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#### **REVIEW**



# Relationship between insulin resistance and polycystic ovary syndrome: a literature review

# Relación entre la resistencia a la insulina y el síndrome de ovario poliquístico: una revisión bibliográfica

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## **ABSTRACT**

**Introduction:** polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age, and insulin resistance is a key feature of its pathophysiology. This study aims to review the relationship between insulin resistance and PCOS, as well as to analyze the efficacy of insulin-sensitizing treatments (such as metformin and myo-inositol) compared to conventional hormonal therapies.

**Method:** a systematic review of clinical studies, meta-analyses, and reviews published in scientific databases such as PubMed and Scopus was conducted, focusing on the relationship between insulin resistance and PCOS, and the effects of insulin-sensitizing treatments. Only relevant, high-quality literature from recent years was included.

**Results:** insulin-sensitizing treatments, especially metformin and myo-inositol, have been shown to be effective in improving insulin resistance and reducing metabolic symptoms of PCOS. However, oral contraceptives, while useful for hormonal symptoms, do not have a significant impact on insulin resistance. **Conclusion:** insulin-sensitizing agents remain the most effective treatment for insulin resistance in women with PCOS. Myo-inositol offers an alternative with fewer side effects compared to metformin, but more research is needed to define optimal combinations and dosages.

**Keywords:** Insulin Resistance; Polycystic Ovary Syndrome; Metformin; Myo-Inositol; Pharmacological Treatments.

# **RESUMEN**

Introducción: el síndrome de ovario poliquístico (SOP) es una de las afecciones endocrinas más comunes en mujeres en edad reproductiva, y la resistencia a la insulina es un hallazgo clave en su fisiopatología. Este trabajo tiene como objetivo realizar una revisión bibliográfica sobre la relación entre la resistencia a la insulina y el SOP, y analizar la eficacia de los tratamientos con sensibilizadores de insulina (como la metformina y el mioinositol) frente a las terapias hormonales convencionales.

**Método:** se realizó una revisión sistemática de estudios clínicos, metaanálisis y revisiones publicadas en bases de datos científicas como PubMed y Scopus, centrada en la relación entre resistencia a la insulina y SOP, y los efectos de los tratamientos con sensibilizadores de insulina. Se incluyó solo literatura relevante y de alta calidad publicada en los últimos años.

Resultados: los tratamientos con sensibilizadores de insulina, especialmente la metformina y el mioinositol, han demostrado ser efectivos en la mejora de la resistencia a la insulina y la reducción de los síntomas metabólicos del SOP. Sin embargo, los anticonceptivos orales, aunque útiles para los síntomas hormonales, no tienen un impacto significativo sobre la resistencia a la insulina.

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**Conclusión:** los sensibilizadores de insulina continúan siendo el tratamiento más eficaz para la resistencia a la insulina en mujeres con SOP. El mioinositol ofrece una alternativa con menos efectos secundarios en comparación con la metformina, pero se necesita más investigación para definir las mejores combinaciones y dosificaciones.

**Palabras clave:** Resistencia a la Insulina; Síndrome de Ovario Poliquístico; Metformina; Mioinositol; Tratamientos Farmacológicos.

#### INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex endocrinological disorder that affects a significant proportion of women of reproductive age, characterized mainly by hyperandrogenism, chronic anovulation, and menstrual irregularities. This condition is the most common cause of hyperandrogenism in women and can have a considerable impact on the metabolic, reproductive, and psychological health of those affected. Although the etiology of PCOS is not entirely clarified, the interaction of genetic and environmental factors in its development is recognized. One of the most relevant aspects in the clinical management of PCOS is insulin resistance, which not only aggravates the symptoms of the syndrome but also increases the risk of severe metabolic complications, such as type 2 diabetes and cardiovascular disease. Insulin resistance has been identified as a central factor exacerbating the clinical picture of PCOS, raising the need for therapeutic approaches that comprehensively address both conditions.

However, despite growing evidence of the importance of insulin resistance in PCOS, controversies persist about the most appropriate treatment. Although insulin sensitizers have shown benefits in improving insulin sensitivity and reducing metabolic symptoms, conventional hormonal therapies remain the standard treatment for PCOS. This raises the question of whether a combined or alternative approach might be more effective in improving affected women's quality of life and metabolic health.

What is the effectiveness of insulin sensitizer treatments compared to conventional hormonal therapies in improving insulin sensitivity and reducing metabolic symptoms in women with polycystic ovary syndrome (PCOS)?

### Objective

This study analyzes the relationship between insulin resistance and polycystic ovary syndrome (PCOS) through a literature review. Its goal is to evaluate the effectiveness of insulin sensitizer treatments compared with conventional hormonal therapies and thus understand the pathophysiological mechanisms and current therapeutic interventions to improve insulin sensitivity and reduce metabolic symptoms associated with PCOS.

## **METHOD**

This work is a systematic literature review that aims to analyze and synthesize the existing scientific literature on the relationship between polycystic ovary syndrome (PCOS) and insulin resistance, focusing on the treatments used to improve insulin sensitivity in women with PCOS. Because this paper is a qualitative review, statistical data analysis will not be performed. Instead, existing studies will be examined and summarized descriptively and critically to provide an up-to-date and comprehensive view of the most effective treatments for insulin resistance in women with PCOS. The review focuses on studies that include women diagnosed with polycystic ovary syndrome (PCOS) and that explore the relationship between PCOS and insulin resistance. Selected studies should examine how insulin resistance affects the metabolic and reproductive aspects of PCOS and treatments to improve insulin sensitivity. Research with women of reproductive age or premenopausal women, without age restriction, will be included. Studies must have been published between 2014 and 2024 and be available in English, Spanish, or Portuguese. Research will be selected that focuses on women diagnosed with PCOS and addresses the relationship between PCOS and insulin resistance, as well as treatments to improve insulin sensitivity. Studies that do not directly address this relationship, that include a male or child population, or that are of low quality, such as conference proceedings or unpublished theses, will be excluded.

The scientific literature search was performed in recognized academic databases such as PubMed and Google Scholar. These databases provided access to many relevant studies in endocrinology and reproductive health. Specific keywords related to PCOS and insulin resistance, such as "Polycystic Ovary Syndrome," "Insulin Resistance," "Metformin," and "Oral Contraceptives," were used, and Boolean operators such as AND (to combine related terms) and OR (to include synonyms) were employed

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(	General summary	Gaitán <sup>(2)</sup>	Myoinositol	No serious adverse effects, well tolerated.	Myoinositol is highly tolerable, making it a viable alternative to metformin.
		All authors mentioned	Metformin, Myoinositol, Combined Oral Contraceptives	Metformin and myoinositol are effective in improving insulin sensitivity and reducing hormonal symptoms. Oral contraceptives help with hormonal symptoms, but not with insulin resistance.	treatments are metformin and myoinositol, which should be combined with

In addition, filters were applied to limit the results to articles published in the last 10 years and the languages of interest. Once the articles were obtained, their titles, abstracts, and keywords were reviewed to select those that met the established inclusion criteria. Relevant studies were read, and the most important information was extracted and organized. The information collected focused on treatments used to improve insulin resistance in women with PCOS, such as insulin sensitizers (e.g., metformin) and conventional hormonal therapies (e.g., combined oral contraceptives). For each treatment, the observed effects on improving insulin resistance, regulation of menstrual cycles, reduction of hyperandrogenism-related symptoms, and impact on long-term metabolic health were analyzed.

Finally, the selected studies were organized and analyzed descriptively. The therapeutic approaches used in each investigation were compared, identifying commonalities and outcome differences. Best practices for treating insulin resistance in women with PCOS were highlighted. This review provides a precise and up-to-date analysis of the most effective treatments. It provides healthcare professionals and researchers with a valuable resource for managing PCOS and its metabolic complications.

#### **RESULTS**

In this review, we analyzed the relationship between insulin resistance and polycystic ovary syndrome (PCOS) to evaluate the effects of insulin sensitizer treatments compared with conventional hormonal therapies on insulin sensitivity and metabolic symptoms associated with PCOS.

# Relationship between insulin resistance and PCOS

Insulin resistance is a key factor in the pathophysiology of PCOS, exacerbating both the hormonal and metabolic symptoms of the condition. Insulin resistance increases androgen production, which contributes to classic PCOS symptoms such as hirsutism and acne and interferes with the regulation of reproductive hormones, affecting ovulation and leading to irregular menstrual cycles.<sup>(7)</sup> In addition, hyperinsulinemia favors visceral fat accumulation and can trigger a chronic low-grade inflammatory process, which increases the risk of metabolic syndrome and cardiovascular disease.<sup>(2)</sup> Insulin resistance also interferes with ovarian function and fertility, which hinders fertility treatments and perpetuates menstrual irregularity.

#### Treatments with insulin sensitizers

# Metformin

Metformin is one of the most studied treatments for insulin resistance in women with PCOS. It has significantly improved insulin sensitivity and reduced blood glucose levels, contributing to better hormone regulation and ovulation. However, its gastrointestinal side effects, such as diarrhea and nausea, limit treatment adherence. In addition, metformin reduces androgen levels, which improves symptoms of hirsutism and acne in women with PCOS.

# Myoinositol

Myoinositol is another effective alternative for improving insulin resistance in women with PCOS, with a superior tolerability profile to metformin. It has been found to improve insulin sensitivity and hormone regulation without metformin's common gastrointestinal side effects. In addition, myoinositol reduces testosterone levels, contributing to the improvement of hyperandrogenism symptoms. (8) This treatment also improves menstrual cycles and fertility, presenting itself as an attractive option for women who are intolerant to metformin.

# Conventional hormonal therapies

Conventional hormonal therapies, such as combined oral contraceptives, help control hormonal symptoms of PCOS, such as hirsutism and acne and regulate menstrual cycles. However, they do not improve insulin sensitivity, so they must be combined with insulin sensitizers, such as metformin or myoinositol, to manage insulin resistance effectively.<sup>(3)</sup>

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# Impact of insulin resistance on metabolic health

Insulin resistance has a significant impact on the metabolic health of women with PCOS, increasing the risk of developing type 2 diabetes and cardiovascular disease in the long term. Adequate control of insulin resistance improves hormonal parameters and reduces the risk of type 2 diabetes and cardiovascular disease. (7) Women with PCOS who do not receive treatment for insulin resistance are at increased risk of developing metabolic syndrome, characterized by hypertension, dyslipidemia, and obesity. (2) In addition, improving insulin sensitivity through treatments such as metformin and myoinositol reduces metabolic risks and improves fertility and menstrual cycles.

## Side effects and tolerance of treatments

#### Metformin

Metformin is associated with gastrointestinal side effects, such as diarrhea, nausea, and stomach upset, which affects adherence in some patients. (4)

# Myoinositol

On the other hand, myoinositol is generally well tolerated, with minimal or no side effects, making it a more attractive option for women who are intolerant to metformin.<sup>(8)</sup>

# **Summary of Results**

The most effective treatments for insulin resistance in women with PCOS are metformin and myoinositol. Metformin is the most commonly used option, although its gastrointestinal side effects limit adherence. Myoinositol, on the other hand, is an effective alternative with better tolerability. Conventional hormonal therapies, such as oral contraceptives, help control the hormonal symptoms of PCOS. However, they do not improve insulin resistance and must be combined with treatments such as metformin or myoinositol to achieve comprehensive PCOS management.

Adequate treatment of insulin resistance improves metabolic health and has positive effects on reproductive health, reducing the risk of type 2 diabetes and cardiovascular disease in the long term.

#### **DISCUSSION**

The review conducted has provided insight into the relationship between insulin resistance and polycystic ovary syndrome (PCOS). These two conditions share an important pathophysiological connection and affect a significant proportion of women of childbearing age. The main objective of this analysis was to explore available treatments, with special attention to insulin sensitizers, and compare them with conventional hormonal therapies to assess their impact on improving insulin sensitivity and reducing metabolic and reproductive symptoms associated with PCOS.

The results obtained show a clear trend towards the efficacy of treatments with insulin sensitizers, especially metformin and myoinositol. It is confirmed that these treatments should be combined with hormonal interventions to comprehensively address both the metabolic and hormonal aspects of PCOS.

The finding most consistent with the literature reviewed is that insulin sensitizers, particularly metformin and myoinositol, remain the most effective therapeutic options for improving insulin resistance in women with polycystic ovary syndrome (PCOS). Several studies have documented these findings, such as those of Vidal-Reyes et al.<sup>(4)</sup> who demonstrated that metformin significantly improves insulin resistance in women with PCOS. In addition, Aguilar-Mor et al. confirmed, through a meta-analysis, that metformin and myoinositol effectively improve insulin sensitivity, with myoinositol showing fewer side effects. Similarly, Retes concluded that metformin improves insulin resistance and reduces androgen levels in these patients, contributing to improving hormonal symptoms of PCOS.

