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P234. Effects of human amnion-derived mesenchymal stem cell (hAD-MSC) transplantation on chemotherapy-induced primary ovarian insufficiency in rats

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Context: Primary ovarian insufficiency (POI) induces multiple health risks and affects about 1% of women under the age of 40 years old. Chemotherapy could induce apoptosis of granulosa cells (GCs), follicle loss, vascular damage and tissue fibrosis in ovary, which can result in POI in young women bearing tumors. Human amnion-derived mesenchymal stem cells (hAD-MSCs) have the features of MSCs. Self-renewal capacity, multipotency, low immunogenicity and noninvasive application make hAD-MSCs promising source of stem cells for transplantation and regenerative medicine. However, whether hAD-MSC transplantation can restore the ovarian function in chemotherapy-induced POI is unknown.

Objective: This study is to explore the effects of hAD-MSC transplantation on chemotherapy-induced POI in rats.

Methods: The animals were divided into the control, POI and hAD-MSCs treatment groups (n=40 each group). POI rat models were established by intraperitoneal injection of cyclophosphamide. hAD-MSCs were injected into the tail vein of POI rats at 24h after chemotherapy. Rats were narcotized, and the organs and blood were collected for test from 24h to 12w after cell transplatation. Secretion of FGF2, IGF-1, VEGF and HGF in hAD-MSCs were detected in vitro.

Patient(s): 120 female Sprague-Dawley rats (10-12weeks).

Intervention(s): PKH26-labeled hAD-MSCs were injected into the tail vein of POI rats.

Main Outcome Measure(s): Estrous cycle, serum sex hormone levels, ovarian pathological changes, GC apoptosis, Bcl2 and Bax expression, and pro-inflammatory cytokine and VEGF levels in ovaries were examined.

Result(s): hAD-MSC transplantation increased the body and reproductive organ weights, improved ovarian function, and reduced reproductive organ injuries in POI rats. Transplantation of hAD-MSCs increased the Bcl-2/Bax ratio, reduced GC apoptosis and ovarian inflammation induced by chemotherapy and promoted VEGF expression in ovaries. hAD-MSCs were only located in the interstitium of ovaries, rather than in follicles, at 24h, 4w, 8w and 12w after transplantation in hAD-MSCs treatment group. hAD-MSCs can secrete FGF2, IGF-1, HGF, and VEGF, which are essential to keep the follicle growing and reduce GC apoptosis in ovaries.

Conclusions: hAD-MSC transplantation can repair ovarian injury and improve ovarian function in rats with chemotherapy-induced POI. The efficacy of hAD-MSCs is more likely to be partially mediated by growth factors produced by hAD-MSCs through the paracrine pathway.

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