Abstract

Polycystic Ovary Syndrome (PCOS) is emerging as a common problem among adolescents today. Its immediate problems range from oligomenorrhoea, hirsutism, acne, seborrhea and obesity but its long term consequences are many. Both gestational diabetes and type 2 diabetes are more common in PCOS women. Though cardiovascular risks have often been cited, actual proof is lacking and morbidity and mortality from cardiovascular disease in women with PCO is not as high as indicated. However women with PCOS are more prone to carcinoma of endometrium and sleep apnoea and image related psychological issues are harsh realities.

Introduction

When close to 20% of our women seem to be affected by Polycystic Ovary Syndrome (PCOS), it is imperative that we sit up and take notice of a public health problem, which has significant repercussions on the life of the woman in her later years as well. At 50 years of age, one lives based on how one lived at 20 years! This adage is extremely applicable to the PCOS woman. When you consider long term sequelle, it is rather difficult to define long term! For a girl who has PCOS at 15 years, 30 years of age is
probably long term, and in her, the most likely problem will be infertility.

The intent of this article is to focus on risks such as type 2 diabetes, cardiovascular risks, cancers, psychological issues and obstructive sleep apnea, and to also examine any remedial strategies that may be adopted to reduce these risks.

Type 2 diabetes

Insulin resistance in PCOS has been linked to the later development of impaired glucose tolerance and type 2 diabetes. Evidence points to a risk in the middle age that approaches 10-20%. This includes a high rate of impaired glucose tolerance, suggesting that further cases of diabetes will develop later, pushing the incidence even further. Increased BMI>30, strong family history of type 2 diabetes, or PCOS women >40 years, are more at risk and should be offered a GTT. However it is surprising to note that the frequency of type 2 diabetes is also increased in the lean PCOS (<27kg/m2), suggesting that PCOS is an independent risk factor for type 2 diabetes. Hence PCOS conditions such as gestational diabetes mellitus (GDM), forms an ideal public health model to screen and detect early, and possibly even prevent type 2 diabetes. Hence the PCOS woman must be counseled to screen with FBS/PPBS or a conventional 75gm WHO GTT regularly – perhaps annually.

It is worthy of note that, there is a higher risk of gestational diabetes in women with PCOS. Such women must be offered screening for GDM as early in pregnancy as is feasible. A recent Meta analysis concluded that women with PCOS also have a significant higher risk of pregnancy complications compared to controls. Metformin when taken throughout pregnancy has been suggested to reduce the risk of miscarriage and GDM in pregnant women with PCOS. Metformin is decreed safe and may reduce the incidence of miscarriage if taken in the first trimester itself. Many practicing clinicians offer metformin in pregnancy for exactly these reasons. However the Royal College of Obstetricians and Gynaecologists does not recommend its routine use in pregnancy as the methodology of these studies was poor and we are yet to see further randomized controlled trials (RCTs) to provide adequate evidence of its safety and efficacy. Being a class B drug, there are no reported instances of fetal toxicity or teratogenicity. There may still be unanticipated risks to the baby from the post natal use of metformin by the breast feeding woman. Further studies are needed before its use can be recommended in the puerperium.

Cardiovascular risk
The woman with PCOS has increased cardiovascular risk factors such as obesity, hyperandrogenism, hyperlipidemia and hyperinsulinism. However clinicians need to be aware that conventional cardiovascular risk calculators have not been validated in women with PCOS. It would be worthwhile nonetheless, to measure blood pressure, cholesterol, triglycerides and HDL, as it has been suggested that overall women with PCOS, may have a higher cardiovascular risk than weight matched controls with normal ovarian function. Their abnormal lipid profiles consist mainly of increased triglycerides, total cholesterol and LDL. The effect of PCOS on HDL is controversial and links to hypertension are less consistent. In clinical practice, hypertension must be treated but lipid lowering treatment is not recommended as a routine, and should only be recommended by a specialist. Hypertension should be treated when persistent blood pressures equal or are >140/90mmHg and not responding to life style measures. But it needs to be understood that when treating PCOS women with diabetes or other high risk factors, BP >130/80 mm Hg will require treatment.

Despite the increase in cardiovascular risk factors, morbidity and mortality from coronary heart disease among women with PCOS, has not shown to be high as indicated.

