysis and a neurophysiology study which was done before termination (8 weeks after nerve repair). Postmortem wet muscle weight was evaluated, and histological examination was performed
Result and Discussion: Three weeks sciatic nerve denervation produce the chronic peripheral nerve injury

model which resulted clinically as gait disturbance and histologically as gastrocnemius muscle degeneration. There was no difference in walking track analysis, compound muscle action potential (CMAP) and muscle weight between two groups. However, the delayed nerve repair combined with stem cell implantation gives a better NMJ and muscle regeneration as the nerve target organ that proven histologically with a significantly lesser acetylcoline receptor (AChR) fragmentation, greater AChR amount and density, as well as larger muscle fiber diameter.

Conclusion: Mesenchymal stem cell direct implantation in neuromuscular junction possibly delayed the end organ degeneration and enhanced regeneration proven by a better morphometry profile in MSCs group.