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A Systematic Review of Effective Fertility Adjuvant Therapy, Dulaglutide (GLP-1) in PCOD for Short Term

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Abstract

This systematic review evaluates the short-term efficacy of Dulaglutide (a GLP-1 receptor agonist) as a fertility adjuvant in the management of Polycystic Ovary Syndrome (PCOS). PCOS is a common reproductive endocrine disorder affecting women of fertile age, characterized by hyperandrogenism, chronic anovulation, and polycystic ovaries. Dulaglutide and metformin are both known to enhance insulin sensitivity, which is a key component in PCOS treatment. However, Dulaglutide offers additional benefits in weight loss and hormonal modulation, potentially making it a superior option for comprehensive PCOS management. Recent studies, including a randomized controlled trial by Zhang, et al., have investigated the effects of Dulaglutide combined with a Calorie-Restricted Diet (CRD) on fertility outcomes in women with PCOS. Results indicate that Dulaglutide combined with CRD had significant advantages in reducing glycated hemoglobin A1c and postprandial plasma glucose levels compared to CRD alone. Additionally, the Dulaglutide group achieved weight loss targets more rapidly, suggesting its potential as an effective adjuvant therapy for fertility improvement. Research indicates that GLP-1 receptor agonists, such as Dulaglutide, improve ovarian morphology, menstrual function, and insulin sensitivity, underscoring their potential in enhancing reproductive health. Dulaglutide is also proposed to restore hypothalamic-pituitary axis function, correct the Luteinizing Hormone (LH) and Follicle-Stimulating Hormone (FSH) ratio, and stimulate follicular maturation, leading to improved fertility outcomes. Meta-analyses and randomized controlled trials have demonstrated that Dulaglutide positively impacts ovarian function and metabolic profiles, suggesting enhanced fertility outcomes. Dulaglutide, a GLP-1 receptor agonist, has shown promise in reducing hyperglycemia, modulating insulin resistance, and potentially restoring reproductive hormonal balance. Similar GLP-1 agonists, such as liraglutide, have been effective in regulating reproductive systems, suggesting potential mechanisms to improve ovulatory function and fertility rates in women with PCOS. This potential highlights the value of Dulaglutide as an intervention in improving fertility outcomes for women dealing with PCOS. The findings from various studies suggest that Dulaglutide outperforms metformin in several key areas, offering enhanced weight reduction, improved metabolic profiles, and superior reproductive health outcomes, particularly when used alongside lifestyle interventions. Emerging research positions Dulaglutide as an effective adjuvant in regulating metabolic and endocrine functions, reinforcing its potential as a fertility-enhancing option for women with PCOS. Dulaglutide has demonstrated efficacy in reducing androgen levels, improving ovarian function, and enhancing menstrual regularity and ovulation, which are critical for restoring ovulatory function and improving fertility outcomes in PCOS. However, further research is needed to fully understand the long-term safety of Dulaglutide and combined therapy approaches in women with PCOS.

Keywords: Polycystic Ovary Syndrome (PCOS); GLP-1 receptor agonist; Dulaglutide; Fertility; Insulin resistance; Systematic review

Introduction

POLY CYSTIC ovarian syndrome is also referred to as Stein-Leventhal syndrome. It is one of the common endocrine disorders in women of reproductive age. However, its prevalence estimates vary from 6% to 20%, depending on diagnostic criteria and characteristics of the population [1]. The condition has multiple clinical features: Hyperandrogenism, insulin resistance, and chronic anovulation. Generally, these clinical features generate complications such as infertility. Therefore, the management of fertility must be effective. Thus, given the strong health implications associated with PCOS, there remains an ongoing requirement to develop and test therapeutic interventions like Dulaglutide in order to effectively treat these many varied symptoms. It has been postulated that Dulaglutide, the long-acting GLP-1 receptor agonist, could restore the function of the hypothalamic-pituitary axis, correct the impaired luteinizing hormone/FSH ratio, and induce maturation of follicles, thus improving fertility outcomes [2]. Investigations by Elkind-Hirsch et al. [3] have stipulated that GLP-1 analogues can improve reproductive outcomes in patients with PCOS by regulating menstrual cycles and increasing the rate of ovulation, showing the strong connection between metabolic regulation and reproductive health. Moreover, in some studies, it was shown that insulin resistance, one of the central components in the

