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Poster Presentations

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The effects of L-carnitine, repaglinide, and mesenchymal stem cell-conditioned medium on in vitro maturation and early embryo development of oocytes derived from normal and endometriosis NMRI mouse

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Background: Endometriosis is an estrogen-dependent chronic inflammatory disorder that adversely affects women in their reproductive age, inducing infertility and pelvic pain. Indeed, oocytes retrieved from endometriosis women are more likely to fail in vitro maturation (IVM), exhibit altered morphology, and lower cytoplasmic mitochondrial content. More importantly, this condition is responsible for 30% of female infertility, and between 30 and 50% of women with endometriosis experience difficulties in becoming pregnant. L-carnitine (LC) is a lysine derivative with anti-oxidative properties that clears hydrogen peroxide and products of lipid peroxidation. Repaglinide (RG) is an anti-diabetic drug that increases intracellular Ca^2+concentration through opening the cells' calcium channels, resulting in insulin release from pancreatic β cells. Mesenchymal stem cell-conditioned media (MSC-CM) contain various growth factors, cytokines, bioactive factors, and tissue regenerative elements generated by mesenchymal stem cells, which can enhance IVM and subsequent embryonic development.

Objective: The current study was aimed to explore the comparative effects of mesenchymal stem MSC-CM, RG, and LC on IVM, in vitro fertilization (IVF), embryo development and formation, as well as on total blastocyst cell numbers.

Materials and Methods: Immature oocytes were collected from two groups of normal and endometriosis induced female NMRI mice ovaries (6-8 weeks old). Oocytes cultured in IVM medium supplemented with 0.0 (control group), 1μM RG, 0.3 and 0.6 mg/ml LC, and 25% and 50% MSC-CM. After 24h of oocyte incubation, the IVM rate was evaluated. Subsequently, MII oocytes were put in the IVF and culture medium then early embryo cleavage was evaluated for 1 to 5 days.

Results: Endometriosis caused a devastating impact upon ovarian histopathology, oocyte maturation, fertilization, early embryo development, and oxidant/antioxidant status ($p < 0.05$). Conversely, in both normal and endometriosis induced mice, different concentrations of RG, LC, and MSC-CM, especially 50% MSC-CM, significantly improved IVM, IVF, and embryo formation rates compared to control groups ($p < 0.05$). Strikingly, better improvement in alleviating EMS-induced injuries was seen in the MSC-CM groups in comparison with other groups.

Conclusion: By way of conclusion, supplementation of IVM medium with RG, LC, and MSC-CM improved oocyte developmental parameters such as maturation, fertilization, and embryo cleavage rates. Our findings indicated that 50% of MSC-CM was the most efficient supplement to reverse endometriosis-evoked deleterious impacts. Indeed, MSC-CM not only does it possesses anti-oxidative properties, but also it contains growth factors, bioactive factors, cytokines and performs anti-inflammatory actions. Present findings have potential applications for improving the clinical trials of humans suffering from endometriosis-related sub/infertility.

Key words: *Endometriosis, In vitro fertilization, Mesenchymal stem cell-conditioned medium, Repaglinide, L-carnitine.*