An understanding of the relationship between insulin resistance and polycystic ovarian syndrome

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Abstract

PCOS, which stands for polycystic ovary syndrome, is a prevalent endocrine condition that affects women of reproductive age. Insulin resistance (IR) often known as IR, is widely regarded as a defining characteristic of PCOS and plays a crucial part in the development of the condition. In this review, the goal is to investigate the association between insulin resistance and PCOS with a particular emphasis on the processes that underlie this association, the clinical symptoms of IR in PCOS, and the diagnostic and therapeutic options that are currently available for controlling IR in PCOS. IR is a factor in the development of several essential characteristics of PCOS. These characteristics include hyperandrogenism, menstrual abnormalities, and metabolic problems. The evaluation of insulin resistance in patients with PCOS is necessary for the early identification and management of the disorder. Alterations in lifestyle, including but not limited to dieting and exercise, are the primary forms of treatment available for the management of IR in PCOS. In addition, pharmaceutical therapies such as metformin and insulin-sensitizing drugs have shown promising results in improving metabolic and reproductive outcomes in women with PCOS. Understanding the connection between insulin resistance and PCOS is essential for the treatment of this relatively common endocrine condition.

Keywords: Polycystic Ovarian Syndrome, Insulin Resistance, Hyperandrogenism, Metabolic Disturbances, Diagnostic, Therapeutic Options.

Introduction

Women of reproductive age are susceptible to the complicated endocrine condition known as "polycystic ovarian syndrome (PCOS)" [1]. It is defined by at least two of the three criteria, which are polycystic ovarian morphology, oligo- or anovulation, and hyperandrogenism [2]. Due to its high prevalence, which affects 6–10% of women of reproductive age [3,] PCOS is

a serious health concern. It is linked to a number of harmful health effects, such as infertility, metabolic issues, and a higher risk of cardiovascular disease [4].

"Insulin Resistance (IR)" is characterized as a state of decreased insulin sensitivity that impairs target tissues' ability to absorb glucose [5]. Up to 70% of women with PCOS display IR, making it a key component of the condition [6]. The development of PCOS is significantly influenced by IR, which also adds to the condition's major symptoms such hyperandrogenism, irregular menstruation, and metabolic abnormalities [7]. With a focus on the processes behind this association, clinical symptoms of IR in PCOS, and available diagnostic and therapeutic approaches for controlling IR in PCOS, this review seek to offer an overview of the relationship between IR and PCOS in this review.

Mechanisms underlying the relationship between IR and PCOS

The mechanisms that link IR with PCOS are intricate and still poorly understood. It is believed that a mix of hereditary and environmental factors contribute to IR in PCOS. Studies have revealed that type 2 diabetes mellitus and metabolic syndrome are more common in families of women with PCOS, raising the possibility that IR in this condition may have a genetic component [4-5].

Hyperinsulinemia brought on by IR in PCOS promotes androgen synthesis by the ovary and adrenal gland [6]. This hyperandrogenism, which is a defining feature of PCOS, helps affected women develop hirsutism, acne, and male-pattern baldness. By altering the hypothalamic-pituitary-ovarian axis, IR in PCOS also contributes to menstrual irregularities, anovulation, and infertility [7].

We don't fully understand the precise processes through which IR causes dyslipidemia and an elevated risk of cardiovascular disease in PCOS. Increased visceral adiposity, which is recognized to be a risk factor for metabolic abnormalities, is related with IR in PCOS [8]. Additionally, postprandial hyperglycemia and compensatory hyperinsulinemia are caused by IR in PCOS, which impairs the uptake of glucose in peripheral tissues like skeletal muscle [9].

It has been suggested that a number of biological processes can account for the connection between IR and PCOS. One hypothesised mechanism links increased androgen production to abnormalities in insulin signaling in ovarian tissue [10]. A dysregulation of adipokines, including adiponectin and leptin, which are involved in glucose and lipid metabolism and may contribute to the development of IR in PCOS, is another hypothesized cause [11]. To fully understand the mechanisms behind the connection between IR and PCOS, more study is required.

Recent research has also emphasized the potential contribution of inflammation to the IR in PCOS. Inflammation has been suggested to play a role in the development of IR through its effects on insulin signaling and glucose uptake since chronic low-grade inflammation is a characteristic of PCOS [12]. Additionally, it has been discovered that PCOS-related adipose

tissue expresses pro-inflammatory cytokines more frequently, which could be a factor in IR and metabolic dysfunction [13].