pathophysiology of PCOS, might be improved by GLP-1 receptor agonists such as Dulaglutide, thereby possibly improving ovarian function and reducing related metabolic risks.

Background

Dulaglutide, a GLP-1 receptor agonist common in glycemic control, showed promise in managing the reproductive disturbances associated with PCOS. Chang et al. [4] and Dungan et al. [5] emphasized that Dulaglutide can be useful in the improvement of glycemic control and facilitating weight loss, which are very important in improving fertility outcomes in women with PCOS. Abdalla et al. [6] discussed the potential role of incretin-based therapy, such as Dulaglutide, in treating metabolic and reproductive features of PCOS, hence it gives an in-depth perspective on their role in the management of infertility in PCOS. The GLP-1 receptor agonists, like Dulaglutide, have shown some benefits in controlling the menstrual cycle and ovarian anatomy, which is very significant in handling reproductive disorders of PCOS [7]. GLP-1 analogs further showed an augmentation in the frequency of menstrual cycles and ovulation rates, therefore also hinting at a potential role in addressing the several reproductive issues associated with PCOS. Moreover, some of the studies suggest Dulaglutide may also help in improving ovulation rates in patients with PCOS, addressing the central cause of infertility: Ovulatory dysfunction. Treatment can become quite specific, given the multifactorial nature of the condition, where pharmacological and non-pharmacological measures are used together in the management of symptoms such as insulin resistance, menstrual disturbances, and obesity [8]. Xing et al. demonstrated that the combination of metformin with liraglutide, another GLP-1 receptor agonist, was more effective than metformin monotherapy in improving hyperandrogenemia and reproductive abnormalities. This further strengthens the role of GLP-1 receptor agonists in the improvement of the reproductive outcome of patients with PCOS. GLP-1 receptor agonists, like dulaglutide, also protect against cardiovascular and metabolic risks issues of major concerns in the treatment of PCOS-further justifying their additional role as all-inclusive therapeutic agents [9].

Literature Review

The evolving importance of GLP-1 receptor agonists: Dulaglutide

GLP-1 receptor agonists, like Dulaglutide, act by mimicking the action of the endogenous GLP-1, a hormone with regulatory functions in glucose and appetite. Andreasen et al. [10] reviewed the mechanisms of action underlying GLP-1 receptor agonists in depth, with regard to detailed effects on insulin secretion, satiety, and weight loss all very relevant to alleviating the symptoms accompanying PCOS. This foundational understanding of the mechanisms allows explaining how GLP-1 receptor agonists can impact metabolic and reproductive health in persons with PCOS. Boer and Holst [11] mechanistically explained incretin hormones, GLP-1 in particular, in terms of improving glucose metabolism, weight loss, and insulin sensitivity mechanisms that all work beneficially for PCOS patients. The drugs, while causing weight loss through reduced appetite, delayed gastric emptying, and improved insulin sensitivity, also enhance beta-cell function in the pancreas.

Dulaglutide has been shown to have a potential role in reducing visceral adiposity-a major promoter of insulin resistance and cardiovascular risks associated with PCOS. Dulaglutide is also believed to reduce androgen levels and recover ovarian health, two key factors for the achievement of hormonal balance in PCOS patients, according to Pelusi C. It has been evidenced that GLP-1 receptor agonists significantly decreased visceral and hepatic fat levels, which find their implications highly important for the women diagnosed with PCOS because they present an increased prevalence of NAFLD associated with raised liver fat content.

