Premature luteinization of follicles and indication for individualization of timing hCG administration based on “ovarian age”

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Why in vitro fertilization (IVF) pregnancy rates suddenly sharply decline after age 43 was for the longest time unknown. The function of granulosa cell (GC) is known as a main regulator and marker of oocyte function. By investigating GC functions in three age groups: young oocyte donors (ages 21-29), middle-aged (ages 30-37) and older infertile patients (ages 43-47), we demonstrated age-related functional declines in GCs, characterized by changes in gene expression, proliferation, apoptosis and sensitivity to FSH during in vitro culture, consistent with premature luteinization (Wu, et al. 2015). To avoid premature luteinization, we, in patients from older infertile group (ages 43-47), advanced oocyte retrieval by administering human chorionic gonadotropin (hCG) at maximal leading follicle size of 16mm instead of 19-21mm. By this earlier retrieval (ER), these patients with very advanced ages exhibited improved embryo quality and, with active utilization of rescue *in vitro* maturation of premature oocytes, despite ER actually improved available embryo numbers for transfer and respectable clinical pregnancy rates (19.3% vs. 8.9%, $P<0.05$). ER to a large degree also avoided premature luteinization in GCs.

Additionally, ER was also tested in younger patients (<age 40) with premature ovarian aging (POA, Wu et al., 2016) . These patients also expressed follicular evidence of premature luteinization in GCs, which was largely avoided by ER and improving clinical pregnancy rated from 7.7% to 41.4%, $P<0.05$). Optimized timing of hCG administration demonstrated that ER with hCG trigger at 16.0-18.0mm of leading follicle size in women with low functional ovarian reserve at all ages appears to significantly improve GC function, oocyte/embryo quality and finally clinical pregnancy rates, while triggering <16.0mm and >18.00mm almost equally reduces pregnancy chances.

References:

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