As for myoinositol, the results of Singh et al.<sup>(8)</sup> corroborate its effectiveness and safety, highlighting its favorable profile in terms of tolerability. These studies reinforce the idea that insulin sensitizers, especially metformin and myoinositol, continue to be fundamental in the treatment of insulin resistance in women with PCOS. Metformin, one of the most widely used and best-studied treatments, has shown significant improvement in insulin sensitivity, as reported by Vidal-Reyes et al. and Retes, who confirmed its efficacy in reducing glucose levels and improving the hormonal profile. However, gastrointestinal side effects, such as diarrhea and nausea, have also been documented to limit their adherence in some patients, which poses a challenge in clinical practice, as noted in the review by Vidal-Reyes et al.<sup>(4)</sup>

On the other hand, myoinositol, a less conventional but promising treatment, has shown significant advantages over metformin in terms of tolerability and reduced side effects. Studies such as those by Aguilar-Mor et al. and Singh et al. (8) corroborate that myoinositol not only improves insulin sensitivity but also has a positive impact on testosterone levels, thus reducing symptoms of hyperandrogenism, such as hirsutism and acne, which are common in women with PCOS. This treatment, due to its safety profile and greater tolerance,

is positioning itself as an effective alternative, especially for those women who do not tolerate metformin, which highlights its therapeutic potential. (9)

A relevant result that this review confirms is that conventional hormonal therapies, such as combined oral contraceptives, continue to be a useful tool for the management of hormonal symptoms of PCOS, especially in the regulation of menstrual cycles and the reduction of hyperandrogenemia. However, as noted in previous studies, oral contraceptives do not directly affect insulin resistance, implying that they are not sufficient on their own to improve the metabolic aspects of PCOS. This underscores the importance of combining these treatments with insulin sensitizers to obtain a more significant and complete improvement of the syndrome. (10,11,12,13)

#### Identification of methodological errors and limitations

Despite the valuable results of this review, it is important to recognize the limitations inherent in the included studies. One of the main limitations is the heterogeneity in study designs and sample characteristics, which could influence the generalizability of the results. Many of the reviewed studies focused on specific populations, which limits the applicability of the results to women with more diverse clinical characteristics, such as those with different PCOS subtypes or comorbidities such as obesity or metabolic syndrome. In addition, most trials focused on evaluating the efficacy of treatments for insulin resistance. However, they did not address the long-term effects on other metabolic and reproductive aspects in depth, which represents a critical area for future research.

Another major methodological challenge is the lack of consensus on optimal therapeutic doses and combinations to treat insulin resistance in women with PCOS. Although metformin and myoinositol are effective, there is no definitive guidance on the most appropriate dosing combination for different patients or PCOS subtypes. In addition, available studies do not always address the interaction between these treatments and other coexisting conditions that women with PCOS often present with, such as obesity or hypertension, limiting the ability to customize therapies.

#### **CONCLUSIONS**

One of the most relevant conclusions of this review is that insulin sensitizers, particularly metformin and myoinositol, remain critical in treating insulin resistance and improving PCOS metabolic symptoms. While metformin remains the gold-standard treatment, its efficacy may be compromised by its gastrointestinal side effects, which limit its tolerability in some patients. Myoinositol, on the other hand, has emerged as an effective and well-tolerated alternative, making it an increasingly relevant therapeutic option, especially for women with PCOS who experience adverse effects with metformin.

Conventional hormonal therapies, such as combined oral contraceptives, should be understood as complementary to insulin sensitizers in the treatment of PCOS since, although they help control hormonal symptoms, they do not significantly impact insulin resistance. Therefore, a combined therapeutic strategy that addresses the syndrome's hormonal and metabolic aspects is recommended.

An important novelty of this analysis is the confirmation that treatments with insulin sensitizers, in addition to improving insulin sensitivity, have a positive impact on reproductive health by contributing to improved fertility and menstrual regularity, underscoring the importance of a comprehensive therapeutic approach that addresses both hormonal and metabolic symptoms.

# Future research needs

Despite advances in the treatment of insulin resistance in women with PCOS, areas for further exploration persist. First, studies involving a larger and more diverse sample of women with PCOS, including both those with more severe PCOS subtypes and associated comorbidities such as obesity, type 2 diabetes, or metabolic syndrome, are needed to assess the efficacy of treatments in these subgroups.