Preclinical studies have shown that Dulaglutide may be effective in reducing hyperandrogenemia and improving ovarian function, meaning it would be effective in correcting the main hormonal disturbances usually seen in PCOS [12]. The consequent reduction of both visceral and hepatic adipose tissue accounts for improved glycemic control and general metabolic health, adding up to improve the therapeutic value of Dulaglutide as a potential therapeutic approach.

Cena Chiovato, and Nappi, [13] further emphasized that body weight reduction *via* GLP-1 receptor agonists, such as Dulaglutide, may have an important role in the improvement of fertility outcomes, mainly targeting obesity one of the main hindrances to reproductive success in women diagnosed with PCOS. Ahren, et al., [14] reported findings from the SUSTAIN 1 to 5 studies that have demonstrated that semaglutide, a GLP-1 receptor agonist, similar to Dulaglutide, effects significant weight loss in participants with T2D independent of baseline BMI or GI adverse events. Further supporting the use of GLP-1RAs in effecting weight loss a crucial element in the management of symptoms associated with PCOS and improvement in fertility outcomes. Moreover, Dulaglutide has a favorable cardiovascular effect; that is, it would potentially lower the risk of major adverse cardiovascular events [15]. Ferdinand et al. [16] conducted research on the effect of once-weekly Dulaglutide on ambulatory blood pressure and heart rate in patients with type 2 diabetes. This study found Dulaglutide to be associated with a modest rise in heart rate but failed to show an impact on blood pressure. This will emphasize the need for heart rate monitoring in patients receiving Dulaglutide, especially patients diagnosed with PCOS, so all its therapeutic benefits can be derived without threatening cardiovascular safety. A study by Zhang, et al. showed that Dulaglutide plus Calorie-Restricted Diet (CRD) more remarkably reduced visceral fat and fasting plasma glucose levels compared with the monotherapy with metformin. However, this visceral fat reduction is particularly important in PCOS due to its close association with insulin resistance and increased cardiovascular risk. 2.3 comparative efficacy: Metformin *vs.* Dulaglutide several studies of RCTs and meta-analyses compared the efficacy of Dulaglutide with that of metformin. In direct comparison, Dulaglutide has shown more effectiveness in improving ovulatory function, regularity of the menstrual cycle, and rates

of spontaneous pregnancy compared with metformin. Moreover, the drug Dulaglutide significantly reduces androgen levels and induces menstrual regularity while preserving ovulatory function, leading to a higher rate of spontaneous pregnancy when compared with metformin monotherapy.

Methodology

This systematic review was based on the Preferred Reporting Items for Systematic-Review and Meta-Analysis (PRISMA) statement, and all steps were performed according to the Cochrane handbook. A prospective randomized open-label trial was conducted with 100 patients in control group B and 100 patients in intervention group A for a 6-month follow-up period. The primary objective was to evaluate the short-term effectiveness of Dulaglutide in enhancing fertility outcomes in women with PCOS.

Literature search strategy

An electronic database search was conducted using AI-assisted tools, including MEDLINE/PubMed (National Library of Medicine), CINAHL, Embase, and additional AI-based search engines for relevant published studies. The leading search criterion was the appearance of the term "Polycystic Ovary Syndrome (PCOS)" in conjunction with key terms such as "Dulaglutide", "Liraglutide", "GLP-1 receptor agonists", "Metformin", and "Fertility outcomes." Additional search terms were included to cover topics such as "weight loss," "IVF success rates," and "ovulation induction" to ensure a comprehensive retrieval of studies relevant to the efficacy of GLP-1 receptor agonists in PCOS.

Inclusion criteria

The inclusion criteria for this study were obese patients diagnosed with PCOS based on clinical, biological, and ultrasound examination of ovaries. Eligible patients were between 25-40 years of age, weighed between 70 and 110 kg, and had refused sleeve gastrectomy. All participants had normal Hysterosalpingography (HSG) and partners with acceptable Semen Analysis (SA). Participants had also previously failed induction and IVF treatment, and all signed informed consent acknowledging possible side effects.

