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흰쥐에서 인간 지방조직유래 간엽줄기세포의 시스플라틴 유도 신독성에 미치는 영향

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Human Adipose Tissue-derived Mesenchymal Stem Cells Protect Kidneys from Cisplatin Nephrotoxicity in Rats

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Cisplatin has multiple cellular targets and modes of action that lead to nephrotoxicity. This suggests novel therapies that act at multiple cisplatin target sites may be effective. We tested whether human adipose tissue-derived mesenchymal stem cells (Ad-MSCs) can affect multiple target sites and protect against cisplatin-induced kidney damage. Rats were divided into four groups: control, infused with Ad-MSCs, injected with cisplatin, and cisplatin followed by infusion of Ad-MSCs. Animal survival and renal function were decreased and histological damage was increased in cisplatin-treated rats at day 3. Infusion of Ad-MSCs ameliorated renal dysfunction and tissue injury caused by cisplatin, leading to increased survival. Apoptotic cell death in the kidney was significantly reduced by Ad-MSCs infusion. Activation of p53, JNK, and ERK, and the expression of inflammation-related molecules were also decreased in the kidney that received Ad-MSCs. Very few Ad-MSCs were detected in the kidney. Conditioned medium from cultured Ad-MSCs had renal protective function in vivo and in vitro. Renal dysfunction and tissue damage caused by cisplatin was significantly reduced in rats treated with Ad-MSCs conditioned medium. The viability of cultured renal proximal tubular cells exposed to cisplatin was also improved by coculture with Ad-MSCs or with conditioned medium. Release of pro-inflammatory mediators induced by cisplatin was inhibited in coculture with Ad-MSCs. Our results show that human Ad-MSCs exert a paracrine protective effect on cisplatin nephrotoxicity at multiple target sites and suggest that human Ad-MSCs might be a new therapeutic approach for patients with acute kidney injury.

Key Words: 지방조직, 간엽줄기세포, 시스플라틴, 신독성
Adipose tissue, MSCs, Cisplatin, Nephrotoxicity