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Short Communication

Polycystic Ovarian Syndrome; A Clinician's Perspective

Svend Lindenberg* and Frederikke Lindenberg

Copenhagen Fertility Center, Research section, Denmark

***Corresponding author:** Svend Lindenberg, Copenhagen Fertility Center, Research Section. Lygten 2c, DK 2400NV, Denmark.

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Abstract

Polycystic Ovarian Syndrome (PCO) is a conglomerate of different predisposing factors, such as infertility, bleeding disorders, diabetes, hypertension etc. which more than 15% of the female population suffers from and seems to increase in prevalence [1]. Moreover, in menopause this condition is not over, as the resulting diabetes, cardiovascular risk, metabolic syndrome etc. will remain an influencing factor in the life in these women. Many factors including genetic susceptibility, maternal milieu, and postnatal environment are likely to synergize in the development of the different PCO conditions. This Presentation Discusses the Following: Genetics in PCO, factors enabling to induce PCO conditions such as the two-hit hypothesis drawing the attention to prenatal and postnatal possible impact. Based on this consideration suggestions for proposed treatments and strategies for ameliorating the PCO now and in the future is presented.

Background

In the clinical setting, several different specialities in medicine are encountering the problem with PCO. Prenatally the problems of hyperandrogenism, gestational diabetes and obesity are present. In adolescent life hirsutism, menstrual disorders and weight gain is seen. Later in fertile life infertility, obesity, menstrual disorders are observed, eventually followed by diabetes and the metabolic syndrome later [2,3]. Thus, the PCO condition in one or another form follows most of these affected women during their entire life span.

The diagnostic criteria for PCOS and PCO has changed during the years, mostly for simplifying the process of diagnosis and treatment. In the present paper, the Rotterdam criteria are used [4,5]. For simplicity, the discussion of handling the PCO condition takes its beginning in the fertile women.

Women with PCO in Childbearing Age

Most women diagnosed with PCO are not infertile and will conceive during their fertile life span [6]. However, parts of PCO women suffer from conditions such as amenorrhea, anovulation, obesity, hirsutism, and mental disorders such as depression. This means that these women often are treated in different disciplines of medicine such as fertility doctors, general practitioners, and endocrinologists as a result of the different needs and original problems these women express in the health system. From a pragmatic, point of view the three basic elements in the care of PCO, the hyperandrogenism, the obesity and the insulin resistance. From a range of publications, it has been seen that weight reduction can be, achieved relatively easy using different dieticians, however the effect is often limited and more than 90% will gain weight again [7]. As obesity is a major key in many of these patients' symptomatology and both a result of and a reason for insulin resistance, weight should be on the top of the treating physicians list when treating PCO patients, providing the patient is overweight.

From a medical point of view lifestyle interventions is important for the long-lasting results but from a short-term perspective often very insufficient as results of lifestyle changes are often months and years underway, which can be problematic in infertility treatment for example. Therefore, new medication such as GLP-1 agonist [8] has been very efficient. This in combination with metformin might even be better in the obese PCO patient [9] having manifest insulin resistance. Bearing in mind the very high number of patients gaining weight after treatment, low dose treatment for a longer time might

be a very good new option in combination with a new lifestyle. The use of Metformin is only to be used in very high androgen levels with or in combination with insulin resistance. The reduction in weight often reduces IR and reintroduce ovulation. Further, the tendency to depression might vanish with reduced weight and better metabolic health [10]. Often misunderstood or forgotten in the predisposition factors of PCO are inflammatory processes effect on the PCO status.

One might regard parts of the PCO condition as inflammatory responses to gut metabolism, resulting in insulin resistance, changed glycose metabolism and change in different metabolic pathways in the ovary [11]. This inflammatory response is often linked to the abdominal fat and the adipocyte responses to lipopolysaccharides leaking from the gut microbiota into the body due to increased intestinal permeability brought about by a changed gut microbiota composition. Therefore, a change in the gut microbiome in the future might be an additional leg in the treatment of PCO [12]. This has in some instances been seen, however real proof is needed. Already proven is the fact that the inflammatory impact on the PCO body is normalized by loosing weight for obese women. The inflammation is also partially treated by the anti-inflammatory properties of metformin, often not recognized [13]. The cardiovascular risk and risk for diabetes also decreases with weight reduction, but also due to the effect from the treatment with GLP 1 agonists and metformin [14].

The importance of regulating the insulin resistance and hyper androgenism in fertile women is not only to reduce their own discomfort and lifelong risk, but also to prevent risks in an eventual offspring. To understand this, we must introduce the two-hit hypothesis [15]. He main issue here is in the early foetal life, maternal hyperinsulinemia, hyperandrogenism, altered placental steroidogenesis and higher number of small for gestational age newborn ads to the predisposition of insulin resistance, obesity and finally PCO and diabetes. All of these might be eliminated in the foetus or reduced by adjusting the endocrine pathology in PCO women before conceiving. Therefore, women in childbearing age are at risk of propagating the PCO condition to their foetus, not only because of genet disposition but also due to endocrine factors. Also, other mental disorders are reported to be transmitted due to the PCO condition in pregnancy [16].

Pre- and Post-Menopausal PCO Women

The insulin resistance, inflammation and obesity remain after menopause. Therefore, the often mislead notion, that after menopause, PCO is no longer a problem is not correct [17]. Women might already have developed blood pressure problems, obesity, and other cardiovascular changes and risk of diabetes. It is therefore important to maintain an interest in these women to avoid these conditions. Here the treatment should again be focusing on lifestyle and weight regulation. Further Hormone Replacement Therapy might be of help, even in this group to reduce thromboembolic events [18]. GLP1 agonist and metformin might also be of great help in this group.

The Postnatal Period and Prepubertal PCO Women

We have already mentioned the Two-hit Hypotheses. In early postnatal life one can see higher concentration of leptin and later prepubertal higher insulin level, hyperandrogenism, increased Anti Müllerian Hormone levels and even early onset of obesity due to this condition. One must also take into consideration the higher frequency of small for gestational age born children from PCO women, which also predispose to these conditions and diabetes. It is therefore important to follow up on family history, birth reports and other relevant information in the prepubertal women suffering from obesity etc. Although not all Rotterdam criteria can be used in the prepuberty, insulin resistance, obesity and bleeding irregularities might give the clinician a hint and start early intervention [19].

Conclusion

The major goals in treatment of PCO women is to normalize in all ages the basal endocrinological disruption comprised of the following: Insulin resistance, obesity, Inflammation and hyperandrogenism individually or in any combinations. Although each period in the women's life has distinct prevalence for different symptoms and needs for treatment, the basic principles in all are the same. The benefits of normalizing these disruptions before conception of a child will probably help the foetus and the offspring an ameliorating the PCO burden in the next generation.

Conflict of Interest

None

Acknowledgement

None

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