

TREATMENT STRATEGIES OF POLYCYSTIC OVARY SYNDROME

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Polycystic ovary syndrome (PCOS) is a common clinical disorder that affects 5 – 10 % of women in the reproductive age. PCOS is a syndrome of ovarian dysfunction associated with hyperandrogenism, polycystic ovary morphology and an increased risk for type 2 diabetes. Its clinical manifestations include menstrual irregularities, signs of androgen excess and obesity. The diagnosis is established if 2 of the following 3 criteria are fulfilled and after excluding other etiologies: 1) oligo/anovulation, 2) hyperandrogenism (clinical or biochemical), and 3) polycystic ovaries. The major problem leading to infertility is chronic anovulation and its therapeutic approach includes life-style changes as well as medical or surgical interventions. Several studies have shown that weight reduction by diet and exercise can effectively restore ovulation in obese PCOS women and should be recommended in these cases before any other treatment. On the other hand, among the medical interventions, clomiphene citrate (CC) still remains the first line approach. Thus, using incremental doses of 50 to 150 mg for 5 days, a cumulative ovulation rate of 77% is observed with pregnancy and live birth rates of 47 and 41%, respectively and 2% multiples (mainly twins). Two recent RCTs have shown that the addition of metformin to CC, has no effect on the ovulation, pregnancy, live birth or spontaneous abortion rates. Conversely, the use of metformin alone was associated with significantly lower ($p < 0.001$) live birth rates than CC alone or in combination with metformin (7.2 vs 22.5 and 26.8%, respectively) and no significant difference in spontaneous abortions (20.8 vs 8.3 and 9.2%, respectively). Nevertheless, approximately 17% of women treated with CC remain anovulatory (clomiphene resistant) and 39% of those ovulating fail to conceive (clomiphene failure). In these cases, the second line treatment usually involves the administration of gonadotropins. Hence, using the low-dose FSH protocols, cumulative ovulation and ongoing pregnancy rates of 82 and 58%, respectively have been reported, with 5% multiples. Alternatively, it has been proposed to apply laparoscopic ovarian drilling (LOD) prior to gonadotropins. The postoperative ovulation rate is reported to be approximately 80%, while the postoperative conception rate 60%. Data from 4 RCTs, comparing the effectiveness of LOD with gonadotropins in CC resistant PCOS women, indicate that there is no difference in ongoing pregnancy, live birth or miscarriage rates. On the other hand, the incidence of multiple pregnancies was significantly lower in women treated with LOD than with gonadotropins. In the cases that the aforementioned treatment modalities have failed or there are other associated causes of infertility (tubal, male, etc), in vitro fertilization (IVF) can be used. Meta-analysis of 9 studies comparing the IVF outcome between PCOS women and controls has shown that the cancellation rate, the number of oocytes retrieved and the days of stimulation are significantly higher in PCOS, whereas there is no difference in the fertilization, miscarriage, pregnancy and live birth rates.

In conclusion, weight reduction by lifestyle changes should be strongly recommended to obese, anovulatory, PCOS women, prior to any intervention. From the medical treatment modalities, clomiphene citrate still remains the first line approach. In those women failing to ovulate or conceive, gonadotropins or laparoscopic ovarian drilling could be applied, followed by IVF. The IVF results in PCOS women seem to be similar to those of controls. Finally, the place of metformin, alone or in combination with other ovulatory agents, in the treatment of anovulatory infertility in women with PCOS needs to be further evaluated.