

HUMAN UMBILICAL CORD PERIVASCULAR CELLS (HUCPVC) REDUCE OVARIAN FIBROSIS AND IMPROVE PREGNANCY RATES IN A MOUSE MODEL OF NATURAL OVARIAN AGING

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Abstract Body

Human umbilical cord perivascular cells (HUCPVC), a rich source of mesenchymal stromal cells (MSC), are gaining interest as cell therapy candidates in fertility preservation strategies. The objective of this study was to determine if the repeated administration of first trimester (FTM) or term HUCPVC during the period of ovarian aging could prevent age-related fertility decline in a mouse model. 6-month-old (6M) ICR mice were randomized in 4 groups (n=10-15 per group) to receive 6 monthly (6x) tail vein injections of 1×10^6 cells resuspended in HBSS (G1, first trimester (FTM) HUCPVC; G2, term HUCPVC; fibroblasts (G3, cell control) or HBSS (G4, vehicle control). A 5th group (G5) received a single injection (1x) of FTM HUCPVC at 11M (n=5). All procedures and assessments were blinded. To assess fertility, mice were bred for 5 days with fertile males at 6-8weeks, 6M and 12M. At 12M, animals that had received 6 injections (6x) of FTM and term HUCPVC showed increased pregnancy rates (100%, 80%) when compared to control HBSS (40%, $P=0.007$; $P=0.048$, respectively), and similar pregnancy rates to 6-8weeks (100%) and 6M (77%) groups. Age-associated declines in litter sizes and ovarian reserve indicators (# follicles per ovary, AMH levels) were observed as expected, but were not rescued by any of the cell treatments. An age-associated increase in ovarian fibrosis was observed by quantification of picosirius red staining in the control groups ($P<0.0001$), and was reduced at 12M in 6x FTM HUCPVC, 6x term HUCPVC and 1x FTM HUCPVC groups when compared to HBSS and fibroblast controls ($P<0.0001$; $P=0.01$; $P<0.0001$, respectively). An age-associated increase in serum c-reactive protein (CRP) levels ($P=0.01$) was significantly decreased in the 6x FTM HUCPVC groups when compared to HBSS at 12M ($P=0.04$). Our data suggest that FTM HUCPVC have anti-inflammatory and anti-fibrotic effects and represent a promising source of MSC to reduce fertility decline associated with advanced reproductive age.