Cancer and PCOS

It is not uncommon to encounter women with PCOS, who menstruate sometimes only every 6-12 months, and that too only on withdrawal with progesterone. These women will be exposed to high unopposed levels of estrogen, and therefore are more at risk for endometrial hyperplasia and carcinoma of endometrium. It is hence good practice to recommend treatment with progesterone, to induce a withdrawal bleeding on a minimum every 3-4 months at least. Regular withdrawal bleeds with monthly progesterone, OCPs or the Mirena IUS, will ensure cyclicity in menstruation and prevent endometrial build up.

Women with PCOS do not have any significant increased risk of developing carcinoma of breast or epithelial ovarian cancer. Hence no additional surveillance is required beyond routine screening.

Sleep apnea

Sleep apnea is an independent cardiovascular risk factor and has been found to be more common in women with PCOS. The difference in the prevalence of sleep apnea between PCOS and controls remained significant even when controlled for BMI. Hence women with PCOS or their partners should be asked about snoring, daytime fatigue, somnolescence and informed about...
the possible risk of sleep apnea offered investigations and treatment where necessary. It has been reported that the strongest predictors for sleep apnea were fasting plasma insulin levels and glucose to insulin ratios.

Image related issues

The obese hirsute PCOS often faces problems with loss of self esteem and depression. They improve dramatically when they start loosing weight. The effects of hyperandrogenism and body image and the consequent psychological implications are to be strongly considered. Hirsutism in the setting of PCOS is distressing and difficult to treat. A recent Cochrane review to compare the use of insulin sensitizing drugs versus combined oral contraceptives (COC) concluded that the limited data available demonstrated no significant difference in effect between metformin and the pill on hirsutism and acne.

Licensed treatment for hirsutism and acne include COC, estrogen and cyproterone combinations and cosmetic treatments like laser, electrolysis, shaving, waxing and topical eflornithine. However there is a paucity of good quality robust placebo controlled trials for hirsutism treatment and often a combination of treatments is resorted to. Metformin as an insulin sensitizer has been shown to have a moderate effect on hirsutism and decreases testosterone levels by 11%.

Strategies for reduction of risk

Exercise and weight control

Drug therapy

Surgery

Life style changes through diet and exercise remain the first line for the treatment of obesity in PCOS. Obesity worsens insulin resistance which will only serve to exacerbate the problem. Loss of even 5% of body weight has been reported to result in spontaneous resumption of ovulation, improvement in fertility, increase in SHBG and decreases basal levels of insulin accompanied by normalization of glucose metabolism. The Diabetes Prevention Trial found that life style modification reduced the risk of diabetes by 58%.

Hence regular exercise aiming for 30 mts of sweat inducing exercises daily or at a minimum of 3-4 times a week, coupled with a balanced diet of hypocalorific meals must be advised.

There is no clear effect of diet and exercise on the long term health of the lean PCOS – although it seems prudent to advise such patients to maintain their body weight in the normal range.
Insulin sensitizing agents like metformin and the thiazolidinediones (troglitazone, rosiglitazone and pioglitazone) while reducing insulin resistance, seem attractive in reducing the risk of diabetes and other metabolic sequelae. Both metformin and troglitazone have been shown to have beneficial short term effects on insulin resistance in women who are not diabetic. Metformin however does not work well in women whose BMI is >37 kg/m². Inference from the Diabetes Prevention Trial suggests that metformin is not superior to lifestyle intervention in reducing cardio metabolic risks and progression to type 2 diabetes. Further a recent Meta analysis suggests an increase in myocardial infarction and death in women with diabetes treated with rosiglitazone. Further research is definitely needed to study the effects of these drugs for the prevention of cardiovascular disease in PCOS.

Orlistat and sibutramine have been shown to significantly reduce body weight and hyperandrogenism in the PCOS. However sibutramine is not advised in women with systolic hypertension. Further research needs to be done on the use of rimonabant in women with PCOS. Bariatric surgery will benefit the morbidly obese woman.

Ovarian electrocautery or drilling has a limited role in the treatment of infertility associated with PCOS, and its role should be reserved for the anovular PCOS with normal BMI. A recent long term cohort study up to 20 yrs after ovarian drilling has shown persistence of ovulation and normalization of serum androgens and SHBG in over 60% of subjects, especially if they have normal BMI. No prospective studies have been powered to look at the cardiovascular risk benefits and it is important to highlighten the fact that ovarian drilling may affect the reproductive capacity of the ovaries in the future, especially with reference to premature ovarian failure.

References

2. Green top guidelines RCOG No:33

