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Review

The root of reduced fertility in aged women and possible therapentic options: Current status and future perspects

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ABSTRACT

It is well known that maternal ageing not only causes increased spontaneous abortion and reduced fertility, but it is also a high genetic disease risk. Although assisted reproductive technologies (ARTs) have been widely used to treat infertility, the overall success is still low. The main reasons for age-related changes include reduced follicle number, compromised oocyte quality especially aneuploidy, altered reproductive endocrinology, and increased reproductive tract defect. Various approaches for improving or treating infertility in aged women including controlled ovarian hyperstimulation with intrauterine insemination (IUI), IVF/ICSI-ET, ovarian reserve testing, preimplantation genetic diagnosis and screening (PGD/PGS), oocyte selection and donation, oocyte and ovary tissue cryopreservation before ageing, miscarriage prevention, and caloric restriction are summarized in this review. Future potential reproductive techniques for infertile older women including oocyte and zygote micromanipulations, derivation of oocytes from germ stem cells, ES cells, and iPS cells, as well as through bone marrow transplantation are discussed.

Abbreviations: aCGH, array comparative genomic hybridization; AFC, antral follicle count; AMH, Anti-Müllerian hormone; ART, assisted reproductive technology; BMT, bone marrow transplantation; CC, clomiphene citrate; CGH, comparative genomic hybridization; Dnmt, DNA methyltransferase; FISH, fluorescence *in situ* hybridization; FSH, follicle-stimulating hormone; DHEA, dehydroepiandrosterone; E2, estradiol; GnRH, gonadotropin-releasing hormone; GV, germinal vesicle; hCG, human chorionic gonadotrophin; HSG, hysterosalpingogram; ICSI, intracytoplasmic sperm injection; IUI, intrauterine insemination; IVF/ICSI-ET, *in vitro* fertilization/fertilization/embryo transfer; IVIG, intravenous immuno globulin; LDA, low-dose aspirin; LH, luteinzing hormone; MCL, menstrual cycle length; OSCs, oogonial stem cells; P, progesterone; PBD, polar body diagnosis; PGCs, primordial germ cells; PGD/PGS, preimplantation genetic diagnosis and screening; PLI, paternal leukocyte immunization; PZD, partial zona dissection; PR, progesterone receptor; PTEN, phosphatase and tensin homolog; SCNT, somatic cell nuclear transfer; SAC, spindle assembly checkpoint; SC, synaptonemal complex; SMC, structural maintenance of chromosomes; SNP, single nucleotide polymorphism; VEGF, vascular endothelial growth factor.

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Contents

1. Introduction

With the world's industrialization, more and more women postphone marriage, childbearing and first birth due to their career priorities, advanced education, contraception, artificial abortion, and financial concerns. The number of women bearing children in their 30- and 40-year age range is clearly increased which is the age range when female fertility is significantly decreased. It has been predicted that the likelihood of infertility of a woman at age 35 is just below 20%; at age 40 it is about 40%; and at age 45 it is 80% (Jansen, 1984).

It is estimated that about 50% of the early embryos undergo miscarriage before or directly after implantation, and in such cases women are not aware of being physiologically pregnant. After pregnancy is established, about 15% of the clinical pregnancies terminate by miscarriage, usually in the first trimester (Jones and Lopez, 2006). The risk of miscarriage increases significantly with advancing maternal age. Several studies have shown an increase in the risk of spontaneous abortion in