

## Polycystic Ovarian Syndrome; an Endocrinologist's Point of View

Ergita Nelaj \*

\* Department of Internal Medicine, University Hospital Center "Mother Teresa",  
University of Medicine, Tirana, Albania

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Polycystic ovarian syndrome (PCOS) is a heterogeneous, endocrine, and metabolic disorder that presents as hyperandrogenemia, anovulation, and/or polycystic ovaries, and affects the lives of women of reproductive age throughout the world. It was first described by Stein and Leventhal in 1935, and its prevalence varies greatly depending on the diagnostic criteria used, from 4–8% according to NIH/NICHD criteria, to approximately 18% according to the Rotterdam criteria (1). Based on these criteria, women must have at least two out of three criteria for diagnosing PCOS, including the presence of oligo-/anovulation, clinical or biochemical hyperandrogenism and/or ovarian cysts. Other possible hormonal disorders should also be excluded. Anti-Müllerian hormone (AMH) is also a marked hormonal indicator and important in maturation and development of ovarian follicles in PCOS women

It is estimated that between 65 and 95% of women with PCOS manifest insulin resistance (2). Insulin resistance, a very common condition in PCOS, is worsened by hyperandrogenism-related adipose tissue accumulation and is involved in both the pathogenesis and the progression of the disease (3). Hyperinsulinemia caused by tissue insulin resistance is central to PCOS pathology. Hyperinsulinemia is the root cause of excess androgens as insulin directly stimulates the action of LH and raise the GnRH indirectly.

PCOS puts the women at a higher risk of metabolic syndrome due to the presence of risk

factors such as central obesity, high blood pressure, atherosclerotic dyslipidemia, and insulin resistance. Because of these risk factors, women with PCOS are exposed to long-term consequences such as type 2 diabetes, heart disease, sleep apnea, and psychological problems including anxiety and depression (3). Therefore, an early diagnosis and treatment of PCOS are crucial to prevent future long-term complications and reduce the healthcare burden.

The treatment presents multiple challenges and varies according to the clinical symptoms and underlying cause which can be divided by treating ovulatory dysfunction, hyperandrogenism, improving insulin resistance, and infertility (4)

Over half of the woman with PCOS are overweight or obese (5), therefore have a higher possibility of increased visceral fat deposition because of impaired glucose tolerance and insulin sensitivity. So, these patients are primarily recommended to reduce their weight, to have balanced diet combined with regular exercise activity in aim to raise their metabolism, improve insulin sensitivity, and help them lose weight safely.

Insulin resistance treatment, including drugs and lifestyle changes, is critical for PCOS treatment. It is the main driver for metabolic and endocrine dysfunction in PCOS, so the therapeutic advantages of glucagon-like peptide 1 (GLP-1) agonists in this population are logical.

Although insulin sensitizers such as metformin have long been used to treat PCOS metabolic

dysfunction, newer medicines such as incretin mimetics (GLP-1 agonists) and Sodium-glucose co-transporter-2 (SGLT2) inhibitors have proven to be more effective at reducing weight and cardiovascular risk (2,6). Metabolic benefits and improvement of parameters of metabolic comorbidities are superior with a combination of lifestyle intervention, metformin, GLP-1 agonists, SGLT-2 inhibitors and bariatric surgery than monotherapy. SGLT-2 inhibitors and GLP-1 agonists are promising therapeutic agents with significant potential advantages in improving metabolic abnormalities in women with PCOS and need further studies (2,6).

In conclusion, it is imperative to know that no single agent can cover the entire spectrum of metabolic disorders in women diagnosed with PCOS. Pharmacological therapies along with a change in the lifestyle ameliorate the overall condition. It's important to collaborate in an interdisciplinary team that can include a family practitioner, a gynecologist, and endocrinologist, a dermatologist, a pediatrician, and a psychologist.

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