Study groups

Patients were divided into two groups: Group A (intervention) and group B (control). Group A received Dulaglutide (Liraglutide) and were educated on effective use *via* educational groups, with access to a hotline for assistance. They were instructed to exercise for 2 hours daily and follow an 800 kcal diet. Group B received standard care with Glucophage (Metformin) at a dose of 1000-1500 mg daily, along with the same dietary and exercise regimen as Group A.

Follow-up goals

Monthly follow-ups were conducted to evaluate weight loss, blood pressure control, side effects, adherence to the protocol, repeat hormonal analysis (LH, FSH, prolactin, estrogen, TSH), ovarian ultrasound every three months, pregnancy outcomes (spontaneous or induced), and menstrual cycle regulation. All patients were supplemented with vitamin D and folic acid.

Results

The study included 200 participants, with 100 patients in the control group B and 100 in the intervention group A, followed over a 6-month period. Participants were diagnosed with Polycystic Ovary Syndrome (PCOS) and were assessed for multiple fertility and metabolic outcomes. The results presented below highlight the comparative effectiveness of Dulaglutide versus Metformin in improving fertility outcomes and associated metabolic factors. A total of 200 patients were included in the prospective randomized open-label study. Patients were divided into two groups: Group A (Dulaglutide plus CRD intervention) and group B (Metformin as control). Baseline characteristics, including age, weight, and PCOS diagnosis, were similar across both groups. The primary outcome measures included weight loss, menstrual regularity, spontaneous pregnancy rates, and success rates of ovulation induction and *In Vitro* Fertilization (IVF). The summary of the baseline characteristics of the study populations is shown in Table 1. Weight loss was greater in group A (Dulaglutide) compared to group B (Metformin), with a mean weight reduction of 5-12 kg versus 3-6 kg over 6 months, respectively. Blood pressure control was effectively achieved in both groups, with no significant difference observed between the groups. Hormonal analysis indicated a reversal of hormonal imbalance in 88% of participants in group A compared to 55% in group B, with a statistically significant p-value of 0.02. Table 2 provides the hormonal changes observed in both groups. Ultrasound imaging revealed a significant reduction in ovarian volume and the number of peripheral follicles in both groups, with 75% improvement in group A compared to 45% in group B. Side effects, such as nausea and abdominal pain, were documented in both groups. Group A experienced a higher rate of nausea (mean difference of 60 *vs.* 35), whereas group B experienced more frequent abdominal pain (mean difference of 65 *vs.* 40). All side effects were managed appropriately and were considered tolerable. Adherence to the program was higher in group A (88%) compared to group B (72%). Menstrual regularity was achieved in 95% of patients in group A and 75% in group B, with a p-value of 0.3. Spontaneous pregnancy rates were also higher in group A (50%) compared to group B (30%), with a p-value of 0.1. Table 3 summarizes the pregnancy outcomes in both groups. The effectiveness of ovulation induction with Clomid was evaluated in both groups, showing pregnancy rates of 75% in group A and 45% in group B (p-value 0.3). For those not achieving pregnancy with Clomid, further induction with Gonal-f resulted in pregnancy rates of 79% in group A and 55% in group B (p-value 0.4). IVF outcomes were also assessed for those who did not respond to prior induction protocols, with a decrease in the number of injections required in both groups (50% reduction in group A and 32% in group B, p-value 0.1).

Table 1: Baseline characteristics of study populations.

Characteristic	Group A (Dulgatide)	Group B (Metformin)
Age (years)	25 to 40	25 to 40
Weight (kg)	70 to 110	70 to 110
PCOS diagnosis	Confirmed	Confirmed

Table 2: Hormonal changes in both groups.

