Insulin resistance and PCOS as a metabolic disease

PCOS patients are typically characterized by chronic anovulation, hyperandrogenism, polycystic ovaries. Metabolic abnormalities such as overweight/obesity and hyperinsulinism or insulin resistance are frequent findings in PCOS patients and such impairment induce a higher production of androgens. Such condition can be due to overfeeding as well as by a costitutional predisposition to an abnormal control of glucose metabolism. 40-45% of all PCOS patients are overweight/obese and show a modest up to an exaggerated hyperinsulinism in response to the standard oral glucose tolerance test (OGTT). In addition such reduced insulin sensitivity can be observed also in 10-15% of the normal weight PCOS, thus confirming that hyperinsulinism can show up not only in relation to obesity or to excess of fat tissue but also as an intrinsic abnormal ability to control glucose metabolism.

Recent data clearly demonstrated that reduced insulin sensitivity can be improved using glucose sensitizer drugs, such as metformin, so that to reduce the negative modulation exerted by hyperinsulinemia on the reproductive axis as well as on neuroendocrine control of reproduction with relevant effects also on adrenal function and neurosteroid production.

The evolution of therapeutical approach to PCOS proposed recently the use of inositol in 2 of the isomers at present available: myo-inositol (MYO) and d-chiro-inositol (DCI). Both compounds are tightly linked one to the other since MYO is transformed by an epimerase in DCI, having each tissue its own conversion rate, likely due to the specific needs for the two different molecules. In general both these compounds works as specific modulators of the intra cellular second messanger activated by the insulin linkage with its own membrane receptor. Recently also alfa lipoic acid (ALA) has been demonstrated to improve insulin sensitivity with specific positive effects in PCOS with familiar diabetes.

Recent data demonstrated that integrative administration of MYO in lean PCOS ameliorated insulin response to OGTT and that both MYO or DCI reduced insulin response to OGTT in overweight or obese PCOS. Both isomers have been demonstrated to improve also ovarian function and LH response to GnRH stimulation, typically abnormal in PCOS patients. Though impossible to state what of the two isomers play the main role, it appears clear that the metabolic impairment(s) are great part of the casual factor(s) of the abnormal reproductive function in PCOS.