INTISARI

Latar Belakang: Gagal ginjal akut (GGA) merupakan masalah kesehatan global dengan angka morbiditas dan mortalitas yang tinggi. Salah satu penyebab utama GGA adalah cedera iskemia-reperfusi (I/R) yang memicu stres oksidatif, aktivasi jalur apoptosis, serta kerusakan struktural ginjal. Terapi GGA saat ini masih bersifat suportif dan belum secara spesifik menargetkan mekanisme molekuler yang mendasari kerusakan ginjal. Eksosom dari *human Wharton's jelly-derived mesenchymal stem cells* (hWJMSC) memiliki potensi terapeutik melalui efek parakrin yang mampu memodulasi stres oksidatif dan apoptosis, namun bukti mekanistiknya pada model GGA akibat cedera I/R masih terbatas.
Tujuan: Penelitian ini bertujuan mengevaluasi pengaruh pemberian eksosom hWJMSC terhadap stres oksidatif, apoptosis, dan cedera tubulus pada model tikus GGA akibat cedera iskemia-reperfusi.
Metode: Penelitian ini merupakan penelitian kuasi-eksperimental dengan rancangan *post-test only with control group design* menggunakan tikus jantan galur Wistar (*Rattus norvegicus*). Hewan coba dibagi menjadi lima kelompok, yaitu *sham-operated* (SO), cedera I/R (IR), serta tiga kelompok cedera I/R yang mendapat eksosom hWJMSC dengan dosis berbeda: dosis rendah (IR-E1), dosis sedang (IR-E2), dan dosis tinggi (IR-E3). Model cedera I/R ginjal dibuat melalui penjepitan pediculus renalis yang diikuti pelepasan klem untuk menginisiasi fase reperfusi. Cedera tubulus dinilai secara semi-kuantitatif menggunakan pewarnaan *Periodic Acid–Schiff* (PAS). Stres oksidatif dan apoptosis dianalisis melalui pemeriksaan ekspresi mRNA SOD2, GPx, BAX, dan Bcl-2 menggunakan RT-PCR, sedangkan ekspresi protein BAX dianalisis secara deskriptif dengan imunohistokimia (IHC).
Hasil: Pemberian eksosom hWJMSC menunjukkan perbaikan struktural ginjal yang ditandai dengan skor cedera tubulus yang lebih rendah. Selain itu, terjadi ekspresi lebih tinggi pada mRNA antioksidan SOD2 dan GPx, disertai ekspresi mRNA proapoptotik BAX yang lebih rendah. Pewarnaan imunohistokimia menunjukkan ekspresi protein BAX pada kelompok IR, IR-E1, IR-E2, dan IR-E3 terlokalisasi di sitoplasma sel epitel tubulus daerah *corticomedullary junction*.
Kesimpulan: Eksosom hWJMSC memberikan efek protektif pada model GGA akibat cedera iskemia-reperfusi melalui perbaikan cedera tubulus, respons antioksidan lebih tinggi, dan inhibisi jalur apoptosis sehingga berpotensi sebagai terapi regeneratif bebas sel pada GGA.
Kata kunci: gagal ginjal akut, cedera iskemia-reperfusi, eksosom hWJMSC, stres oksidatif, apoptosis, cedera tubulus.

ABSTRACT

Background: Acute kidney injury (AKI) is a global health problem associated with high morbidity and mortality. One of the main causes of AKI is ischemia-reperfusion (I/R) injury, which induces oxidative stress, activation of apoptotic pathways, and structural renal damage. Current therapies for AKI remain largely supportive and do not specifically target the underlying molecular mechanisms of renal injury. Exosomes derived from human Wharton's jelly-derived mesenchymal stem cells (hWJMSCs) have shown therapeutic potential through paracrine effects that modulate oxidative stress and apoptosis. However, mechanistic evidence in AKI models induced by I/R injury remains limited.

Objective: This study aimed to evaluate the effects of hWJMSC-derived exosomes on oxidative stress, apoptosis, and tubular injury in a rat model of acute kidney injury induced by ischemia-reperfusion.

Methods: This quasi-experimental study employed a post-test only with control group design using male Wistar rats (Rattus norvegicus). The animals were divided into five groups: sham-operated (SO), ischemia-reperfusion injury (IR), and three ischemia-reperfusion groups treated with different doses of hWJMSC-derived exosomes: low dose (IR-E1), intermediate dose, IR-E2, and high dose (IR-E3). Renal ischemia-reperfusion injury was induced by clamping the renal pedicle followed by clamp release to initiate the reperfusion phase. Tubular injury was assessed semi-quantitatively using Periodic Acid–Schiff (PAS) staining. Oxidative stress and apoptosis were analyzed by measuring the mRNA expression of SOD2, GPx, BAX, and Bcl-2 using reverse transcriptase polymerase chain reaction (RT-PCR), while BAX protein expression was descriptively evaluated using immunohistochemistry (IHC).

Results: Administration of hWJMSC-derived exosomes resulted in structural improvement of the kidney, as indicated by lower tubular injury scores. In addition, higher mRNA expression of the antioxidant enzymes SOD2 and GPx was observed, accompanied by lower expression of the proapoptotic marker BAX. Immunohistochemical analysis demonstrated that BAX protein expression in the IR, IR-E1, IR-E2, and IR-E3 groups was predominantly localized in the tubular epithelial cell cytoplasm at corticomedullary junction.

Conclusion: Administration of hWJMSC-derived exosomes exert protective effects in a rat model of acute kidney injury induced by ischemia-reperfusion by improving tubular injury, repairing antioxidant responses, and inhibiting apoptotic pathways. These findings support the potential of hWJMSC-derived exosomes as a cell-free regenerative therapy for AKI.

Keywords: acute kidney injury, ischemia-reperfusion injury, hWJMSC-derived exosomes, oxidative stress, apoptosis, tubular injury.