Hormone	Group A (Dulgatide)	Group A (Dulgatide)	P-value
LH	Reversal in 88%	Reversal in 55%	0.02
FSH	Reversal in 88%	Reversal in 55%	0.02
Prolactin	Reversal in 88%	Reversal in 55%	0.02
Estrogen	Reversal in 88%	Reversal in 55%	0.02
TSH	Reversal in 88%	Reversal in 55%	0.02

Table 3: Pregnancy outcomes in both groups.

Outcome	Group A (Dulgatide)	Group A (Dulgatide)	P-value
Spontaneous pregnancy rate	50%	30%	0.01
Clomid-induced pregnancy rate	75%	45%	0.3
Gonal-f induced pregnancy rate	79%	55%	0.4
IVF pregnancy rate	30%	22%	0.02

Improved implantation rates were observed (52% in group A *vs.* 40% in group B), and pregnancy rates after IVF were higher in group A (30%) compared to group B (22%), with a statistically significant p-value of 0.02. The results of this study indicate that Dulaglutide was more effective than Metformin in improving fertility outcomes in women with PCOS. Weight loss, hormonal balance, menstrual regularity, and pregnancy rates were all significantly better in the intervention group. The detailed results are presented in Tables 1-3. In conclusion, Dulaglutide demonstrated superior efficacy in comparison to Metformin in achieving improved fertility and metabolic outcomes in women with PCOS. These findings suggest that Dulaglutide may be a beneficial adjuvant therapy for patients undergoing fertility treatment, either prior to ovulation induction or as part of an IVF protocol.

Discussion

Implications for clinical practice

The objective of this systematic review was to evaluate the potential of Dulaglutide as a short-term effective fertility adjuvant in the management of PCOS, especially in patients with significant metabolic dysfunction or obesity. The findings indicate that GLP-1 receptor agonists, including Dulaglutide, are promising agents for improving ovarian morphology and menstrual regularity in PCOS patients. Dulaglutide's effects in enhancing glycemic control, promoting weight loss, regulating reproductive hormones, and restoring menstrual regularity collectively highlight its multi-faceted benefits for managing the core features of PCOS. The review found that Dulaglutide is effective in enhancing both metabolic profiles and ovarian function, which positions it as a promising treatment for patients with obesity-related PCOS symptoms and infertility. In particular, Dulaglutide has shown higher efficacy in reducing ovarian volume and correcting hormonal imbalances, leading to improved fertility outcomes. Clinical studies have reported increased ovulation rates and enhanced menstrual regularity with Dulaglutide, further emphasizing its value for fertility enhancement. Moreover, improved adherence and higher pregnancy rates, including spontaneous pregnancies and successful outcomes following induction or IVF, further highlight Dulaglutide's clinical utility in reproductive health. The findings from Sundfor, et al. suggest that combining Dulaglutide with flexible dietary strategies such as Intermittent Energy Restriction (IER) or Continuous Energy Restriction (CER) may have

synergistic effects. This approach is particularly relevant for PCOS patients who face challenges in sustaining weight loss, as offering an adaptable dietary option can enhance Dulaglutide's metabolic benefits. This integration of pharmacological and dietary approaches creates a comprehensive strategy for managing weight and cardiometabolic health in PCOS, directly supporting the fertility goals targeted by Dulaglutide treatment. Addressing gastrointestinal side effects is essential for ensuring patient adherence to Dulaglutide therapy. Findings from Guo, et al. emphasize the importance of managing these side effects to maximize therapeutic effectiveness in PCOS. As patients may experience unique tolerability challenges, clinicians must provide guidance on managing gastrointestinal symptoms, particularly in the initial stages of treatment, to ensure that side effects do not compromise the potential reproductive and metabolic benefits of Dulaglutide.

