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# **Polycystic Ovarian Syndrome: Evaluating the optimal therapy**

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**Abstract:**

This report reviews the treatment of Polycystic Ovarian Syndrome (PCOS) and early diagnosis helps in the effective treatment. Polycystic ovarian syndrome affects women's ovulation and also leads to infertility. Treatment-resistant acne and acanthosis nigricans are symptoms for this disorder. A number of cases have discussed this issue thoroughly and results concluded that dietary changes, metformin and clomiphene are all effective ways in the treatment of this disorder.

## Introduction:

Polycystic Ovarian Syndrome, formerly called (Stein-Leventhal syndrome) is a heterogeneous and complex disorder that has adverse reproductive and metabolic implications for affected women. This disorder has an unclear etiology<sup>1</sup>. The most accurate and widely accepted clinical definition of PCOS is the association of hyperandrogenism with chronic anovulation in women without an underlying disease of pituitary or adrenal glands, along with the presence of polycystic ovaries. If two of these three criteria were present then the patient can be diagnosed with PCOS<sup>2</sup>. PCOS affects 5-10% of women of reproductive age. Hyperandrogenism is characterized clinically by hirsutism, acne, and androgen-dependent alopecia and biochemically by elevated serum concentrations of androgens, particularly testosterone and androstenedione<sup>3</sup>. Obesity is common but not universal. Typically, these features are associated with hypersecretion of luteinizing hormone and androgens but with normal or low serum concentrations of follicle-stimulating hormone<sup>3</sup>. Ironically, although the

early descriptions of the syndrome were based on ovarian morphology, this has not been considered an essential requirement<sup>3</sup> for the diagnosis. However technology and the availability of ultrasonography has allowed the ovarian morphology to be studied in more depth without the need of a gross morphology which comes to the favor of clinical professional diagnosis-(figure 1)<sup>3</sup>. PCOS has many complications, infertility being



**Figure 1. Ultrasonography (Panel A) and Gross Histologic (Panel B) Appearance of a Typical Polycystic Ovary.**

its most common. Other complications could include: miscarriage, sleep apnea and depression<sup>3</sup>. PCOS treatment is not restricted to a certain drug, as there are variable drugs and hormonal influences that could help in its treatment. Dietary changes are one of the effective approaches for obese women.

## Aim of the study:

The aim of this report is to cover how the disorder affects women's fertility and why it affects their physical appearances, possibly helping readers self-diagnose themselves

or their relatives. As there are different ways of treating PCOS, this report should talk about and compare between them.

### **Material and methods:**

Multiple studies have been conducted where a group of randomly picked women have been involved. In the dietary treatment, 24 women were picked to participate in the trials. These women had to be obese and meet the criteria for PCOS as mentioned above. The duration of the study was 6-7months and no external materials used.

On the other hand, the second study involved a group of 60 women who previously were not given any medications for the disorder. The study involved giving the patients drugs over a period of 60days. It also involved oral glucose intolerance test before and after administering the drug. The drug was also given thrice daily. The 60 people were divided into three groups of 20s. The first was given *metformin*, second was given *clomiphene* ± placebo, last group was given both drugs together.

### **Discussion:**

Obese women suffering from PCOS have been found to have menstrual disturbance as well as hirsutism more commonly than age matching women with lean bodies having the same condition. Insulins' elevation correlates to weight gain as its side effect and hence insulin increases in level with increasing weight. The bodies' response is to cause some cells to be intolerant to the insulin "insulin resistant", such as: liver and muscle cells<sup>3</sup>. However the pituitary gland does not become resistant to insulin and would still be sensitive to it. This would mean that the gland would be stimulated to produce high levels of hormones that impair fertility by disturbing ovulation<sup>3</sup>. These hormones include androgens and androstenedione, the former leading to acne, hirsutism and androgen related alopecia, while the latter increases the production of the testosterone hormone. These factors lead to amenorrhea and reduces possibilities of ovulation in women within the reproductive age.

### **Case 1: Changing diets**

There are many approaches to PCOS treatment that have impacted positively on the women's reproductive life. One approach is dietary change in obese women. The first case included 24 obese women with a mean mass of 91.5kg that were scheduled for

treatment for 6-7 months with a restricted 1000kcal, low fat diet. Of the 24 patients; 19 were hirsute, 19 had menstrual disturbances and 12 were infertile. Of the patients that lost weight, sex hormone binding globulin has increased and free testosterone levels reciprocally decreased. This change is linked to the presence of increasing levels of sex hormone binding globulin which is a hormone that controls the function of sex hormones by binding to them and removing them from the circulation, hence the reason behind testosterone level drop in the blood. Moreover, there is a decrease in the levels of serum insulin that in turn reduce their effect on pituitary glands. This in turn reduces hyperandrogenism's symptoms and patients have been found to conceive or ovulate more normally than before; periods were also regulated therefore there were not any cycle disturbances.

