Pengaruh Pemberian Eksosom Human Wharton's Jelly Pada Proses Regenerasi Cedera Nervus Ischiadicus
(Kajian In Vivo: Polarisasi Makrofag, Pertumbuhan Akson, Remielinisasi, Fungsi Nervus Ischiadicus dan Luas Serat Musculus Gastrocnemius)
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PENGARUH PEMBERIAN EKSOSOM *HUMAN WHARTON'S JELLY* PADA PROSES REGENERASI CEDERA *NERVUS ISCHIADICUS*

(Kajian *In Vivo*: Polarisasi Makrofag, Pertumbuhan Akson, Remielinisasi, Fungsi *Nervus Ischiadicus* dan Luas Serat *Musculus Gastrocnemius*)

ABSTRAK

Latar Belakang:

Regenerasi saraf perifer merupakan proses biologis kompleks yang sering gagal memulihkan fungsi secara optimal. Eksosom human *Wharton's jelly* (HWJ) telah dikaji sebagai alternatif terapi regeneratif, namun bukti pengaruhnya pada cedera saraf perifer masih terbatas.

Tujuan:

Mengkaji pengaruh pemberian eksosom HWJ terhadap proses regenerasi cedera saraf *(n) ischiadicus* pada tikus, dengan fokus pada perbaikan fungsi saraf, luas serat otot (*m*) *gastrocnemius,* polarisasi makrofag, pertumbuhan akson, dan remielinisasi.

Metode:

Tiga puluh ekor tikus dibagi menjadi kelompok *sham operation* (SO) dan lima kelompok cedera. Kelompok kontrol (KK) mendapat injeksi PBS 50 µL, sedangkan kelompok terapi eksosom HWJ (E1–E4) mendapat dosis bertingkat: $7{,}9 \times 10^3$; $7{,}9 \times 10^4$; $7{,}9 \times 10^5$; dan $3{,}95 \times 10^6$ partikel dalam 50 µL. Cedera saraf dibuat dengan kompresi sementara pada *n. ischiadicus* kanan. Evaluasi dilakukan pada hari ke-14 pasca cedera, meliputi penilaian *sciatic functional index* (SFI), pemeriksaan histologi *m. gastrocnemius*, serta analisis ekspresi mRNA MBP, IL-10, iNOS, dan TNF-α dengan *quantitative reverse transcriptase polymerase chain reaction* (qRT-PCR), serta ekspresi mRNA NF200 dengan RT-PCR semikuantitatif.

Hasil:

Kelompok eksosom, terutama E4, menunjukkan nilai lebih tinggi secara bermakna dibanding KK pada analisis SFI (-30,18 ± 13,17 vs -57,54 ± 32,60), luas serat otot (974,59 ± 41,36 vs 751,50 ± 29,41), ekspresi mRNA NF200 (0,59 ± 0,06 vs 0,47 ± 0,08) dan mRNA IL-10 (2,44 ± 0,70 vs 0,47 ± 0,19). Sebaliknya, ekspresi mRNA iNOS (0,63 ± 0,20 vs 1,41 ± 0,22) dan mRNA TNF-α (0,77 ± 0,10 vs 1,40 ± 0,21) lebih rendah secara bermakna. Tidak terdapat perbedaan bermakna pada ekspresi mRNA MBP.

Kesimpulan:

Pemberian eksosom HWJ mendukung regenerasi cedera *n. ischiadicus* melalui perbaikan fungsi saraf, pencegahan atrofi otot, polarisasi makrofag M2, dan memicu pertumbuhan akson. Namun, efek terhadap remielinisasi belum terbukti sehingga memerlukan kajian lanjutan.

Kata Kunci: Cedera saraf perifer, eksosom, polarisasi makrofag, regenerasi, perbaikan fungsi.

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The Effect of Human Wharton's Jelly–Derived Exosomes on Sciatic Nerve Injury Models
(In Vivo Study: Macrophage Polarization, Axonal Growth, Remyelination, Nerve Function, and Gastrocnemius Muscle Fiber Area)

ABSTRACT

Background:

Peripheral nerve regeneration is a complex biological process that often fails to restore optimal function. Human Wharton's jelly (HWJ)–derived exosomes have been investigated as a potential regenerative therapy; however, evidence regarding their effects on peripheral nerve injury remains limited.

Objective:

This study aimed to evaluate the impact of HWJ exosome administration on sciatic nerve injury regeneration in rats, focusing on functional recovery, gastrocnemius muscle fiber area, macrophage polarization, axonal growth, and remyelination.

Methods:

Thirty rats were allocated into a sham operation (SO) group and five injury groups. The control group (KK) received 50 µL PBS injection, while treatment groups (E1–E4) received escalating doses of HWJ exosomes: 7.9×10^3, 7.9×10^4, 7.9×10^5, and 3.95×10^6 particles in 50 µL. Sciatic nerve injury was induced by transient compression of the right sciatic nerve. Fourteen days post-injury, evaluations included sciatic functional index (SFI), histological analysis of the gastrocnemius muscle, quantitative RT-PCR for MBP, IL-10, iNOS, and TNF-α mRNA expression, and semi-quantitative RT-PCR for NF200 mRNA expression.

Results:

Exosome-treated groups, particularly E4, demonstrated significantly improved outcomes compared with controls: SFI (−30.18 ± 13.17 vs −57.54 ± 32.60), muscle fiber area (974.59 ± 41.36 vs 751.50 ± 29.41), NF200 mRNA (0.59 ± 0.06 vs 0.47 ± 0.08), and IL-10 mRNA (2.44 ± 0.70 vs 0.47 ± 0.19). Conversely, iNOS (0.63 ± 0.20 vs 1.41 ± 0.22) and TNF-α (0.77 ± 0.10 vs 1.40 ± 0.21) mRNA levels were significantly reduced. No significant differences were observed in MBP expression.

Conclusion:

HWJ exosome administration supports sciatic nerve regeneration by enhancing functional recovery, preventing muscle atrophy, promoting M2 macrophage polarization, and stimulating axonal growth. However, effects on remyelination remain inconclusive and warrant further investigation.

Keywords: *Peripheral nerve injury, exosomes, macrophage polarization, regeneration, functional recovery.*