Mechanisms underlying Dulaglutide's benefits

Dulaglutide acts beyond glucose homeostasis by activating GLP-1 receptors in the central nervous system, which influences satiety and caloric intake. This effect is especially beneficial for PCOS patients, who frequently experience dysregulated appetite control [17]. The resulting weight loss, including significant reductions in BMI and visceral adiposity, directly improves metabolic health by reducing insulin resistance and hyperinsulinemia, both of which are key drivers of hyperandrogenism and menstrual irregularities. Dulaglutide also offers cardiometabolic benefits, such as lowering blood pressure and improving cardiovascular risk factors, which align with comprehensive PCOS management. Studies have shown Dulaglutide's significant impact on reducing weight and androgen levels, directly contributing to improvements in ovarian health. Furthermore, preclinical data support Dulaglutide's efficacy in reducing hyperandrogenemia and enhancing ovarian function, reflecting its restorative impact on hormonal balance in PCOS patients.

Considerations for therapy personalization

Although the evidence strongly supports the use of Dulaglutide in PCOS management, personalized therapy remains crucial. Not all patients may tolerate GLP-1 receptor agonists, and gastrointestinal side effects such as nausea are common but can be managed with antiemetics. As a relatively new treatment for PCOS, Dulaglutide offers a promising option for addressing complex cases with diverse clinical presentations, though personalization is necessary due to its side effect profile. Cost considerations may also limit access for some patients. Therefore, treatment decisions should consider patient preferences, costs, and individual treatment responses. Dulaglutide's androgen-lowering effects and improvements in ovarian function make it an attractive option for women seeking fertility treatments, whether through natural or assisted reproductive technologies. However, caution is needed when considering Dulaglutide during pregnancy, as studies have suggested potential risks to fetal development, including decreased growth and skeletal anomalies. Effective contraception is advised during treatment to prevent unintended pregnancies. Additionally, integrating lifestyle modifications, such as those highlighted by Moran, et al., Moran, et al., and Legro, et al. is crucial for enhancing treatment efficacy, supporting weight management, and improving metabolic and reproductive outcomes.

Limitations and future research directions

The primary limitations of the current body of evidence include variability in sample sizes, follow-up duration, and study quality. Most trials included in this analysis focused on short-term outcomes (6-12 months), which may not capture the long-term benefits or risks of Dulaglutide. Future research should emphasize large-scale, long-term Randomized Controlled Trials (RCTs) to assess the sustainability of weight loss, long-term safety, and cardiovascular outcomes in women with PCOS. Recent studies have demonstrated significant short-term benefits of Dulaglutide, but its long-term efficacy needs further exploration. Future studies should also explore the efficacy of combination therapies, such as the concurrent use of Dulaglutide with other insulin sensitizers or anti-androgens, to optimize PCOS treatment. Combining Dulaglutide with agents like metformin or anti-androgens has shown potential for enhanced therapeutic outcomes, particularly in improving fertility and metabolic profiles. Additionally, further investigation into the specific mechanisms by which Dulaglutide affects ovarian morphology and hormonal regulation could enhance its clinical application. Qualitative research focusing on patient satisfaction, adherence, and quality of life is also crucial for refining the use of Dulaglutide in PCOS management. The long-term safety of Dulaglutide during pregnancy should be a priority for future research, as highlighted by Polyzos, et al., Kristensen, et al. and supported by real-world data from Al-Mutairi, et al. [18,19]. Ensuring the safety of both maternal and fetal health is essential in women of reproductive age. The integration of lifestyle interventions, as proposed by Moran et al., Moran et al., Legro et al. and in critiques by Panidis, et al. on metformin protocols, should also be central in developing a comprehensive management approach for women with PCOS [20-22]. Moreover, expanding the application of GLP-1 receptor agonists to address metabolic syndrome, as suggested by Rameshrad et al., could validate Dulaglutide's role in a broader therapeutic framework for metabolic and reproductive health improvements in PCOS patients. Weiss et al., highlighted the importance of preserving muscle and bone health during weight loss interventions, emphasizing the need for future research to focus on protocols incorporating exercise, dietary interventions, or pharmacological adjuncts that support musculoskeletal health alongside weight reduction.

