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The Impact of GLP-1 Receptor Agonists on Reproductive Function in Women with Obesity and Metabolic Disorders: A Narrative Review

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Abstract

Background: Obesity and related metabolic disorders, including insulin resistance and polycystic ovary syndrome (PCOS), impair female fertility and increase the risk of adverse obstetric outcomes. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are a class of anti-obesity medications effective in promoting weight loss and improving metabolic control.

Aim: To summarize current evidence on the effects of GLP-1 receptor agonists on female reproductive function, particularly in PCOS and the preconception period.

Materials and Methods: A literature search was performed using the PubMed database to identify relevant studies published in English within the last 10 years. The selected studies were analyzed to summarize current evidence regarding the potential role of GLP-1 RAs in preconception care and female fertility.

Results: GLP-1 receptor agonists promote weight loss, improve insulin sensitivity, and reduce androgen levels. In women with PCOS, treatment has been associated with improved menstrual regularity and increased ovulation rates, and may enhance endometrial receptivity. Current evidence does not indicate a clear increase in congenital malformations after first-trimester exposure; however, discontinuation before planned conception is recommended due to limited safety data.

Conclusions: GLP-1 receptor agonists may improve metabolic health and reproductive outcomes in women with obesity and PCOS. However, most studies focus on surrogate outcomes, while evidence for definitive endpoints-particularly live birth rates-remains limited. Further prospective studies are needed to clarify their role in preconception care.

Keywords: Obesity; GLP-1 receptor agonists; Female fertility; Polycystic ovary syndrome (PCOS); Insulin resistance; Hyperandrogenism; Ovulation; Hormonal profile; Preconception care; Pregnancy outcomes.

1. Introduction

Obesity is one of the most serious public health challenges of the 21st century. Its prevalence has nearly tripled since 1975, and the proportion of women of reproductive age who are overweight or obese continues to rise steadily [1,9]. Obesity is now regarded as a chronic, multifactorial metabolic and endocrine disease that leads to disturbances in carbohydrate and lipid metabolism and contributes to chronic low-grade inflammation [25]. In the context of reproductive health, excess body weight represents an important, modifiable risk factor for subfertility and infertility [2,12,23].

The mechanisms by which obesity affects female fertility are complex and include dysfunction of the hypothalamic-pituitary-ovarian (HPO) axis, hyperinsulinemia, insulin resistance, hyperandrogenism, and disturbances in gonadotropin secretion [4,9,11]. Excess adipose tissue-particularly visceral fat-promotes insulin resistance and contributes to a self-perpetuating metabolic-hormonal vicious cycle, which is especially evident in polycystic ovary syndrome (PCOS) [9,10,19]. Chronic inflammation, lipotoxicity, and oxidative stress impair oocyte quality, disrupt meiosis, induce mitochondrial dysfunction, and reduce endometrial receptivity, resulting in lower implantation efficiency and an increased risk of miscarriage [4,18,25].

Outcomes of infertility treatment using assisted reproductive technologies (ART) are significantly poorer in women with obesity than in women with normal body weight. These patients require higher doses of gonadotropins, experience cycle disturbances more frequently, yield fewer oocytes, and have lower pregnancy and live birth rates [9,12,23]. At the same time, evidence regarding the effect of preconception weight reduction on live birth rate remains inconclusive-although lifestyle interventions improve ovulation frequency and spontaneous conception, they do not consistently translate into higher live birth rates (LBR) in ART populations [11,12].

Particular attention has been drawn to visceral obesity and cardiometabolic indices as predictors of infertility. Novel measures such as the cardiometabolic index (CMI) and the weight-adjusted-waist index (WWI) show significant positive associations with infertility risk, underscoring the role of metabolic dysfunction as a key link in pathogenesis [24,27].