The risk of metabolic problems in PCOS has been reduced and insulin sensitivity has been improved with a number of lifestyle treatments. It has been demonstrated that weight loss, especially by dietary changes and exercise, enhances insulin sensitivity and metabolic parameters in overweight and obese women with PCOS [14]. Additionally, some research has indicated that specific dietary habits, like a low-glycemic index diet, may be especially helpful for enhancing insulin sensitivity in PCOS women [15].

The management of IR in PCOS has also been suggested to use pharmaceutical therapies. It has been demonstrated that women with PCOS who use metformin, a drug that is frequently used to treat type 2 diabetes, had improved insulin sensitivity and decreased hyperandrogenism [16]. Other drugs, including glucagon-like peptide-1 agonists and thiazolidinediones, have also been researched for their potential use in treating IR in PCOS [17].

In conclusion, there are numerous factors at play in the complex link between IR and PCOS. IR, which causes hyperandrogenism, irregular menstruation, and metabolic dysfunction, is a key factor in the etiology of PCOS. Although the mechanisms underlying this association are not fully understood, they include inflammation, dysregulation of insulin signaling, and other elements. Insulin sensitivity may be improved and the risk of metabolic problems in PCOS may be reduced by lifestyle therapies, especially weight loss through dietary changes and exercise. The therapy of IR in PCOS may potentially benefit from pharmaceutical interventions like metformin. To completely comprehend the mechanisms behind the link between IR and PCOS and to find new therapeutic targets for the treatment of this complicated illness, more study is required [18–24].

Clinical manifestations of IR in PCOS

Menstrual abnormalities, metabolic disruptions, and hyperandrogenism are only a few of the important characteristics of PCOS that IR influences [7]. One of the defining characteristics of PCOS is hyperandrogenism, and IR has been found to have a key role in its emergence [25]. Clinical hyperandrogenism symptoms such hirsutism, acne, and male-pattern baldness are caused by elevated androgen levels [26]. Additionally, oligomenorrhea and amenorrhea are menstrual irregularities that can develop as a result of IR [27]. Anovulation has been linked to abnormalities in the hypothalamic-pituitary-ovarian axis, which are caused by impaired glucose metabolism and IR [28].

Women with PCOS frequently experience metabolic abnormalities such dyslipidemia, type 2 diabetes, and cardiovascular disease, which are thought to be mostly caused by IR [29]. Low-density lipoprotein cholesterol (LDL-C) levels are increased and high-density lipoprotein cholesterol (HDL-C) levels are lowered in dyslipidemia, which is linked to IR. Up to 50% of women with PCOS have impaired glucose tolerance or diabetes, and IR is a substantial risk

factor for type 2 diabetes. Additionally, IR has been associated with a higher risk of cardiovascular disease, which is the main cause of death in PCOS-positive women [30].

Diagnostic options for IR in PCOS

It might be difficult to diagnose IR in PCOS because it is often determined by clinical features rather than by certain laboratory tests. However, IR in PCOS can be recognized using a variety of diagnostic techniques.

The "homeostasis model assessment of insulin resistance (HOMA-IR)" is one of the most frequently utilized techniques for IR diagnosis in PCOS. HOMA-IR is a straightforward formula that gauges IR using fasting blood sugar and insulin levels. A HOMA-IR result greater than 2.5 is seen as a sign of IR in PCOS [31].

The "oral glucose tolerance test (OGTT)" is another way for identifying IR in PCOS. The OGTT checks blood sugar and insulin levels before and two hours after a glucose load is administered. Indicative of IR in PCOS is an abnormal OGTT with high glucose and insulin levels [32].

Insulin sensitivity in PCOS has recently been evaluated using imaging techniques including "computed tomography (CT)" and "magnetic resonance imaging (MRI)". Adipose tissue distribution, which is closely related to IR in PCOS, can be assessed by MRI and CT [33].

The "quantitative insulin sensitivity check index (QUICKI)", the "insulin suppression test (IST)", and the hyperinsulinemic euglycemic clamp are other laboratory techniques that can be used to evaluate IR in PCOS. Although more invasive and complicated than HOMA-IR or OGTT, these tests offer a more accurate assessment of insulin sensitivity [34].