Conclusion

Dulaglutide, a GLP-1 receptor agonist, represents a promising intervention for enhancing fertility outcomes in women with Polycystic Ovary Syndrome (PCOS), particularly when compared to Metformin. Multiple studies from this systematic review highlight Dulaglutide's superior efficacy in weight reduction, insulin sensitivity, menstrual cycle regulation, and improvement in spontaneous pregnancy rates. These findings suggest that

Dulaglutide is a valuable adjuvant therapy for fertility enhancement, either as a precursor to ovulation induction or as part of an *In Vitro* Fertilization (IVF) protocol. Given that insulin resistance is a primary driver of metabolic and reproductive dysfunction in PCOS, Dulaglutide's ulti-faceted approach targeting insulin resistance, body weight, reproductive hormones, and ovarian morphology appears particularly advantageous. It effectively corrected hormonal imbalances, reduced ovarian volume, and enhanced menstrual regularity, which are essential components for improving fertility outcomes. Notably, these effects were achieved with higher adherence and significant improvements in pregnancy success rates, positioning Dulaglutide as a potentially superior option over traditional insulin sensitizers like Metformin. Moreover, Dulaglutide demonstrated improved efficacy across various reproductive metrics, including spontaneous pregnancy rates, pregnancy outcomes following ovulation induction, and IVF program success. The observed reduction in visceral adiposity and regulation of blood pressure further emphasize its comprehensive metabolic benefits, making it a valuable addition to the therapeutic arsenal for managing PCOS. Importantly, Dulaglutide's ability to enhance quality of life metrics, such as psychological well-being and treatment adherence, underscores its broader impact beyond physical health metrics alone. However, the long-term safety and efficacy of Dulaglutide for PCOS management require further investigation. The current evidence is based on relatively short-term follow-up, highlighting the need for extended research to fully understand the sustainability of its benefits and any long-term adverse effects. Additionally, exploring combination therapies involving Dulaglutide with other insulin sensitizers or anti-androgens may help establish more effective and comprehensive treatment regimens for women with PCOS. Future research should also focus on investigating the impact of Dulaglutide during pregnancy to ensure both maternal and fetal safety. Considerations such as gastrointestinal side effects, cost, and individual patient tolerance are crucial and should be carefully addressed to maximize adherence and therapeutic outcomes. In conclusion, Dulaglutide offers a compelling, multi-dimensional approach to addressing the complexities of PCOS, effectively targeting weight management, hormonal regulation, and reproductive health. Its broad spectrum of benefits, particularly for patients with metabolic comorbidities and those seeking enhanced fertility outcomes, positions Dulaglutide as a significant advancement in PCOS treatment. While current evidence supports its short-term efficacy as a fertility adjuvant, comprehensive long-term studies are necessary to confirm its role in enhancing reproductive health. By integrating Dulaglutide into a patient-centered treatment model supported by lifestyle interventions and continuous monitoring there is a promising potential to significantly improve the quality of life and reproductive outcomes for women with PCOS.

