Enhancement of oocyte developmental competence under metabolic stress conditions using omega-3 fatty acids in vitro

Waleed F. Marei1,2, Jessie De Bie1, Karolien L.J. Desmet1, Peter E.J. Bols1, Jo L.M.R. Leroy1

1Department of Veterinary Sciences, University of Antwerp, Belgium
2Department of Theriogenology, Cairo University, Egypt

We have shown that omega-3 α-linolenic acid (ALA) enhance oocyte competence via several molecular pathways. In contrast, high saturated (stearic, palmetic) and monounsaturated (oleic) non-esterified fatty acids (HNEFAs) which are predominant during metabolic stress conditions have detrimental effects on oocyte quality. Here, we examined the combined effects of HNEFAs and ALA (at patho-physiological concentrations). COCs (n=1529 in 5 repeats) were matured in the presence of ALA (50µM), HNEFAs (425µM), HNEFAs+ALA, or in fatty acid-free solvent control. Cumulus cell expansion was scored after oocyte maturation (0-3: 0; not expanded, 3; fully expanded). Cleavage and fragmentation rates were recorded on day 2 post-fertilization. Blastocyst rates were recorded on day 7 and 8. Day 8 blastocysts (n=179) were immunostained with anti-cleaved-caspase-3 antibody and Hoechst. Total cell counts and apoptotic cell indices were calculated. Compared with controls, HNEFA supplementation resulted in (P<0.05): inhibition of cumulus cell expansion (score: 1.7±0.2 vs. 2.8±0.04); higher fragmentation rates (16.8% vs. 9.5%); and lower blastocyst rates on day 7, expressed as a proportion from total fertilized oocytes (15.6% vs. 22.8%) or from total cleaved embryos (20.4% vs. 30.6%). Hatched and expanded blastocysts produced from HNEFA-exposed oocytes had higher apoptotic cell indices. In contrast, these negative effects were alleviated in the presence of ALA in the HNEFA+ALA group, where cumulus expansion score (2.4±0.16), fragmentation (6.9%), blastocyst rate on day 7 (21.4% from total fertilized oocytes and 28.7% from cleaved embryos), and apoptotic cell index were similar to the controls. In addition, HNEFA+ALA group had significantly higher total cell numbers in expanded and normal blastocysts compared with HNEFA group. In conclusion, ALA supplementation protects COCs matured under metabolic stress conditions and enhance their subsequent developmental potential. These results propose the use of dietary omega-3 fatty acids to improve fertility in animals and humans suffering from metabolic disorders associated with lipolysis.