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PCOS IN ADOLESCENT GIRLS

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Polycystic Ovary Syndrome (PCOS) is a prevalent endocrinopathy in adolescent girls, commonly presenting with hirsutism and menstrual irregularity. The pathophysiology of PCOS is complex and involves the interaction of genetic/epigenetic alterations and endocrine- metabolic abnormalities such as insulin resistance and adiposity, including ectopic accumulation of fat in the liver and other organs.
There is no licensed therapy for PCOS. The baseline treatment should consist of lifestyle measures that reduce body adiposity. The most prescribed addition is an oral estro-progestagen contraceptive (OC), even for girls who do not need contraception. An alternative addition in girls who are not sexually active is the combination of insulin sensitizers plus an anti-androgen to reduce hepatic and visceral fat excess. In non-obese girls with PCOS and without pregnancy risk, we have explored the effects of low-dose combinations of insulin-sensitizers and anti-androgens, as compared to the effects of OC. A decade ago, a low-dose combination of flutamide (Flu) and metformin (Met) was found to be superior to a drospirenone-OC in attenuating endocrine-metabolic and body composition abnormalities. The subsequent addition of low-dose pioglitazone (Pio) to FluMet resulted in a triple treatment (PioFluMet) with a broader spectrum of on-treatment and post-treatment benefits than cyproteroneacetate-OC.
More recently, and because some of the explored medications (such as flutamide and cyproterone acetate) are not available in many countries, we have compared the effects of SPIOMET -a low-dose combination of three generics: spironolactone (50 mg/d), Pio (7.5 mg/d) and Met (850 mg/d), that targets the reduction of hepatic fat-, to those of a widely prescribed OC (20 mcg ethinylestradiol + 100 mcg levonorgestrel). The on-treatment normalization of hyperandrogenemia as well as the post-treatment increase in androgen levels were slower with SPIOMET. Visceral fat and insulinemia normalized only with SPIOMET. Body weight, lean mass, and abdominal subcutaneous fat did not change significantly in both treatment groups. SPIOMET was followed by a 2.5-fold higher ovulation rate and by a 6-fold higher prevalence of normovulation than OC. Higher post-treatment ovulation rates associated to more on-treatment loss of hepatic fat. In PCOS adolescents, early reduction of ectopic fat may prevent in part subsequent oligo-anovulatory subfertility.

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