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Normalization of Ovulation Rate in Adolescent Girls with Polycystic Ovary Syndrome

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The authors have nothing to disclose

BACKGROUND

Study registered as *ISRCTN29234515*

- Oligo-ovulatory androgen excess in women [Polycystic Ovary Syndrome (PCOS) by NIH definition] is a major cause of subfertility and relates to hepatic steatosis and visceral adiposity. In adolescent girls, PCOS-by-NIH is the most common cause of hirsutism and menstrual irregularity.
- There is no licensed therapy for PCOS-by-NIH in adolescent girls. Prime recommendation is to reduce body adiposity with lifestyle measures. Most girls receive in addition an oral contraceptive (OC); an alternative treatment in girls who are not sexually active is a combination treatment with spironolactone (50 mg/d), pioglitazone (7.5 mg/d) and metformin (850 mg/d) (SPIOMET), that aims at reducing ectopic fat and thus at a further lowering of insulin, gonadotropin and androgens.

AIM & STUDY DESIGN

- To compare the on-treatment and post-treatment effects of a widely prescribed OC [ethinylestradiol (20 µgr) + levonorgestrel (100 mg)], to those of low-dose SPIOMET.
- Randomized, controlled, open-label study (12 mo on treatment, 12 mo post-treatment) in an Adolescent Endocrinology Unit.

SUBJECTS AND METHODS

- Adolescent girls with hirsutism and oligomenorrhea; >2 yr beyond menarche; no sexual activity; PCOS by NIH; n=36 of whom 34 completed the study; at start, mean age was 16 yr; body mass index 23.5 Kg/m^2.
- Prime outcome was the ovulation number (in the second and fourth trimester of the post-treatment year), as inferred from menstrual diaries and weekly progesterone concentrations in saliva. Secondary outcomes were body composition (DXA); abdominal fat partitioning (MRI); insulinemia (oGTT); and circulating androgens (LC-MS/MS).

RESULTS

Figure 1. Longitudinal changes in hepatic fat and free androgenemia Z-scores in adolescent girls with PCOS, who received an OC (red circles; N=17) or low-dose SPIOMET (blue circles; N=17) for 12 mo, and who remained subsequently untreated for 12 mo. OC and SPIOMET had opposing effects on hepatic fat; OC lowered free androgenemia faster than SPIOMET, but was also followed by a faster rebound. Results are means and SEM. P values refer to differences between treatment subgroups (0-24 mo). Symbols along the X-axis (*p<0.05, &p<0.01, #p<0.001), refer to differential changes between 0-6 months and between 12-18 mo.

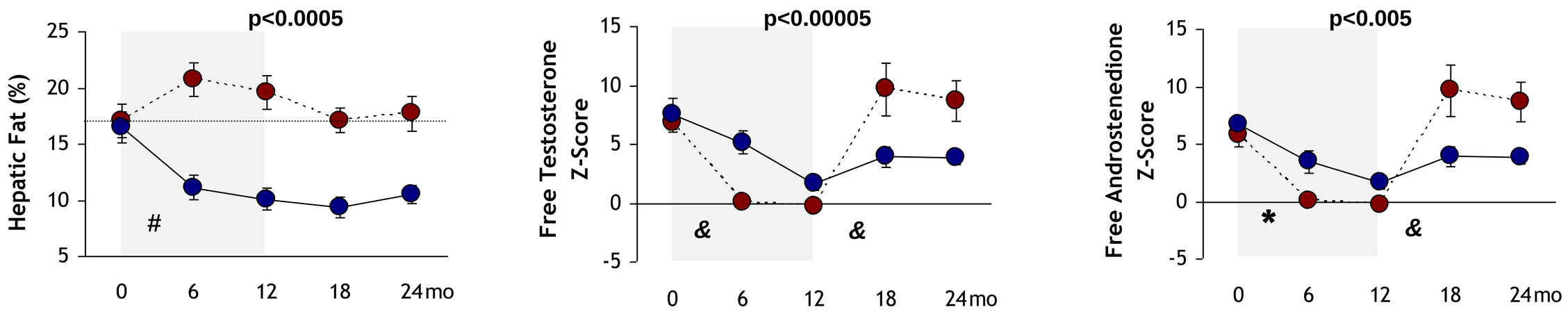
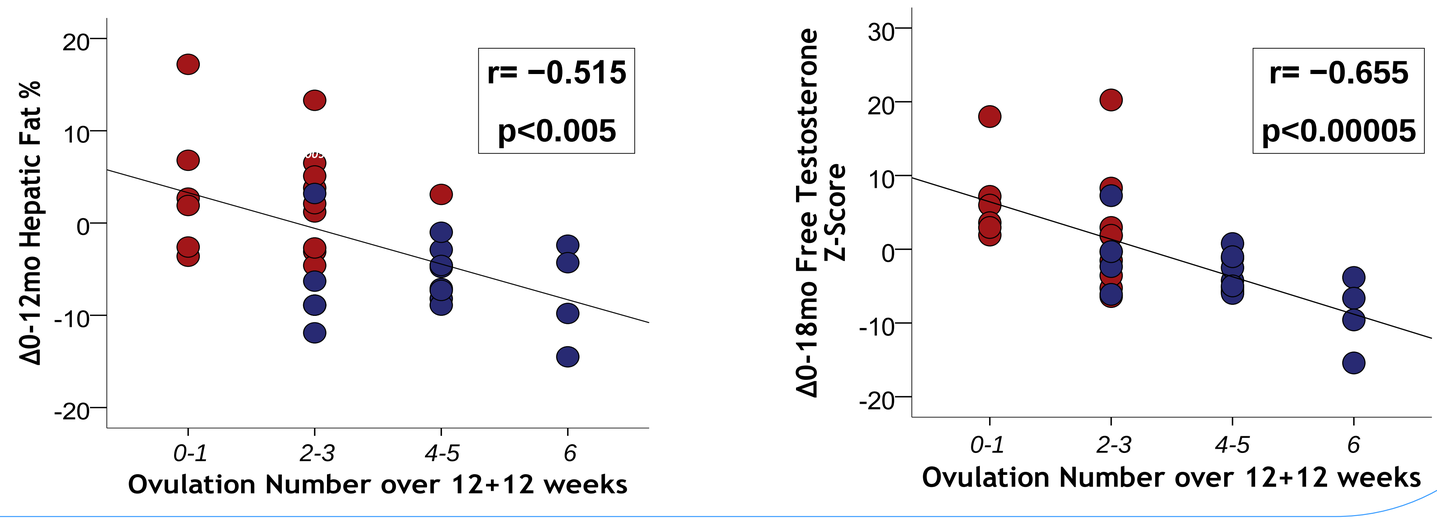


Figure 2. Numbers of inferred ovulations over 12+12 post-treatment wk associated to on-treatment changes of hepatic fat (left panel), and to post- *vs* pre-treatment changes of free testosteronemia (right panel).

Results from OC girls (N=17) are shown in red circles, and those from SPIOMET girls in blue circles (N=17). P and R values are from Pearson correlations.



CONCLUSION

- Early in PCOS, normalization of hepatic fat with SPIOMET is followed by a normal ovulation rate.
- SPIOMET treatment in adolescent girls with PCOS (and without sexual activity) is accompanied and followed by a more normal endocrine-metabolic state than OC treatment.

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