

ABSTRACT

Endometriosis, a common gynecological disorder, is characterized by the presence of endometrial tissue outside the uterine cavity. In vitro fertilization (IVF) is believed to be an effective therapy for endometriosis associated infertility. Oxidant-antioxidant balance in the oocyte environment is considered to have a significant impact on IVF outcome in these women. However, the definitive role of trace elements in women with endometriosis remains largely unknown. In view of this, relationship between oxidative stress and trace elements and possible role of these parameters on IVF outcome was investigated. Intrafollicular reactive oxygen species (ROS)/nitric oxide (NO) showed deleterious effect on IVF outcome parameters. A cut-off ROS level ~105 cps beyond which good quality oocyte formation is unlikely, was established. Further, follicular levels of lead and cadmium showed a negative association with IVF pregnancy outcome, highlighting the toxicity of environmental pollutants. Development of ovarian follicles and follicular walls breakdown to release oocytes at the time of ovulation is determined greatly by the activity of the enzymes, matrix metalloproteinases (MMPs) and their inhibitors, tissue inhibitors of metalloproteinases (TIMPs). Mature oocytes retrieved from women with endometriosis associated with a significant decrease in MMP-2 and MMP-9 and increase in TIMP-1 activity as compared with immature oocytes. Further, the imbalance in MMP-9/TIMP-1 ratio was found to decrease significantly following progesterone supplementation. A large number of cytokines and angiogenic factors present in the follicular fluid are associated with follicular development, oocyte maturation and embryo formation. Using multivariate analysis, IL-8, IL-12 and adrenomedullin were identified as the major factors contributing to endometriosis and were negatively associated with oocyte maturity and embryo quality and pregnancy outcome. Treatment of endometriosis yet remains a challenge. The efficacy of dual drug-loaded Doxycycline-EGCG nanoparticles therapeutics is demonstrated in endometriosis mouse model. The dual agent nanoparticles appeared to be effective in decreasing oxidative stress, MMP activity and angiogenesis in mice induced with the disease. Further, the molecule reduced endometrial glands and microvessels density considerably and improved the oocyte quality. This combination of nanoparticles emerges as a promising molecule with potential application in clinical treatment of endometriosis and warrants further research.

Keywords: *Endometriosis, Infertility, Follicular fluid, Oxidative stress, Antioxidants, Trace elements, In vitro fertilization, Matrix metalloproteinases, Cytokines, Nanoparticles*