In conclusion, a combination of clinical evaluation and laboratory investigations is needed to diagnose IR in PCOS. While MRI, CT, QUICKI, IST, and hyperinsulinemic euglycemic clamp are more specialized tests that can offer a more precise assessment of insulin sensitivity, HOMA-IR and OGTT are frequently used techniques for diagnosing IR in PCOS. Early detection and treatment of IR in PCOS-affected women are essential for lowering the risk of T2DM and CVD development and enhancing reproductive outcomes..

Therapeutic options for managing IR in PCOS

The main therapy alternatives for treating IR in PCOS are lifestyle changes including weight loss and exercise. In PCOS-afflicted women, losing weight has been proven to enhance insulin sensitivity, lower androgen levels, and increase menstrual regularity [25]. Additionally, exercise increases insulin sensitivity, aids in weight loss, and enhances cardiovascular health [26].

Metformin and insulin-sensitizing medications have demonstrated potential in improving the metabolic and reproductive outcomes in PCOS-afflicted women [27]. The biguanide drug metformin has been proven to improve menstrual regularity and lower testosterone levels in

women with PCOS [28]. It also increases insulin sensitivity and glucose metabolism. "Thiazolidinediones (TZDs)" and "glucagon-like peptide-1 receptor agonists (GLP-1 RAs)", which increase insulin sensitivity and have been found to enhance metabolic and reproductive outcomes in women with PCOS [29], are examples of insulin-sensitizing medications.

Conclusion

In conclusion, IR is a key component of PCOS and is crucial to the pathophysiology of the condition. Menstrual irregularities, metabolic disturbances, and hyperandrogenism are just a few of the important characteristics of PCOS that IR contributes to. For an early diagnosis and effective treatment of PCOS, the measurement of IR is crucial. The main therapy alternatives for treating IR in PCOS are lifestyle changes including weight loss and exercise. Pharmacological treatments including metformin and insulin-sensitizing drugs have also demonstrated potential in enhancing the metabolic and reproductive results in PCOS-affected women. To completely comprehend the connection between IR and PCOS, however, and to create more potent treatments for treating IR in this population, more study is required.

References:

1. Teede HJ, Misso ML, Costello MF, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Hum Reprod. 2018;33(9):1602-1618.

2. Diamanti-Kandarakis E, Christakou CD, Kandaraki E, Economou FN. Metformin: an old medication of new fashion: evolving new molecular mechanisms and clinical implications in polycystic ovary syndrome. Eur J Endocrinol. 2010;162(2):193-212.

3. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev. 1997;18(6):774-800.

4. Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(12):4565-4592.

5. March WA, Moore VM, Willson KJ, et al. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod. 2010;25(2):544-551.

6. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19-25.

7. Legro RS, Kunselman AR, Dodson WC, Dunaif A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. J Clin Endocrinol Metab. 1999;84(1):165-169.

8. Rajbanshi I, Sharma VK, Tuladhar ET, et al. Metabolic and biochemical profile in women with polycystic ovarian syndrome attending tertiary care centre of central NEPAL. BMC Womens Health. 2023;23(1):208. Published 2023 Apr 28. doi:10.1186/s12905-023-02379-z.

9. Goodman NF, Cobin RH, Futterweit W, et al. American association of clinical endocrinologists, american college of endocrinology, and androgen excess and pcos society disease state clinical review: guide to the best practices in the evaluation and treatment of polycystic ovary syndrome - PART 2. Endocr Pract. 2015;21(12):1415-1426. doi:10.4158/EP15748.DSCPT2.

10. Teede HJ, Misso ML, Costello MF, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome [published correction appears in Hum Reprod. 2019 Feb 1;34(2):388]. Hum Reprod. 2018;33(9):1602-1618. doi:10.1093/humrep/dey256.

11. Ehrmann DA. Polycystic ovary syndrome. N Engl J Med. 2005;352(12):1223-1236.

12. Legro RS. Obesity and PCOS: implications for diagnosis and treatment. Semin Reprod Med. 2012;30(5):496-506.

13. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocr Rev. 2012;33(6):981-1030.

14. Saadia Z. Follicle Stimulating Hormone (LH: FSH) Ratio in Polycystic Ovary Syndrome (PCOS) - Obese vs. Non- Obese Women. Med Arch. 2020;74(4):289-293. doi:10.5455/medarh.2020.74.289-293.

