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The role of GLP-1 analogues in the treatment of obesity in women with Polycystic Ovary Syndrome

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ABSTRACT

GLP-1 receptor agonists have newly appeared in the treatment for metabolic disorders of polycystic ovary syndrome (PCOS), including obesity and insulin resistance. It has got a lot of benefits, weight loss, increased insulin sensitivity, make better lipid profiles, regulars menstrual cycles. GLP-1 receptor agonists may offer better metabolic-endocrine effects than standard treatment, such as metformin. More research is needed to confirm safety and identify optimal treatment strategies, however. The review highlights the significance of GLP-1 receptor agonists for managing PCOS and suggests future research priorities.

Keywords: GLP-1 receptor, PCOS, metabolic, menstrual cycles

1. INTRODUCTION

Polycystic ovary syndrome (PCOS) ranks among the most prevalent endocrine disorders affecting women of reproductive age, with a global prevalence estimated between 6% and 20% (Szczesnowicz et al., 2023). The condition is typified by a combination of hyperandrogenism, disruptions in ovulation, and the characteristic appearance of polycystic ovaries, as outlined by the Rotterdam Criteria in 2003 (Geng et al., 2023). The disorder is often associated with significant metabolic disorders. These consist of all types like Lyu et al., (2021): insulin resistance (IR), obesity, dyslipidemia, enhanced susceptibility for developing type 2 diabetes mellitus (T2DM), diseases related to the cardiovascular system (Han et al., 2019).

And more than just these repercussions: These impair the overall effectiveness of the huge gap in what we know about long-term health and quality of life of women suffering from PCOS (Nauck et al., 2021). Diabetes and

lifestyle modifications were typically the central focus of PCOS management. That's due to insulin resistance, for instance with metformin (Cena et al., 2020). Not only does a wide clinical spectrum show by PCOS, rich dynamic nature. As treatment protocols must be more efficient and personalized (Bader et al., 2024). Glucagon-like peptide-1 receptor (GLP-1 RA) drugs, which were pioneered to treat type 2 diabetes, are now showing promise. These people places can help patients return from catastrophes with Greco et al., (2019): Weight loss, increased sensitivity to insulin, better lipid levels.

Therefore, these agents may be of specific benefit to PCOS women if they are obese or have different metabolic diseases (Siamashvili and Davis, 2021). Experiments have shown that glucagon-like peptide-1 (GLP-1) receptor agonists could help prevent some of the obesity and metabolic derangements manifesting in conditions like PCOS, including via studies of their mechanisms of action, clinical utility and comparisons to conventional therapy (Mozaffarian, 2024). Additionally, it identifies gaps in current research and suggests directions for future investigations to guide clinical decision-making and support personalized treatment strategies (Abraham et al., 2021).

2. MATERIALS

This review article synthesises the findings from peer-reviewed studies and meta-analyses on the efficacy and safety of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in the treatment of polycystic ovary syndrome (PCOS). The study design comprises a systematic review of the available literature and a descriptive analysis of data from a range of sources. A comprehensive literature search was conducted in major academic databases, including PubMed, Scopus, and Web of Science, to identify relevant articles published between January 2019 and August 2024. Keywords included:

"GLP-1 receptor agonists"
"PCOS treatment"
"Metabolic regulation in PCOS"
"Weight loss in PCOS"
"GLP-1 and reproductive outcomes".

Inclusion and Exclusion Criteria

And all studies included in this review were retrieved from peer-reviewed journals. This review aims to assess the efficacy of GLP-1 RAs for the management of polycystic ovary syndrome (PCOS) and summarize their effects on metabolic, reproductive, and endocrine parameters. The following review is on high-order study designs:

Randomised controlled trials (RCTs)
Meta-analyses
Cohort studies
Systematic reviews

These techniques provide a comprehensive overview of the therapeutic applications of GLP-1 RAs according to the distinct, multidimensional barriers resulting from PCOS, highlighting potential pathways for further exploration.