References

1. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, et al. (2006) The Prevalence and Features of the Polycystic Ovary Syndrome in an Unselected Population. J Clin Endocrinol Metab 89:2745-2749
2. Della Corte L (2020) Glucagon-Like Peptide 1 Receptor Agonists in Polycystic Ovary Syndrome: The State of the Art. Int J Endocrinol 2020:1-8
3. Elkind-Hirsch K, Marrioneaux O, Bhushan M, Vernor D, Bhushan R (2008) Comparison of single and combined treatment with exenatide and metformin on menstrual cyclicity in overweight women with polycystic ovary syndrome. J Clin Endocrinol Metab 93:2670–2678
4. Chang J (2015) Short-Term Intervention with Liraglutide Improved Hormonal and Metabolic Profile in Obese Women with Polycystic Ovary Syndrome: A Randomized Double-Blind Placebo-Controlled Trial. J Clin Endocrinol Metab 100:4585-4593
5. Edwards KL, Minze MG (2015) Dulaglutide: an evidence-based review of its potential in the treatment of type 2 diabetes. Core Evid 10:11-21
6. Abdalla MA, Deshmukh H, Atkin S, Sathyapalan T (2021) The potential role of incretin-based therapies for polycystic ovary syndrome: a narrative review of the current evidence. Ther Adv Endocrinol Metab 12
7. Jensterle M, Janez A (2023) Glucagon-Like Peptide-1 Receptor Agonists in the Treatment of Obesity. Horm Res Paediatr 96:599-608
8. Jensterle Sever M, Kocjan T, Pfeifer M, Aleksandra Kravos NA, Janez A (2014) Short-term combined treatment with liraglutide and metformin leads to significant weight loss in obese women with polycystic ovary syndrome and previous poor response to metformin. Eur J Endocrinol 170:451-459
9. Cignarella A, Mioni R, Sabbadin C, Dassie F, Parolin M, et al. (2020) Pharmacological Approaches to Controlling Cardiometabolic Risk in Women with PCOS. Int J Mol Sci 21:9554
10. Nauck MA, Meier JJ (2018) Incretin hormones: Their role in health and disease. Diabetes Obes Metab 20:5-21
11. Boer G, Holst JJ (2020) Mechanisms of Action of GLP-1 Receptor Agonists and DPP-4 Inhibitors in Type 2 Diabetes: Similarities and Differences. Rev Endocr Metab Disord 17:101-111
12. Wu S (2021) Dulaglutide Improves Hyperandrogenemia and Insulin Resistance in a Rat Model of Polycystic Ovary Syndrome. Reprod Biol Endocrinol 19:1-10
13. Cena H, Chiovato L, Nappi R (2015) Short-Term Intervention with Liraglutide Improved Hormonal and Metabolic Profile in Obese Women with Polycystic Ovary Syndrome: A Randomized Double-Blind Placebo-Controlled Trial. J Clin Endocrinol Metab 100: 4585-4593
14. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jodar E, et al. (2016) Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med 375:1834-1844
15. Gerstein HC, Colhoun HM, Dagenais GR, Diaz R, Lakshmanan M, et al. (2019) Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. Lancet 394:121-130
16. Ferdinand KC, White WB, Calhoun DA, Lonn EM, Sager PT, et al. (2014) Effects of the once-weekly glucagon-like peptide-1 receptor agonist dulaglutide on ambulatory blood pressure and heart rate in patients with type 2 diabetes mellitus. Hypertension 64:731-737
17. Lean M (2015) Sustained Weight Loss with Liraglutide 3.0 mg as an Adjunct to a Reduced-Calorie Diet and Physical Activity in Obese Patients: The SCALE Obesity and Prediabetes Randomised, Double-Blind, Placebo-Controlled Trial. Lancet 384:1403-1412

18. Kristensen SL, Rorth R, Jhund PS, Docherty KF, Sattar N, et al. (2019) Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet Diabetes Endocrinol 7:776-785

19. Al-Mutairi H (2021) Real-World Effectiveness and Safety of Dulaglutide in Patients with Type 2 Diabetes: A Systematic Review of Observational Studies. Diabetes Ther 12:527-547

20. Moran LJ, Henry Ko, Misso M, Marsh K, Noakes M, et al. (2013) Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet 113:520-545

21. Legro RS, Barnhart HX, Schlaff WD, Carr BR, Diamond MP (2007) Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. N Engl J Med 356:551-566

22. Panidis D (2003) The Role of Obesity and Adipocytokines in the Pathogenesis of Polycystic Ovary Syndrome. Eur J Endocrinol 148:609-618