The international Academy of Human Reproduction

17th World Congress of the Academy of Human Reproduction

15–18 March 2017

Rome, Italy

TITLE

PROTEOMICS OF FOLLICULAR FLUID: NEW INSIGHT IN GONADOTROPHIN SIGNALING AND POTENTIAL TRANSLATION INTO CLINICAL PRACTICE

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ABSTRACT

Purpose: to evaluate if r-LH supplementation during COS in poor-ovarian-responders(POR) may influence post-receptor signalling and messenger pathways involved in follicular growth and oocyte maturity, to identify the follicular pathways involved and determine whether the above factors could explain the clinical advantages observed with r-LH supplementation in this cohort of patients.

Methods: we conducted an observational-cohort-study on infertile women aged ?40 years expected poor-responders. First COS cycle was done by standard-long-agonist protocol(s-COS) using recombinant-FSH and, in case of treatment failure, a second cycle(LH-COS) was performed by r-LH supplementation. Follicular fluid levels of EGF,ERK-1/2,AKT-1/2 and their phosphorylated isoforms(p-ERK-1/2 and p-AKT-1/2) were assessed. As main outcome measures we considered differences in levels of the above mentioned biomarkers between stimulation protocols and their association with the number of MII oocytes and 1st degree embryos.

Results: S-COS and LH-COS showed significant differences in terms of FF levels of EGF[$p<0.05$], ERK-1/2[$p<0.001$], p-ERK-1/2[$p<0.001$], AKT-1/2[$p<0.001$] and p-AKT-1/2[$p<0.001$]. FF levels of EGF[$p<0.01$], ERK-1/2[$p<0.05$], AKT-1/2[$p<0.05$], p-ERK-1/2[$p<0.001$], p-AKT-1/2[$p<0.05$] correlated significantly with the number of MII oocytes retrieved. p-ERK-1/2 [r2:0.973; $p<0.0001$] and p-AKT-1/2 [r2:0.624; $p<0.05$] also showed a significant association with the highest rate of 1st degree embryos.

Conclusions: EGF downstream signalling PI(3)K-AKT1/2-mTOR and cAMP-PKA-ERK1/2 cascades are strongly enhanced by r-LH supplementation during COS. These pathways may have a fundamental role in the acquisition of oocyte competence and potentially influence the number and quality of obtained embryos. r-LH supplementation might represent a strategy to improve the cost-efficacy of IVF in POR patients.

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