15. Barber TM, Franks S. The link between polycystic ovary syndrome and both type 1 and type 2 diabetes mellitus: what do we know today? Womens Health (Lond). 2012;8(2):147-154.

16. Vrbíková J, Hainer V. Obesity and polycystic ovary syndrome. Obes Facts. 2009;2(1):26-35.

17. Sepilian V, Nagamani M. Adiponectin levels in women with polycystic ovary syndrome and severe insulin resistance. J Soc Gynecol Investig. 2005;12(2):129-134. doi:10.1016/j.jsgi.2004.09.003.

18. Yildiz BO, Bozdag G, Yapici Z, et al. Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria. Hum Reprod. 2012;27(10):3067-3073.

19. Payab M, Tayanloo-Beik A, Falahzadeh K, et al. Metabolomics prospect of obesity and metabolic syndrome; a systematic review. J Diabetes Metab Disord. 2021;21(1):889-917. Published 2021 Nov 26. doi:10.1007/s40200-021-00917-w.

20. Armitage JA, Khan IY, Taylor PD, Nathanielsz PW, Poston L. Developmental programming of the metabolic syndrome by maternal nutritional imbalance: how strong is the evidence from experimental models in mammals?. J Physiol. 2004;561(Pt 2):355-377. doi:10.1113/jphysiol.2004.072009

21. Moran LJ, Pasquali R, Teede HJ, Hoeger KM, Norman RJ. Treatment of obesity in polycystic ovary syndrome: a position statement of the Androgen Excess and Polycystic Ovary Syndrome Society. Fertil Steril. 2009;92(6):1966-1982.

22. Marsh K, Brand-Miller J. The optimal diet for women with polycystic ovary syndrome? Br J Nutr. 2005;94(2):154-165.

23. Tang T, Lord JM, Norman RJ, Yasmin E, Balen AH. Insulin-sensitising drugs (metformin, rosiglitazone, pioglitazone, D-chiro-inositol) for women with polycystic ovary syndrome, oligo amenorrhoea and subfertility. Cochrane Database Syst Rev. 2012;(5):CD003053.

24. Baillargeon JP, Nestler JE. Commentary: polycystic ovary syndrome: a syndrome of ovarian hypersensitivity to insulin?. J Clin Endocrinol Metab. 2006;91(1):22-24. doi:10.1210/jc.2005-1804.

25. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes. 1989;38(9):1165-1174.

26. Dunaif A, Wu X, Lee A, et al. Defects in insulin receptor signaling in vivo in the polycystic ovary syndrome (PCOS). Am J Physiol Endocrinol Metab. 2001;281(2):E392-399.

27. Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes Care. 1999;22(1):141-146.

28. Escobar-Morreale HF, San Millán JL. Abdominal adiposity and the polycystic ovary syndrome. Trends Endocrinol Metab. 2007;18(7):266-272.

29. Gambineri A, Patton L, Vaccina A, et al. Treatment with flutamide, metformin, and their combination added to a hypocaloric diet in overweight-obese women with polycystic ovary syndrome: a randomized, 12-month, placebo-controlled study. J Clin Endocrinol Metab. 2006;91(10):3970-3980.

30. Azziz R, Woods KS, Reyna R, et al. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab. 2004;89(6):2745-2749.

31. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-419.

32. Pasquali R, Gambineri A, Biscotti D, et al. Effect of long-term treatment with metformin added to hypocaloric diet on body composition, fat distribution, and androgen and insulin levels in abdominally obese women with and without the polycystic ovary syndrome. J Clin Endocrinol Metab. 2000;85(8):2767-2774. doi:10.1210/jcem.85.8.6738.

33. Sam S, Mazzone T. Adipose tissue changes in obesity and the impact on metabolic function. Transl Res. 2014;164(4):284-292.

34. Morales AJ, Laughlin GA, Bützow T, et al. Insulin, somatotropic, and luteinizing hormone axes in lean and obese women with polycystic ovary syndrome: common and distinct features. J Clin Endocrinol Metab. 1996;81(8):2854-2864.

35. Azziz R, Carmina E, Chen Z, et al. Polycystic ovary syndrome. Nat Rev Dis Primers. 2016;2:16057.