Inclusion Criteria

The studies included in this review met the following criteria:
Published in peer-reviewed journals between January 2019 and August 2024.
Focused on the application of GLP-1 RAs in women diagnosed with PCOS.
Reported clinical outcomes related to metabolic regulation, weight loss, reproductive health, and lipid profiles.
Included human subjects with clearly defined diagnostic criteria for PCOS.

Exclusion Criteria

Studies were excluded if they:
Focused exclusively on non-human subjects.
Lacked statistical analysis or reported clinical outcomes.

Were review articles without original data or presented outdated findings.

Data Extraction

Key data points were extracted and systematically organized into tables. The extraction process focused on:
Study Design: Categorization as RCTs, cohort, or observational studies.
Population Characteristics: Age range, BMI, and criteria used for diagnosing PCOS.
Type and Dosage of GLP-1 RAs: Including agents such as liraglutide, semaglutide, and exenatide.
Measured Outcomes: Assessing parameters such as weight loss, BMI changes, insulin sensitivity, lipid profiles, ovulation rates, and adverse events.

Search Strategy

A detailed literature search was conducted on the PubMed, Scopus, and Web of Science databases to identify eligible studies.
Details of the Search Strategy: The search strategy including keywords and Boolean operators (AND/OR) to refine results.
Keywords included: "GLP-1 receptor agonists" "PCOS treatment" "metabolic regulation in PCOS" "weight loss in PCOS" "GLP-1 and reproductive outcomes".
Using relevancy keywords for filtering, articles were considered based on the topic-specific keywords that were used at the stages of abstract screening and full-text screening.

Statistical Analysis

The findings from the selected studies were synthesized to create a comparative analysis of the efficacy and safety of GLP-1 receptor agonists. Statistical significance and effect sizes were highlighted to demonstrate the therapeutic benefits and areas where additional research is warranted.

Ethical Considerations

As this study is a review of previously published data, it did not involve human or animal subjects directly and is exempt from ethical approval. Data were sourced from publicly accessible peer-reviewed studies, and no personal or identifiable information was utilized.

3. RESULTS AND DISCUSSION

This section outlines the results regarding the effectiveness of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in treating polycystic ovary syndrome (PCOS), emphasizing their role in weight loss, metabolic improvements, and lipid profile regulation. These findings are based on robust, high-quality research identified during the review process and are further supported by comprehensive tables.

Weight Loss and BMI Reduction

Weight management constitutes a fundamental element of the treatment of PCOS, particularly in the case of overweight or obese patients. GLP-1 receptor agonists (GLP-1 RAs), in particular liraglutide and semaglutide, are highly efficacious in promoting weight loss when compared to standard treatments such as metformin.
Liraglutide (1.2–3 mg/day): Several studies have demonstrated the efficacy of liraglutide in reducing body mass index (BMI) among women with polycystic ovary syndrome (PCOS). BMI reductions ranged between 1.1 kg/m² and 3 kg/m² over treatment periods of 26 weeks to 12 months. For instance, a randomized controlled trial conducted by Jensterle et al., (2014) revealed that liraglutide significantly outperformed metformin in lowering BMI (1.1 ± 1.26 kg/m² vs. 0.1 ± 0.67 kg/m²; $p < 0.05$), with the most notable effects observed in women with higher baseline BMIs.
Semaglutide (2.4 mg/week): Emerging research highlights the enhanced weight-loss potential of semaglutide compared to liraglutide. A recent study by Frøssing et al., (2018) demonstrated that semaglutide achieved a greater weight reduction of 7.9%, compared to a 5.2% reduction observed with liraglutide. These findings suggest that semaglutide may offer superior benefits in weight management for PCOS patients.

The weight loss effects were dose-dependent and correlated with improved appetite regulation, delayed gastric emptying, and reduced energy intake.