In recent years, the rapid development of anti-obesity pharmacotherapy-especially glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dual GLP-1/GIP receptor agonists-has created new therapeutic opportunities in the preconception period [5,6,13]. GLP-1 receptor agonists, including semaglutide and liraglutide, have demonstrated effective weight reduction and favorable effects on cardiovascular parameters, which led to their approval by the FDA for obesity treatment [7]. These agents can induce substantial weight loss (often exceeding 15-20%), improve insulin sensitivity, reduce inflammation, and produce favorable changes in hormonal profiles [13,19,22]. In women with PCOS, GLP-1 RAs may help reduce hyperandrogenism, improve cycle regularity, and increase ovulation and pregnancy rates; in some studies, beneficial effects have also been observed with combination therapy including metformin [15,16,19]. Moreover, a meta-analysis of seven randomized trials (n = 464) found that GLP-1 RAs were more effective than metformin in reducing BMI, HOMA-IR, and waist circumference, while no significant differences were observed in menstrual frequency or androgen parameters; additionally, combined therapy with GLP-1 RAs and metformin did not outperform GLP-1 RA monotherapy for the assessed outcomes [21].

Importantly, growing evidence suggests that the effects of GLP-1 RAs may extend beyond weight loss alone. Preclinical and clinical studies point to a possible direct influence of these agents on the hypothalamic-pituitary-gonadal axis, ovarian tissue, and endometrial receptivity [18,31]. However, the safety of GLP-1 RAs around conception remains under active investigation. Available observational data have not demonstrated a clear increase in congenital malformations following unintended early pregnancy exposure, yet given the limited number of studies, planned discontinuation before conception is recommended [28,29].

In light of these findings, comprehensive care for women with obesity who are planning pregnancy is needed, including lifestyle modification, assessment of metabolic risk factors, psychological support, and, in selected cases, pharmacotherapy for obesity [5,17]. The aim of this paper is to present the current state of knowledge on the impact of obesity on female fertility and to discuss the potential role of GLP-1 receptor agonists in optimizing metabolic and reproductive health in the preconception period, with particular emphasis on women with PCOS.

2. Epidemiology

Obesity is one of the fastest-growing health problems worldwide. Its prevalence has nearly tripled since 1975 and currently affects hundreds of millions of adults, including an increasing proportion of women of reproductive age [1,9]. In this population, excess body weight is associated not only with an increased risk of cardiovascular and metabolic diseases but also with impaired fertility, a higher incidence of pregnancy complications, and adverse health outcomes in offspring [1,3,9,12].

At the same time, the prevalence of metabolic disorders such as insulin resistance, prediabetes, and type 2 diabetes is rising, further amplifying the negative impact of obesity on reproductive function [14]. A particularly important condition in this context is polycystic ovary syndrome (PCOS), the most common endocrine disorder in women of reproductive age and a leading cause of anovulatory infertility. The global prevalence of PCOS is estimated at 4-20%, depending on the diagnostic criteria used, and approximately half of affected women present with overweight or obesity as well as insulin resistance [10,15,19]. This coexistence creates a population at particularly high risk of infertility, obstetric complications, and future metabolic disease.

Infertility remains a significant global public health concern, and its association with obesity has been well documented, although it varies depending on population characteristics, age, and diagnostic definitions [11,12]. Epidemiological data indicate that increasing BMI is associated with a reduced probability of spontaneous conception, a higher prevalence of ovulatory disorders, and poorer reproductive outcomes in both natural conception and assisted reproductive technologies (ART) [9,12,25,26]. In addition, central obesity has emerged as a stronger predictor of reproductive risk than BMI alone. Population studies show that novel indices of visceral and cardiometabolic adiposity, such as the weight-adjusted waist index (WWI) and cardiometabolic index (CMI), are associated with an increased risk of infertility, and this relationship may be non-linear [24,27].

The growing scale of this problem also has systemic implications. In many countries, BMI thresholds have been introduced as criteria for eligibility or reimbursement for infertility treatment, despite inconclusive evidence that short-term weight reduction improves hard clinical outcomes such as live birth rate [11,12,17]. Consequently, the epidemiology of obesity in the reproductive-age population highlights the need for integrated models of preconception and reproductive care that combine metabolic risk assessment, obesity management, and individualized infertility treatment strategies [5,14,28,17].

3. GLP-1 Receptor Agonists – Mechanism of Action

Glucagon-like peptide-1 (GLP-1) is an incretin hormone secreted by L-cells of the small intestine in response to food intake. