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Review Article

The story of polycystic ovary syndrome: A challenging condition with numerous consequences for women of childbearing age

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Abstract

As the name implies, polycystic ovarian syndrome (PCOS) is a chronic hormonal disorder that mostly affects women of childbearing age. However, symptoms suggestive of androgen overproduction and ovarian dysfunction have been identified. It has a huge public health issue. Women with PCOS are more likely to have co-occurring diseases, as well as various other long-term metabolic and health issues. Prevalence has risen steadily during the last decade, and it's expected to continue rising. Many health care providers and individuals might avoid it if they shared more information. Everything from the initial diagnosis to pathogenesis to effects and treatment options is still up for debate. The study's purpose is to provide a detailed analysis of current and upcoming diagnostic tools, as well as speculate on future strategies. We searched the Cochrane Database of Systematic Reviews and meta-analyses, as well as the most recent international recommendations, to get a fresh look at PCOS.

KEYWORDS: *Polycystic ovary syndrome, menstrual irregularity, hirsutism, infertility*

Introduction

PCOS is a chronic endocrine disorder that disproportionately affects women of childbearing age and those who have recently became pregnant. More than a third of women with the condition go untreated because of the difficulty in getting a timely diagnosis. Depending on the criterion used and the population studied, the influence could range from 6 to 20 percent. It's a disorder that's both heterogeneous in form and characterized by a wide range of androgen overproduction and ovarian dysfunction symptoms, but no specific cause has been identified. Youth and early adulthood are often plagued by oligomenorrhea, acne, and infertility in women with PCOS [1-5]. Prior to recent research, PCOS was considered to be a disease of adult females, but it now appears to be a lifelong condition that begins in girls from birth. It's dangerous for the public's health. PCOS, on the other hand, might persist even after menopause, with or without the previously stated symptoms. Psychological characteristics of women include things like sadness, anxiety, and body image issues, all of which can lead to things like poorer quality of life. Female characteristics relating to reproductive health include things like hirsutism, irregular menstrual cycles, infertility, and pregnancy difficulties. These are all examples of female characteristics that fall under this category. One further group of feminine characteristics involves metabolic health, such as diabetes, hypertension, and weight gain (insulin resistance, prediabetes, metabolic syndrome, type 2 diabetes mellitus and cardiovascular risk factors). As a result, these people are at greater risk for weight gain or obesity if they have PCOS diagnosed with them. As a result, many patients experience increased anxiety and are more concerned about maintaining a healthy lifestyle. Endometrial

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hyperplasia and neoplasia are more common in those with PCOS [5-12].

The progression of diagnostic criteria

Numerous diagnostic criteria have been proposed as a result of the condition's intricacy and the numerous debates it has generated over the last three decades. When Stein and Leventhal initially identified PCOS as a syndrome in 1953, they identified it as having symptoms such as oligomenorrhea and polycystic ovaries as well as hirsutism and acne on the face. After ruling out other diseases, the National Institutes of Health (NIH) set out to diagnose PCOS for the first time in 1990. Both hyperandrogenism (HA) and oligo- or anovulation were utilized as diagnostic criteria. When the Rotterdam PCOS Consensus Workshop Group issued the Rotterdam criteria in 2003, it included polycystic ovarian morphology (PCOM), an ultrasound finding of polycystic ovaries. PCOS can be diagnosed with just two of the three possible symptoms (ovulation failure, HA, and PCOM) [13-15]. All clinical and biochemical symptoms of hyperandrogenism (such as oligoanovulation or PCOM) are included in the Rotterdam criteria. One year after AE-PCOS was founded, the organization released a report saying that only two criteria should be used to determine whether someone has PCOS: clinical or biochemical hyperandrogenism with polycystic ovarian syndrome (PCOS) or clinical anovulatory syndrome (CSA). Those who have hyperandrogenism but no anovulatory symptoms (ovulatory PCOS), which accounts for about 10 percent of women with oligo-anovulation or PCOM, are also included in this group. As reported by the National Institutes for Health, 8.7 percent of women suffer from PCOS, which rises to 17.8 percent when using the Rotterdam criteria and 13 percent when using the AE-PCOS diagnosis [15-17]. If androgen excess cannot be ruled out, it is necessary to rule out other conditions such nonclassical congenital adrenal hyperplasia, hyperprolactinemia, androgen secreting ovarian or adrenal tumors, hypothyroidism, Cushing's syndrome, and acromegaly. According to NIH consensus in 2012, new Rotterdam / ESHRE/ ASRM 2003 criteria with clear diagnosis of PCOS phenotype should be used in all PCOS patients to close the diagnostic gap between the two organizations. Two of the three criteria for PCOS diagnosis (hyperandrogenism, ovulatory dysfunction and PCOM) must be met for a diagnosis to be made, according to this theory, and each case must be classified into its own subtype [18-20]. Teenage girls with PCOS are more likely to develop it. While there are three widely accepted criteria for diagnosing PCOS, applying them to teenagers may be tricky. In adolescents, a diagnosis of PCOS is difficult to make because anovulation and PCOM are both lacking. Clinical and laboratory testing is required to confirm cases of chronic oligomenorrhea, especially when it persists for more than two years following menarche. Menopausal women do not have diagnostic criteria that apply to them. When a woman has a documented history of oligomenorrhea and hyperandrogenism during her reproductive years, a PCOS diagnosis can be made. Diagnoses can only be made after a comprehensive clinical examination that includes a detailed medical history, an in depth physical examination, and all relevant laboratory tests. AACE and the androgen Excess and PCOS Society (AES) recommended in their 2015 best clinical practices guidelines that free testosterone levels are more sensitive to the development of hyperandrogenism than total testosterone levels. Monitoring androgen levels other than testosterone in PCOS patients is limited in its utility. Prior to this study, PCOM could only be diagnosed in women who had at least 25 little follicles (ranging in size from 2 to 9 mm) spread across the ovary. Patients with ovarian fluid in excess of 10 mL can now be diagnosed with this condition because the ovarian size criteria are unchanged. 17-Hydroxyprogesterone and anti-Müllerian hormone (AMH) blood tests can help detect PCOS [15, 21, 22].

These standards have a few flaws that need to be addressed. Many commercial testosterone tests are erroneous, and the results vary from facility to facility. Blood testosterone levels have a distinct profile depending on how often and when they are measured. Even if there are a variety of other circumstances where hyperandrogenemia can be found, it is especially hard for teenagers to document since the mature levels are attained around one year following menarche. With next-generation high-resolution imaging modalities that establish the necessity of antral follicle count, a sonographic definition of PCOM may lead to a higher than average diagnosis of PCOS. The use of PCOM as a diagnostic criterion should be avoided in adolescent girls since anovulatory criteria should be linked to age and puberty. Finally, none of these standards takes into consideration the possibility that PCOS can show signs of ovarian malfunction such as polycystic ovarian syndrome (PCOS) without showing any clinical symptoms of the condition [23-25].

Pathogenesis

PCOS has no known cause and is considered to be difficult to treat. There is no one cause for polycystic ovarian syndrome's many symptoms (PCOS). IR and hyperandrogenism are the two most common hormonal issues associated with PCOS, although other aspects including as obesity, heredity, and way of life can also play a part in the condition. PCOS, increased androgen levels due to ovarian cell abnormalities (most likely theca cells) and IR are all possible hereditary illnesses associated with polycystic ovaries. Prenatal factors including fetal androgen exposure & intrauterine growth restriction influence phenotypic development, while postnatal obesity is a major environmental

influence on phenotypic progress [5, 9, 26, 27]. Epigenetic remodeling of fetal reproductive tissue caused by in utero androgen exposure may activate the hypothalamic-pituitary-ovarian axis and lead to PCOS later in life. It appears that these contributing elements have interconnections that approximate autosomal dominant features, with the exception of varying penetrance. When it comes to disease prevalence and phenotypic heterogeneity, ethnic variety makes a difference. Women of Spanish, Native American, and Mexican descent had a higher risk of PCOS [20, 28].

Hyperandrogenism

PCOS patients' ovarian theca cells overproduce androgens in response to elevated luteinizing-hormone stimulation. When luteinizing hormone levels surpass follicle-stimulating hormone levels, the ovaries preferentially generate androgen. There is a decrease in the amount of luteinizing hormone in polycystic ovarian syndrome women due to a higher frequency of luteinizing hormone pulse, which favors the transcription of luteinizing-hormone over the transcription of follicle-stimulating hormone. These women may have low progesterone levels as a result of irregular ovulation or an issue with the GnRH pulse generator. Theca cells in the ovaries of women with PCOS convert androgenic precursors to testosterone at a higher rate than those in healthy individuals [26, 29, 30].

Insulin resistance

Because to insulin resistance (IR), which is also known as hyperinsulinemia, theca cells in the ovary create an excessive amount of testosterone in conjunction with luteinizing hormone, leading to hyperandrogenism symptoms (hirsutism, acne, alopecia). However, total testosterone levels remain stable or just slightly higher when free testosterone levels grow due to insulin limiting SHBG (sex hormone-binding globulin) synthesis in the liver [26, 31].

Inflammation

Inflammation may exacerbate PCOS symptoms, according to current thinking. CRP, leukocyte TNF-α, ferritin, IL-6, and IL-18 have all been linked to the onset of PCOS, as have other inflammatory factors including CRP and ferritin. One of the most recent discoveries is a link between PCOS and iron excess symptoms. Increased ferritin and transferrin levels have been found, as well as a higher frequency of the HP2/HP2 haptoglobin α-chain genotype. These findings lead to a drop in anti-inflammatory cytokines as well as antioxidant molecules, eventually leading to an inflammatory process [32, 33].

Genetic factors

Many lines of evidence suggest that polycystic ovarian syndrome is heritable. In PCOS moms and sisters, metabolic syndrome affects 3 percent-35 percent of women and 25 percent of PCOS sisters have metabolic syndrome. Researchers recently discovered that certain genes (like INSIG2 and MC4R) are associated with an increased risk of infertility in the reproductive years (IR). They also discovered that PCOS patients with the TCF7L2 SNP are more likely to develop T2DM or gain weight, with a per-allele weight gain of 1.56 kg/m2. Another study proposed insulin receptor autophosphorylation, reduced levels of phosphatidylinositol-3-kinase in muscle tissue, and visceral obesity as plausible explanations. The biology of the disease is still a mystery, but it appears to be a multigenic illness. In a few rare situations, a single gene mutation is to blame for the syndrome's symptoms. PCOS has been the subject of several genome-wide association studies (GWAS), although the findings have been ambiguous. These GWAS focused on genes implicated in androgen synthesis and activity, metabolism (including insulin and insulin receptor genes), and inflammatory cytokines like tumor necrosis factor-alpha (TNF-∞) and interleukin-6 (IL-6) production [34-38].

Clinical features

Hyperandrogenism, including oligo/amenorrhea, clinical or endocrine signs of it, and polycystic ovaries are all signs of the disorder. Women with PCOS are more likely to have menstrual abnormalities (amenorrhea or oligomenorrhea), which can lead to abdominal obesity (30%-70%), infertility (73%-75%), and type 2 diabetes (approximately 10 percent) [27, 36].

Comorbidities and long-term health issues

According to the preceding claims, PCOS has long been linked to a slew of gynecological, metabolic, psychological, and anthropometric problems in women. Insulin resistance, dyslipidemia, and a change in glucose metabolism are all typical in PCOS patients who have already developed type 2 diabetes as a result of their metabolic consequences. Women with PCOS are prone to gaining weight, which exacerbates the condition's symptoms even further. A higher incidence of cardiovascular disease is shown in women who have chronic inflammation, oxidative stress, and poor fibrinolysis. These factors appear to be associated to an increased risk of cardiovascular disease in these women. Those who are depressed or anxious, as well as those who have body image problems or sexual dysfunction, are more prone to suffer from depression and anxiety, which can range in severity from mild to moderate. The health-related quality of life (HRQoL) of certain PCOS women is impacted by other medical concerns, making it difficult for them to maintain a healthy lifestyle [39-45].

Metabolic consequences

Obesity as well as insulin resistance is both associated with polycystic ovarian syndrome, which increases the risk of various health issues like cardiovascular disease. In addition, PCOS may be considered a sex-specific metabolic syndrome, with the idea that PCOS be referred to as "syndrome XX" in order to emphasize this link. In the end, the chance of diabetes and metabolic syndrome increases, as does the risk of having high cholesterol or having any of the other conditions associated with them, such as nonalcoholic fatty liver disease (NAFLD) or having any clotting problems [15, 26].

Insulin resistance and diabetes mellitus

Insulin resistance (IR) affects 30 percent of lean women with PCOS and 70 percent of obese women with PCOS. Many women with PCOS develop IR. Women with PCOS were more likely than healthy women of the same age and weight to have IR and glucose intolerance. The metabolic profile linked to IR appears to be influenced by ethnicity. Hispanics are more likely than non-Hispanics to suffer from a severe case of PCOS. Insulin resistance and amenorrhea/anovulation are more common in hyperandrogenic and anovulatory women, regardless matter their weight or body mass index (BMI) [46-48]. Large studies of 1,212 women with PCOS found that phenotype 1 (all three Rotterdam criteria) was associated with more severe insulin resistance and hyperandrogenism. Women with phenotypes 4 and 2 (hyperandrogenaemia and oligo or anovulation) were shown to have higher IR than BMI-matched healthy women who did not have oligo or anovulation or PCOM (hyperandrogenaemia and PCOM). Adrenal hyperandrogenemia appears to have no effect on IR [49, 50].

Dyslipidemia

PCOS women are far more likely than healthy women to have lipid abnormalities, with a prevalence of 70 percent. A higher level of low-density lipoprotein cholesterol (LDL-C) is associated with higher levels of blood triglycerides (Tg) and free fatty acids (FFAs), while HDL-C, specifically HDL2-C has been connected to lower levels of apolipoprotein I (apoA-I) (apoA-I). In addition, PCOS women, regardless of BMI, have higher levels of oxidized LDL-C, which increases the risk of heart disease. The atherogenic phenotype is exacerbated by obesity and IR. Those with PCOS who were obese exhibited higher levels of atherogenic dyslipidemia, suggesting that obesity-related PCOS is associated with higher rates of lipid issues [51-53].

Obesity

Clinical and metabolic symptoms of PCOS are heavily influenced by obesity. Obesity is more common in women with PCOS, according to two systematic reviews. According to a meta-analysis, PCOS women are two to three times more likely than non-PCOS women to be overweight or obese, and this risk varies by ethnicity, with Caucasian women being more likely than Asian women to be overweight or obese. The distribution of adipose tissue on the body is critical due to the link between abdominal obesity and cardiovascular disease (CVD). Higher BMI and waist-hip ratios are associated with PCOS, increasing the risk of being overweight or obese. PCOS also enhances the risk of being overweight or obese. All studies and analyses agree that obesity is a major contributor to the worsening of PCOS reproductive, metabolic, and psychological effects. Women who are overweight or obese should receive priority treatment that focuses on weight loss, according to the international PCOS guideline, and avoiding weight gain is critical [9, 40, 54-56].

Metabolic syndrome (MetS)

PCOS sufferers are more likely than the general population to develop metabolic syndrome (MetS) (ranging from 33 percent to 47 percent in most studies, increasing to 53 percent in ages 30-39 years). T2DM patients are five times more likely to develop the metabolic syndrome (MS) and are two times more likely to have cardiovascular disease (CVD). Anovulatory hyperandrogenic women with PCOS had a greater incidence of the syndrome than non-hyperandrogenic anovulatory women with PCOS, indicating that androgens are important in the development of MetS in PCOS (24.8 percent vs 0 percent) [44, 57, 58].

Cardiovascular disease

PCOS comorbidities and effects were examined in detail by Gilbert, et al. in their systematic review and meta-analysis. n = 23 reviews were analyzed, and there were 575 studies and over a million people in all (1,090,072). The study found that women with PCOS had a greater prevalence of CVD and a higher risk of surrogate indicators for CVD. Some research shows PCOS patients are more likely than controls to have subclinical atherosclerosis, as measured by indices like coronary artery calcification scores, arterial stiffness, carotid artery intima-media thickness (CIMT), and endothelial dysfunction as measured by flow-mediated dilation (FMD). Though it remains controversial, the association between cardiovascular disease and PCOS has been shown in various prospective cohort studies, the results of which have been mixed [40, 59, 60]. Perimenopausal women are more likely to show indications of cardiovascular disease than women with PCOS. Few long-term, well-characterized cohort studies are available due to the lag time between PCOS diagnosis and cardiovascular disease symptoms. We urge the development of long-term studies that examine the relationship between certain clinical characteristics, such as obesity and insulin

resistance (IR), and the risk of cardiovascular disease [40, 60].

Nonalcoholic fatty liver disease (NAFLD)

Nonalcoholic fatty liver disease is more common in PCOS women (between 27% and 62%) than in healthy women (NAFLD). Girls with NAFLD (nonalcoholic fatty liver disease) are more likely to have PCOS, according to new research (polycystic ovarian syndrome). In spite of obesity, insulin resistance, or the body's cells becoming resistant to insulin's actions, has been demonstrated to be a major contributing factor to nonalcoholic fatty liver disease (NAFLD) (BMI or waist circumference) [61-63].

Hypertension and vascular dysfunction

Women with PCOS are at greater risk of developing hypertension later in life. In comparison to the general population, premenopausal women with PCOS develop hypertension at a rate of 9 percent-25.7 percent higher. It's likely that IR (together with obesity) is the most significant contributor to hypertension, while androgens affect blood pressure through activating the renin-angiotensin system. In a number of investigations, researchers discovered that women with PCOS had lower vascular compliance and endothelial dysfunction than those without the condition. Obese women were shown to have larger levels of cognitive impairment [64, 65].

Coagulation disorders

One reason that PCOS has been linked to increased levels of plasminogen activator inhibitor 1 (PAI-1) and fibrinogen in women with the condition is because of this association. PCOS has been linked to higher-than-normal amounts of the homocysteine amino acid regardless of one's BMI. Women with PCOS are more likely to develop deep vein thrombosis (DVT) if they use OCPs, which increase the risk of blood clots (three to six fold greater RR). Increasing the ethinyloestradiol dose and the created amount of third-generation OCP enhances the hazard. This raises the danger level. In other investigations, researchers have found contradictory results about the role of OCP in inflaming the system, increasing IR, altering the lipid profile, and maybe raising the risk of cardiovascular disease by increasing TG and HDL levels while decreasing the LDL/HDL ratio. The most secure way is to use progestogen pills or hormone-releasing intrauterine devices [66-69].

Infertility

If a woman has PCOS, her fertility may be affected by ovulatory problems and other endocrine illnesses. According to a recent study, women with PCOS are 10 times more likely than healthy controls to have infertility. There has not been enough research done to say whether or not PCOS causes infertility in women [6, 70].

Pregnancy outcome

Women with PCOS have an increased risk of miscarriage, according to study. Women are more likely to have diabetes complications during pregnancy. Food consumption and metabolism during pregnancy have an impact on the fetus' weight, which may have long-term consequences for the child's health. Fetal mortality, neonatal hypoglycemia and gestational diabetes are problems that women with PCOS face throughout pregnancy, childbirth and the newborn period due to pregnancy-induced high blood pressure, preeclampsia and pregnancy-induced high blood pressure [9, 40].

Relation with cancer

Endometrial cancer is more common in women with PCOS, according to numerous research. It is possible that premenstrual insulin resistance, oligomenorrhea, and the presence of an unopposed estrogen during anovulation all have a role in endometrial development. One study found a link between PCOS and breast and ovarian cancer, and another found it to be associated with prostate cancer. There are three main symptoms of PCOS: obesity, infertility, and anovulation. Obesity and infertility are both common in PCOS patients, as are those who need hormone therapy to conceive. Because they share so many characteristics, it's difficult to tell which malignancies have distinct risks [71].

Psychological disorders

Numerous scientific reviews as well as meta-analyses have found that women with PCOS have a lower quality of life and are more likely to have depression and anxiety symptoms, both of which are linked to having a higher BMI (BMI). This demonstrates how important it is to lose weight in order to treat PCOS as a first line of defense. People who lose weight according to research, report feeling better. Obesity and living with a chronic illness can both worsen the symptoms of polycystic ovarian syndrome (PCOS), which affects mental well-being in women. Most PCOS sufferers, according to studies conducted outside the U.S., are dissatisfied with long-term medical and mental health counseling. According to the findings, women with PCOS should be counseled about their increased risk of experiencing mild to moderate depressive and anxiety symptoms, as well as insomnia [42, 72-74].

Obstructive sleep apnea

Studies have shown that polycystic ovarian syndrome (PCOS) is more likely than previously thought to suffer from obstructive sleep apnea (OSA). A key risk factor for sleep apnea in nonobese individuals is insulin resistance (rather than age, BMI, or testosterone levels in the blood) [75].

Screening recommendations

PCOS necessitates treatment that addresses both immediate symptoms as well as long-term prevention of problems. PCOS screening recommendations are crucial during the therapeutic phase.

Screening for type 2 DM and GDM

All obese PCOS women, regardless of their family history of type 2 diabetes, and all lean PCOS women under the age of 40, regardless of previous gestational diabetes or familial type 2 diabetes, should have an oral glucose tolerance test (OGTT) performed because it may reveal whether they have type 2 diabetes (ESE). All women with PCOS should have an OGTT because of the increased risk of type 2 diabetes and insulin resistance, according to these endocrine associations. Use of HbA1c (HbA1c) as a screening test is not approved by any organization. Regardless of whether a person has diabetes risk factors or not (approximately three to five years apart), or if a person does have diabetes risk factors, evaluation is required for diabetes prevention (about every year) [76, 77]. According to the most recent international guidelines for PCOS, an OGTT must be conducted prior to conception or during the first trimester of pregnancy, which lasts between 24 and 28 weeks [9].

Screening for CVD

All women with PCOS should have their cardiovascular risk factors tested under current global standards, regardless of the variances. They advocate a thorough lipid panel, smoking assessment, body weight and BMI assessment, blood pressure monitoring, and a comprehensive lipid panel as part of the treatment plan for hypercholesterolemia. The Australian Guideline prioritizes CVD screening, which includes yearly blood-pressure readings if BMI is ≤ 25 kg/m2, or at each visit if BMI is ≥ 25 kg/m2, and lipid profile checks every two years if first normal, or annually if abnormal before [51, 77].

Screening for psychological wellbeing

Women with PCOS should be tested for depression and anxiety before receiving a diagnosis so that treatment can begin as soon as possible. To make sure they are getting the proper care, these ladies should be evaluated for everything from depression to anxiety to eating problems to erectile dysfunction to sexual dysfunction. If a woman's screening results are positive, she should see a doctor and talk to a specialist about her options. There have been a few studies that show depression among teenagers is more common, and parents should be aware of this. Since the unknown long-term health consequences of NAFLD screening in women with PCOS have not yet been determined, current guidelines and special interest groups have chosen not to recommend routine NAFLD screening in these women [77, 78].

Treatment of PCOS

Doctors should concentrate on treating PCOS symptoms if they want to see results. The best treatment is a combination of many treatments, including the assistance of a family practitioner, endocrinologist, gynecologist, dermatologist, nutritionist, pediatrician and psychiatrist. The treatment suggestions are mostly based on two guidelines: the American Task Force Guidelines and the PCOS Australian Alliance Guidelines, according to the American Task Force and the PCOS Australian Alliance Guidelines. Added care is given to contemporary requirements as well [77].

Lifestyle changes

Making small changes to your lifestyle can go a long way toward managing your disease. The American Congress of Obstetricians and Gynecologists advises women with PCOS who are obese to engage in regular exercise treatment and follow a low-calorie diet to help control their weight. Menstrual cycles, fertility, insulin and testosterone levels all fluctuate significantly in women who drop 5 percent of their body weight [79-81].

Medical treatment

Medications may be used if lifestyle changes do not alleviate symptoms enough.

Oral contraceptive pills

Oral contraceptive pills (OCPs) have now been approved as the first-line treatment for hyperandrogenism and irregular menstrual cycles in women with PCOS by the Endocrine Society Task Force, Australian Alliance, and PCOS Consensus Group. A woman taking an oral contraceptive pill (OCP) has higher levels of the sex hormone-binding globulin (SHBG) and lower levels of free testosterone in her body because the birth control pill (OCP) suppresses the luteinizing hormone (LH) synthesis. People with acne, hirsutism, and irregular menstruation cycles may all benefit from this medication due to hyperandrogenism. Treatment for acne and hirsutism should continue six months or longer. The most efficient way to treat PCOS is to use OCP as an antiandrogenic or neutral progestin alone [82, 83].

Metformin

Biguanides, such as metformin, are used to treat diabetes by being taken orally. Metformin is a first-line treatment for PCOS-related skin diseases and pregnancy concerns in women, despite the opinions of some doctors. When used with clomiphene citrate, it can enable people who have become resistant to clomiphene citrate

work more effectively again [84].

Spironolactone

OCPs or not, this is the strongest antiandrogen for reducing hirsutism that researchers have come across. The drug has been effective in treating both acne and alopecia. To avoid menstrual irregularities, it should be combined with OCP, which is widely tolerated. However, the current guidelines provide no explicit recommendations on the use of spironolactone in treating PCOS [85].

Cyproterone acetate

While pregnant, it works as an antiandrogen. A dosage of 50-100 mg daily, either alone or with ethinyl- oestradiol, is effective. Hepatotoxicity is a rare complication of the drug. Hair loss and hirsutism are two common conditions for which it is prescribed [20].

Flutamide

In spite of its name, flutamide is neither an anabolic nor an androgenic steroid. When it comes to treating PCOS symptoms, flutamide and metformin work better than OCP alone. Toxicities of the liver are, nevertheless, common adverse effects [20].

Finasteride

When used with OCPs, the antiandrogen finasteride is more potent than when used alone. There have been studies done on finasteride and spironolactone that show they are effective when estrogen is not allowed [20].

Cosmetic/local therapy

It's possible to remove unwanted hair through medical means or physically by using treatments such as shaves or threading, plucking, bleaching, or shaving. Laser thermolysis, electrolysis, and photoepilation are all methods of permanently removing hair in which the hair follicle is vaporized [20].

Infertility treatment

Anovulatory infertility is treated with clomiphene citrate, which is suggested by the American Task Force and the PCOS Australian Alliance Guidelines as a first-line treatment. Clinical care guidelines for PCOS patients taking letrozole to promote ovulation have been updated by the ACOG, the American College of Obstetricians and Gynecologists. When compared to clomiphene citrate, the live birth rate of letrozole is greater, hence it is recommended as the first-line ovulation induction medication. For women who have tried clomiphene citrate and letrozole and are still unable to get pregnant, second-line treatments include using exogenous gonadotropins, IVF, or laparoscopic ovarian surgery. Ultrasound-guided transvaginal ovarian needle drilling, ovarian biopsy and electrocautery, laparoscopic ovarian drilling, and multi-needle laparoscopic ovarian intervention have all been shown to successfully trigger ovulation when used in conjunction with laparoscopic ovarian operations [86, 87].

Treatment in adolescents

In the treatment of adolescent PCOS, no placebo-controlled randomized controlled studies are currently available. According to the recommendations, each adolescent with PCOS should receive individualized care. Adopting a healthier lifestyle and losing weight are recommended as the first line of treatment, especially for overweight or obese youth. OCPs are a critical part of treating adolescent PCOS. However, it's unclear which OCPs work best for adolescents and for how long they should use them. Despite the fact that metformin is widely used no data exists on how long patients remain on the medication. Better preventative outcomes have been linked to early lifestyle changes and the use of metformin medication [76].

New therapeutic options

The intramuscular injection of 0.5-1 mg/kg/dL isotretinoin was tested on female acne patients by Cakir, et al. It was a highly effective method of treating the condition. Acne-prone women with PCOS may benefit the most from using this supplement as a first line of defense against the symptoms of their disease. As a result, persons with low AMH levels may find isotretinoin to be advantageous. When used to treat severe acne, isotretinoin, on the other hand, does not work as well. Because it is costly and leads to increased body weight and cholesterol, this medication is not extensively utilized in PCOS at this time [88, 89]. Vinaixa, et al. have developed a new polytherapy that combines a three-month flutamide-metformin-pioglitazone treatment with a three-month ester-progestogen treatment. It has been shown to lower LDL cholesterol, raise HDL cholesterol, boost testosterone levels, and thicken CIM, all of which minimize the chances of atherosclerosis and the difficulties it brings. Thiazolidinedione derivatives can increase insulin sensitivity as well. It is not recommended for women who are trying to conceive to use these medicines, despite the benefits they may offer. With metformin and GLP-1 agonists, new weight loss, improved insulin sensitivity, and improved reproductive function can be achieved. However, they have a poor safety record in women who are fertile [90-92]. Numerous studies have looked into the usefulness of vitamin D supplementation for women with PCOS who have low levels of vitamin D or insulin resistance. PCOS is frequently linked to lipid problems and obesity, thus statin therapy may be beneficial. For those who have been diagnosed with conditions like "inflammatory," "antioxidant," "antiproliferative," or "cholesterol lowering," the standard treatment is statins. Researchers Celik

and Acbay found that a metformin-based 12-week treatment reduced research participants' total testosterone, DHEA-S, body weight, CRP, TG, and LDL cholesterol. Omega-3 fatty acids, α-lipoic acid, and N-acetylcysteine are found in these supplements, which may improve insulin sensitivity and lipid profile for PCOS women [93-95]. PCOS, its symptoms, and therapy are all linked to having a highly active sympathetic nerve system. The ovaries of some women with PCOS produce higher levels of NGF than normal, which causes increased muscle sympathetic nerve activity, which leads to fat storage problems, insulin resistance, OSA, and other metabolic issues (MSNA). It's possible for a patient to benefit from nonpharmacological treatments (like CPAP for OSA and weight loss) as well as pharmaceutical treatments (like insulin sensitizers) and surgical treatments (like renal denervation). FGFs 1, 10, 19, and 21 have been found to regulate glucose and lipid metabolism and operate as a cardioprotective factor, according to the findings (FGF-21). Fibroblast growth factors (FGFs) are implicated in hyperactive sebaceous glands, as well. An analogue of FGF-21 called LY2405319 has been shown to aid in the treatment of insulin resistance, lipid problems, and obesity. Clinical investigations have indicated that hypoglycemia is reduced, and the lipid profile of the blood and the production of hormones such as LH, DHEA, testosterone, and progesterone are also enhanced. When the follicular milieu has high levels of myo-inositol, the overall number of oocytes increases. myo-inositol has a large amount of the fertility-enhancing compound inositol [96, 97].

Conclusion

The polycystic ovarian syndrome is a endocrine disorder, but extensive research and studies are conducted to determine the cause and remedies because no one understands what causes it, multiple diagnostic criteria are used, and treatment is difficult. There is a knowledge gap between patients and healthcare providers, as well as a recurring failure of healthcare providers to meet the often inadequate important patient needs. It is important to remember that this can be prevented rather than cured. Women with PCOS should be counseled, evaluated, and treated by healthcare providers who are aware of the long-term health issues associated with PCOS.

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