Metabolic Regulations

Most studies found that GLP-1 GAs improved metabolic parameters, including:

Insulin resistance

Fasting glucose

Hyperandrogenism

Increased Insulin Sensitivity: The AIP has been associated with increased insulin sensitivity, mostly measured by homeostasis model assessment of insulin resistance (HOMA-IR). For example, Frøssing et al., (2018) reported that liraglutide decreased HOMA-IR scores by 28% from baseline, compared with a 15% reduction with metformin.

Glycemic Control

Fasting glucose levels were found to decrease by 10% to 15% across multiple studies, with the most pronounced improvements seen in participants with pre-existing glucose intolerance. Additionally, GLP-1 receptor agonists (GLP-1 RAs) were associated with reductions in glycated hemoglobin (HbA1c) levels by approximately 0.8% over a 26-week treatment period.

Reproductive Function

Ovulation rates showed significant enhancement in women treated with GLP-1 RAs, especially when combined with metformin. In a study conducted by Elkind-Hirsch et al., (2021), ovulation occurred in 58% of women in the liraglutide group, compared to just 20% in the placebo group ($p < 0.01$).

Lipid Profile

The lipid-modifying effects of GLP-1 RAs were significant across the studies analyzed, contributing to cardiovascular risk reduction.

Triglycerides

Research highlights that liraglutide contributes to a 20–30% decrease in triglyceride levels, as supported by findings from (Frøssing et al., 2018). In addition, semaglutide has been identified as even more effective, particularly for women with severe hyperlipidemia, showcasing its potential in lipid management.

LDL Cholesterol

Studies consistently show that LDL cholesterol levels decrease by 15–18%, reflecting the lipid-lowering properties of GLP-1 receptor agonists, as demonstrated in research by (Elkind-Hirsch et al., 2021).

HDL Cholesterol

Improvements in HDL cholesterol, with an average increase of about 10%, have been associated with liraglutide use, as evidenced by the study conducted by (Frøssing et al., 2018). These findings underline its role in enhancing overall lipid profiles. These improvements in lipid profiles are attributed to both direct effects of GLP-1 RAs and associated weight loss.

Comparative Efficacy

GLP-1 RAs were compared with metformin, lifestyle interventions, and placebo across studies.

GLP-1 RAs, Comparison with Metformin

Liraglutide works so well for obesity and insulin resistance, one of the main issues for women with PCOS.

Other Adjuvant Therapeutic Modalities: Metformin

Showed among 193 pubertal girls treated with either metformin or two different classes of oral agents that metformin augments the efficacy of GLP-1 receptor agonist therapy, producing greater reductions in BMI, HOMA-IR, and hyperandrogenism.

The study highlights that the addition of the second agent to the treatment regimen adds value to the existing treatment, since these agents might work synergistically on one or more fronts, including better response to metabolic derangements.

GLP-1 RAs Compared to Placebo

By FDA class vs placebo, GLP-1 receptor agonists are efficacious on metabolic parameters. This comes with benefits such as increased control over fasting blood sugar, a significant drop in circulating triglycerides, and overall reductions in total cholesterol levels. Studies such as Frøssing et al., (2018) demonstrated that liraglutide treatment decreases liver fat by nearly 50% in an unbiased manner, while liver fat remained unchanged with placebo. The results underline the powerful effect of GLP-1 receptor agonists on the metabolic aspect of the PCOS spectrum.

Safety and Tolerability

GLP-1 RAs appeared to be safe with few adverse events.

Gastrointestinal Symptoms: Nausea, vomiting, and diarrhea were the most common side effects and affected 10 percent to 20 percent of participants. These symptoms were transient and dose related.

Long-Term Safety: Short-term safety data are available for diabetes patients; however, long-term data of GLP-1 RAs use in the non-diabetic PCOS population is absent.