This treatment is effective and is financially efficient. It has various advantages as mentioned above, moreover, it has no side effects. This treatment both helps PCOS patients lead a normal reproductive life as well as allow them to restore a healthy and fit life.

## **Case 2: Taking tablets**

The second case involves a group of 60 patients who had started taking *metformin* and *clomiphene*. These drugs are both taken orally as tablets. They both help women to ovulate normally and reduce the symptoms for PCOS.

*Metformin* has been found to treat PCOS in obese women who have developed type 2 DM. Insulin's elevation correlates to weight gain as its side effect and hence insulin increases in level with increasing weight. The bodies' response is discussed above. *Metformin* is found to inhibit hepatic glucose production<sup>4</sup>, although it also decreases intestinal glucose uptake and increases insulin sensitivity in peripheral tissues. *Metformin* likely plays its role in improving ovulation induction in women with PCOS through a variety of actions, including reducing insulin levels and altering the effect of insulin on ovarian androgen biosynthesis; it inhibits ovarian gluconeogenesis and thus reduces ovarian androgen production<sup>4</sup>.

*Metformin* has many advantages, but it also has its drawbacks. Its common side effects include: lactic acidosis, diarrhea, nausea, vomiting and flatulence<sup>4</sup>. Other side effects include: asthenia and decreased vitamin B12 serum concentration.

On the other hand, *Clomiphene* citrate is a selective estrogen receptor inhibitor. It antagonizes the effect of the negative feedback of estrogen on hypothalamus and leads to a consequence increase of gonadotrophins. This leads to increased production of follicles which increases the ovulation rates. Therefore, administering this drug would increase the possibilities for women to have more follicles hence increasing their chances of conceiving.

*Clomiphene* as any other drug has side effects; they include: bloating, pelvic pain and hot flashes. Less commonly: breast discomfort, dizziness, headache, nausea and may also lead to heavy menses.

Both drugs mentioned above can be administered either individually or given in conjunction to achieve optimum results.

## **Results:**

A study has been conducted to observe the importance of diet in oversized women. The weight loss average for 13 of 24 patients was between 5.9-22% of their original weight. In this group there was not a significant change in the gonadotropin (they stimulate the gonads (testes and ovaries) and increase the production of the sex hormones) and testosterone levels. However there was a marked increase in the levels of sex hormone binding globulin 23.6-36.3nmol/l and a reciprocal change in the free testosterone levels 77-53pmol/l. This change is linked to the presence of increasing levels of sex hormone binding globulin which is a hormone that controls the function of sex hormones by binding to them and removing them from the circulation, hence the reason behind testosterone level drop in the blood. Moreover fasting serum insulin levels decreased significantly from 11.2-2.3mU/l in the patients that lost more than 5% of their pretreatment<sup>6</sup> weight. Predictably the patients that lost less than 5% of their original weight did not experience a significant drop in their fasting serum insulin levels.

Of the 13 women who lost > 5% of their pretreatment weight, 11 had menstrual dysfunction. Amongst these women, nine of 11 showed an improvement in reproductive function, i.e. they either conceived or experienced a more regular menstrual pattern<sup>6</sup>. There was a reduction in hirsutism in 40% of the women in this group. By contrast, in the group who lost less than 5% of their initial weight, only one

of the eight with menstrual disturbances noted an improvement in reproductive function and none had a significant reduction in hirsutism.

A second study has been conducted to observe the importance of *metformin* and *clomiphene*.

In the first phase of the study, first 35 days the patients that were treated with metformin only did not ovulate. So clomiphene was given to these patients. Among the 20 women given metformin plus clomiphene, the mean serum insulin curve after oral glucose administration decreased from  $6745 \pm 2021$  to  $3479 \pm 455$   $\mu\text{U}$  per milliliter per minute, but it did not change significantly in the 20 women given placebo plus clomiphene. Nineteen of the 20 women (90 percent) who received metformin plus clomiphene ovulated (mean peak serum progesterone concentration,  $23.8 \pm 3.4$  ng per milliliter). Two of the 20 women (10 percent) who received placebo plus clomiphene ovulated. Overall, 18 of the 20 women (90 percent) treated with metformin ovulated spontaneously or in response to clomiphene, as compared with 3 of the 20 women (15 percent) treated with placebo.

Both treatments were effective and efficient, however, dietary treatment is the safer, more applicable, patient preferred and expense friendly option, although some patients would need to be treated with the drugs.

## **Conclusion:**

In this study, the report discussed the various approaches to treating PCOS. Dietary changes are effective and efficient in the disorder's treatment. Moreover, the ovulatory response to clomiphene can be increased in obese women with the polycystic ovary syndrome by decreasing insulin secretion with metformin. Therefore, giving these drugs in conjunction is very helpful, only if the patient's insulin is high and no ovulation occurs.



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