EFFECTS OF CO-ADMINISTRATION OF METFORMIN AND CLOMIPHINE CITRATE (CC) ON HORMONAL PROFILE AND PREGNANCY RATES IN NON-OBESE PATIENTS WITH POLYCYSTIC OVARY SYNDROME (PCOS): RESULTS OF A CLINICAL TRIAL

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Objective: Insulin resistance, and its compensatory hyperinsulinemia, plays a key role in the pathogenesis of infertility in women with PCOS. Metformin is an insulin-sensitizing agent, which appear to ameliorate the biochemical profile and improve reproductive function in obese patients with PCOS. The objective of this study was to examine the effects of combined metformin and CC treatment on endocrine function and pregnancy rates in non-obese infertile women with PCOS.

Design: Prospective study in a private practice.

Materials/Methods: Our study included 102 non-obese (BMI <25 Kg/m2) women with PCOS. Blood samples were obtained in the early follicular phase of the cycle. Basal blood estradiol, follicle stimulating hormone (FSH), luteinizing hormone (LH), insulin, thyroid stimulating hormone (TSH) and prolactin were determined using commercially available kits. Diagnosis of PCOS was based on a history of oligohypomenorrhea, and/or anovulation, pelvic ultrasound and reversed LH/FSH ratio (>2). The patients received no treatment for at least 3 months prior to recruitment. Patients were categorized into 2 groups: group I received CC 50 mg/day from day 3 to day 7 of the cycle and metformin 1000 mg/day (n = 51). Group II received CC 50 mg/day from day 3 to day 7 of the cycle and a placebo (n = 51). A second hormonal profile was performed in non-pregnant women after 6 months of treatment.

Results: The mean (± SD) age of patients was 28 ± 6 in group I and was 31 ± 7 in group II. The 2 groups were comparable regarding basal levels of insulin, estradiol, LH, FSH and LH/FSH ratio. Levels of TSH and prolactin were normal for all patients. A clinical pregnancy was found in 24/51 (47%) patients in group I within 6 months of treatment (per cycle pregnancy rate = 9.8%) compared to 13/53 (25.5%) in group II (per cycle pregnancy rate = 4.8%) (P = 0.023). Basal LH/FSH ratio in pregnant women from group I (n = 24) was significantly lower than the basal ratio in non-pregnant women from the same group (n = 27) (P = 0.026). However, LH/FSH ratio of non-pregnant women in group I at 6 months following treatment was not significantly different from the basal ratio of pregnant women in the same group (P = 0.651). LH and LH/FSH ratio of non-pregnant women, at 6 months, were significantly lower than basal values only in group I (P = 0.008 & 0.019; respectively).

Conclusions: Our data indicate that co-administration of metformin with CC results in a significant increase in pregnancy rates than CC alone. Such improvement in pregnancy rates may be related, at least in part, to reduction of LH level and LH/FSH ratio. The lack of significant difference between basal LH/FSH ratio in pregnant women and that of non-pregnant women after 6 months of treatment, suggests that the later group may benefit from longer duration of therapy.

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