INTISARI

Pendahuluan: Siklofosfamid dapat menyebabkan kerusakan jaringan ovarium melalui aktivasi jalur inflamasi NF-κB dan memicu proses *Epithelial Mesenchymal Transition* (EMT) yang berkontribusi dalam pembentukan fibrosis dan penurunan fungsi ovarium. Eksosom *Human Wharton's Jelly-Mesenchymal Stem Cells* (HWJ-MSCs) berpotensi dalam memperbaiki jaringan ovarium. Namun, hingga kini belum banyak penelitian yang secara spesifik menilai efek eksosom dalam mengurangi inflamasi dan EMT serta dosis optimal yang efektif terhadap perbaikan jaringan ovarium pascainjeksi siklofosfamid.

Tujuan: Menganalisis efek pemberian eksosom HWJ-MSCs terhadap ekspresi mRNA IL-6, E-Cadherin, dan Vimentin pada jaringan ovarium mencit pascainjeksi siklofosfamid.

Metode: Penelitian eksperimental in vivo menggunakan 20 ekor mencit betina galur BALB/c yang dibagi menjadi 5 kelompok: kontrol tanpa perlakuan (A); injeksi siklofosfamid tanpa eksosom (B); injeksi siklofosfamid + eksosom $1{,}7\times10^6$ partikel (C); injeksi siklofosfamid + eksosom $3{,}4\times10^6$; partikel (D); dan injeksi siklofosfamid + eksosom $6{,}8\times10^6$ partikel (E). Injeksi siklofosfamid diberikan dengan dosis 120mg/kg pada hari ke-8 dan ke-15. Selanjutnya, eksosom diberikan secara intraperitoneal pada hari ke-22. Mencit di terminasi pada hari ke-36 untuk diambil ovariumnya dan dilanjutkan analisis ekspresi gen menggunakan metode qPCR dengan perhitungan $2^{-\Delta\Delta Ct}$.

Hasil: Eksosom HWJ-MSCs khususnya dosis $6{,}8\times10^6$ partikel menunjukkan ekspresi mRNA IL-6 lebih rendah signifikan dibandingkan kelompok tanpa eksosom ($p = 0{,}048$). Pada EMT, seluruh dosis eksosom HWJ-MSCs menunjukkan ekspresi mRNA E-Cadherin lebih tinggi signifikan pada kelompok C ($p = 0{,}001$), D ($p = 0{,}002$) dan E ($p = 0{,}001$) serta ekspresi mRNA Vimentin lebih rendah signifikan kelompok C ($p = 0{,}005$), D ($p = 0{,}003$) dan E ($p = 0{,}006$) dibandingkan kelompok tanpa eksosom.

Kesimpulan: Pemberian eksosom HWJ-MSCs berpengaruh terhadap ekspresi mRNA IL-6, E-Cadherin dan Vimentin dengan dosis $6{,}8\times10^6$ partikel sebagai dosis optimal dalam mengurangi inflamasi dan EMT pada jaringan ovarium mencit pascainjeksi siklofosfamid.

Kata Kunci: eksosom HWJ-MSCs, siklofosfamid, Inflamasi, EMT, IL-6, E-cadherin, Vimentin.

ABSTRACT

Introduction: *Cyclophosphamide induces ovarian tissue damage through activation of the NF-κB inflammatory pathway and triggers Epithelial–Mesenchymal Transition (EMT), which contributes to ovarian fibrosis and impaired ovarian function. Human Wharton's Jelly–Mesenchymal Stem Cell (HWJ-MSC)-derived exosomes have the potential in promoting ovarian tissue repair. However, there have been few studies that specifically assess the effects of exosomes in reducing inflammation and EMT, as well as the optimal effective dose for ovarian tissue repair after cyclophosphamide injection.*

Objectives: *Analyzing the effects of HWJ-MSC–derived exosome administration on the mRNA expression of IL-6, E-Cadherin, and Vimentin in the ovarian tissue of mice after cyclophosphamide injection.*

Methods: *The in-vivo experimental study used 20 female BALB/c mice, divided into five groups: untreated control (A); cyclophosphamide injection without exosome (B); cyclophosphamide injection + 1.7×10^6 exosome particles (C); cyclophosphamide injection + 3.4×10^6 exosome particles (D); and cyclophosphamide injection + 6.8×10^6 exosome particles (E). Cyclophosphamide was administered at 120 mg/kg on days 8 and 15. Exosomes were administered intraperitoneally on day 22. Mice were euthanized on day 36, ovaries were collected, and gene expression analysis was performed using qPCR method with the $2^{\wedge\text{-}\Delta\Delta Ct}$ calculation.*

Results: *HWJ-MSCs exosomes particulary at a dose of 6.8×10^6 particles showed significantly lower IL-6 mRNA expression compared to the group without exosomes ($p = 0.048$). In EMT, all doses of HWJ-MSCs exosomes showed significantly higher E-Cadherin mRNA expression in groups C ($p = 0.001$), D ($p = 0.002$) and E ($p = 0.001$) groups, as well as significantly lower Vimentin mRNA expression in groups C ($p = 0.005$), D ($p = 0.003$), and E ($p = 0.006$) compared to the group without exosomes.*

Conclusion: *Administration of HWJ-MSC-derived exosomes affected the mRNA expression of IL-6, E-Cadherin and Vimentin, with a dose 6.8×10^6 particles being the optimal dose for reducing inflammation and EMT in mice ovarian tissue after cyclophosphamide injection.*

Keywords: *HWJ-MSC exosomes, cyclophosphamide, inflammation, EMT, IL-6, E-Cadherin, Vimentin.*