In addition, it would be valuable to investigate further the pathophysiological mechanisms underlying the relationship between insulin resistance and PCOS. A better understanding of these mechanisms will allow the identification of potential additional therapeutic targets and the development of more specific and personalized treatments. Long-term follow-up studies are also needed to assess the impact of current treatments, such as metformin and myoinositol, on metabolic and reproductive health over time, particularly on the prevention of chronic diseases, such as type 2 diabetes and cardiovascular disease.

## Speculation on future developments

With the advancement of research in PCOS and insulin resistance, new therapeutic strategies are likely to emerge that focus not only on improving insulin sensitivity but also on addressing other metabolic pathways, such as chronic inflammation or oxidative stress, which are also implicated in the pathophysiology of PCOS. The development of treatments targeting these pathways could offer a more comprehensive and effective solution for treating the syndrome.

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In turn, the growing interest in personalized medicine and the use of advanced technologies, such as genomics and biotechnology, could open new possibilities for developing more specific treatments tailored to patients' individual characteristics. In this context, the integration of biotechnology in the treatment of PCOS could facilitate better-personalized treatments, improving both metabolic and reproductive outcomes, which would mark a significant advance in the management of the polycystic ovarian syndrome.

### **REFERENCES**

- 1. Baltazar DLS, Ku AJM, Perez DCP. Síndrome de ovario poliquístico y la resistencia a la insulina. Cienc Lat Rev Cient Multidiscip. 2024;8(5):3300-21.
  - 2. Gaitán ES. Actualización del manejo de síndrome de ovario poliquístico. Rev Med Sinergia. 2019;4(12):322.
- 3. Navarrete Telenchana JG. Resistencia a la insulina en mujeres con síndrome de ovario poliquístico [trabajo de conclusión de curso]. Ambato: Universidad Técnica de Ambato, Facultad de Ciencias de la Salud, Carrera de Laboratorio Clínico; 2023.
- 4. Vital-Reyes VS, Flores GF, Guzmán JJ, Pérez CM, Martínez FJ. Frecuencia de resistencia a la insulina en pacientes con síndrome de ovario poliquístico con el clamp hiperinsulinémico euglucémico. Ginecol Obstet Mex. 2014;82(12):785-90.
- 5. Mayorga Carrasco MF. Resistencia a la insulina y su relación con los factores de riesgo del síndrome de ovario poliquístico en pacientes que acuden a la consulta externa de ginecología del centro médico PUCE SALUD en el año 2023 [trabajo académico]. 2024.
- 6. Aldama-González PL, Hernández-Marín I. Correlación de la morfología ovárica y la resistencia a la insulina en pacientes con síndrome de ovario poliquístico. Rev Mex Med Reprod. 2015;7(4):153-9
- 7. Creo Menéndez R. Revisión bibliográfica: relación entre la resistencia a la insulina y el síndrome del ovario poliquístico (SOP) [trabajo académico]. 2022
- 8. Singh JR, Sharma S, Gupta P, Patel M. La resistencia a la insulina como factor etiológico en el síndrome del ovario poliquístico: un estudio de casos y controles. Adv Lab Med Av Med Lab. 2022;3(2):205-9
- 9. García García Y, Fernández López C, Martínez Pérez L, Sánchez Rodríguez M. Evaluación de las alteraciones lipídicas en el síndrome de ovarios poliquísticos y su relación con la resistencia a la insulina. Rev Cubana Endocrinol. 2010;21(2):145-53.
- 10. Veloz González AD. Relación de la resistencia a la insulina y síndrome de ovario poliquístico en mujeres latinoamericanas [trabajo de conclusión de curso]. Riobamba: Universidad Nacional de Chimborazo; 2024.
  - 11. Gutiérrez AZ, Santizo AS. Síndrome de ovario poliquístico. Rev Med Sinergia. 2022;7(1).
  - 12. Flores MR. Síndrome de ovario poliquístico: el enfoque del internista. Med Int Mex. 2012;28(1).
- 13. Telenchana JGN, Veloz APM. Resistencia a la insulina en mujeres con síndrome de ovario poliquístico. Rev Cient Arbitr Multidiscip Pentacienc. 2023;5(4):673-86.

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#### **CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

## **AUTHORSHIP CONTRIBUTION**

Conceptualization: Lucas de Castro Reuter, José Posturivo. Data curation: Lucas de Castro Reuter, José Posturivo. Formal analysis: Lucas de Castro Reuter, José Posturivo. Research: Lucas de Castro Reuter, José Posturivo.

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