Table 1 Weight Loss Across Studies

Study	Drug	Dose	BMI Reduction (kg/m²)	Duration (weeks)	p-value
Jensterle et al.,	Liraglutide	1.2 mg/day	1.1 ± 1.26	26	< 0.05
Frøssing et al.,	Liraglutide	1.8 mg/day	2.9	26	< 0.01
Elkind-Hirsch et al.,	Liraglutide	3 mg/day	3.0	52	< 0.001

The following table presents a comparative analysis of the efficacy of liraglutide in reducing body mass index (BMI) in women with PCOS, as evidenced by three distinct studies (Table 1). The following points merit particular attention:

In their investigation, Jensterle et al., administered liraglutide at a dosage of 1.2 mg per day for a period of 26 weeks, resulting in a modest reduction in BMI of 1.1 ± 1.26 kg/m² ($p < 0.05$).

Frøssing et al., (2018) employed a higher dosage of liraglutide (1.8 mg/day) for an equivalent period and observed a more pronounced reduction of 2.9 kg/m² ($p < 0.01$).

The greatest reduction in BMI (3.0 kg/m²) was demonstrated by Elkind-Hirsch et al., (2021) with a 3 mg/day dose of liraglutide administered over 52 weeks ($p < 0.001$).

These results show a dose-response relationship, where higher doses and longer treatment durations yielded better outcomes in BMI reduction.

Table 2 Lipid Profile Improvements

Study	Drug	Triglycerides (%)	LDL (%)	HDL (%)	Duration (weeks)
Frøssing et al.,	Liraglutide	-20	-15	+10	26
Elkind-Hirsch et al.,	Liraglutide	-30	-18	NA	52

Table 2 summarizes the impact of liraglutide on lipid parameters:

Triglycerides: Both studies report significant reductions, with Elkind-Hirsch et al., (2021) showing a 30% decrease, outperforming the 20% reduction reported by Frøssing et al., (2018)

LDL Cholesterol: Liraglutide reduced LDL levels by 15% to 18%, contributing to a better cardiovascular profile.

HDL Cholesterol: An improvement of 10% was observed in Frøssing et al., (2018) indicating enhanced lipid metabolism.

The data substantiates the assertion that liraglutide not only facilitates weight loss but also addresses dyslipidaemia in women with PCOS.

4. CONCLUSION

This review highlights the emerging role of GLP-1 receptor agonists (GLP-1 RAs) in the management of polycystic ovary syndrome (PCOS), representing another pathway for counteracting the entangled metabolic and reproductive pathophysiologies of this condition. Focusing on factors resembling insulin sensitivity, satiety, and hyperandrogenism, GLP-1 RAs embrace the multifactorial nature of PCOS that is reflected in the transition from merely 'the pill' based treatment to certainly more comprehensive and refined disease approaches. The results highlight the interesting effectiveness of GLP-1 RAs, but several important issues must still be resolved, notably about the long-term effect of these new therapies on weight maintenance and metabolic normalization.

Moreover, the best incorporation of these agents in multi-drug regimens with metformin or inositols has yet to be determined. Given the substantial heterogeneity in presentation of PCOS, future studies should emphasize phenotyping to pinpoint the subgroups that would benefit most. The ability of GLP-1 RAs to target the metabolic and reproductive aspects of PCOS represents an important and promising treatment opportunity in the field. Nonetheless, their role in therapeutic regimens requires careful patient selection and monitoring, especially considering the risk of gastrointestinal adverse events and contraindications.

Author's Contributions

Martyna Koszyk: Conceptualization; writing - rough preparation; supervision
Zuzanna Kudas: Writing - rough preparation
Paweł Nowocin: Writing - rough preparation
Nikola Perchel: Writing - rough preparation
Aleksandra Litwin: Writing - rough preparation
Karolina Krzywicka: Writing - rough preparation
Dawid Wiktor Kulczyński: Writing - rough preparation
Natalia Dąbrowska: Writing - review and editing
Paulina Kumięga: Writing - review and editing

Informed Consent

Not applicable.

Ethical approval

Not applicable.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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