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Polycystic ovaries and obesity

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Almost 50% of the women with polycystic ovary syndrome (PCOS) are obese. Obesity in PCOS affects reproduction via various mechanisms. Hyperandrogenism, increased luteinizing hormone (LH) and insulin resistance play a pivotal role. Several substances produced by the adipose tissue including leptin, adiponectin, resistin and visfatin may play a role in the pathophysiology of PCOS. Infertility in PCOS is related to anovulation. For induction of ovulation, clomiphene citrate and human gonadotrophins are first- and second-line treatments, respectively. Other treatment modalities include the use of insulin sensitizers, such as metformin as well as aromatase inhibitors and laparoscopic ovarian drilling, while in vitro fertilization is the last resort. Obesity can adversely affect infertility treatment in PCOS. Diet and lifestyle changes are recommended for the obese women before they attempt conception. The use of anti-obesity drugs and bariatric surgery in PCOS require further evaluation.

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Introduction

The polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women. Based on the Rotterdam consensus workshop the prevalence of PCOS comes up to 15% [1].

Women with PCOS are overweight (35–80%; body mass index (BMI) above 25 kg/m [2]) or obese (20–69%; BMI above 30 kg/m [2]) and the rate is affected by various parameters including ethnicity [2–4]. Obesity in women with PCOS not only involves the peripheral tissue but also a significant increase occurs in the intra-abdominal fat, which is independent of obesity [5].

Impact of obesity on reproduction

Women with PCOS, particularly those with regular menstruation, are not necessarily infertile. However, women with menstrual irregularities may have difficulties to conceive. The main cause of infertility in PCOS is the anovulation. Obesity seems to be an additional factor that contributes to the reduced fecundity [6]. There are several mechanisms via which obese women with PCOS may have fertility problems.

Hyperandrogenism

Ovarian hyperandrogenism is a cardinal feature of PCOS. Intrinsic amplified steroidogenetic capacity of theca cells results in increased ovarian androgen secretion. Endocrine mechanisms may contribute to hyperandrogenism and these include pituitary luteinizing hormone (LH) hypersecretion, relative follicle-stimulating hormone (FSH) insufficiency, high levels of insulin and anti-Müllerian hormone (AMH) inhibiting aromatase activity. Ovarian hyperandrogenism in PCOS may arrest folliculogenesis through inhibition of granulosa cell proliferation and maturation, oestrogen and progesterone secretion, aromatase action and increase of 5a-reductase activity [7–9].

Obesity amplifies hyperandrogenism in PCOS resulting in increased total testosterone, free androgen index and decreased sex hormone-binding globulin (SHBG) [10]. Obese women with PCOS exhibit a higher degree of insulin resistance and compensatory hyperinsulinaemia which contributes to androgen excess [10]. It is obvious that obesity may deteriorate hyperandrogenism in women with PCOS, which is involved in anovulatory infertility.

Hypersecretion of LH

In women with PCOS, LH levels are frequently elevated due to anovulation and lack of progesterone [11] and hyperandrogenaemia, which attenuates the progesterone negative feedback effect [12]. However, obese PCOS women demonstrate a blunted LH secretion, through mechanisms acting at the pituitary and not the hypothalamic level [13]. These mechanisms may involve insulin and leptin [14,15]. According to the ceiling hypothesis, high LH levels in circulation may cause premature luteinization and anovulation [16]. It seems than in lean but not obese women with PCOS, elevated LH is a significant mechanism of anovulation.

Hyperinsulinaemia

Obese women with PCOS demonstrate higher insulin resistance and hyperinsulinaemia than lean women with PCOS. Elevated insulin levels may cause premature maturation of granulosa cells, because they respond prematurely to LH (small follicles of 4 mm), which is in contrast to the normal response that occurs when follicles reach the 10-mm diameter [17]. Furthermore, high insulin levels amplify LH-stimulated androgen secretion from the theca cells [18,19]. A recent meta-analysis showed that obese/overweight PCOS women had lower insulin-like growth factor (IGF)-binding protein-1 (IGFBP-1) levels as compared to normal-weight PCOS women [20]. This is another link between hyperinsulinaemia and hyperandrogenaemia, as it is known that insulin stimulates ovarian androgen synthesis through also its interaction with the IGF system and IGF-I potentiates LH-stimulated ovarian androgen synthesis, while this action may be negatively modulated by the IGFBP-1 [21]. The role of hyperinsulinaemia is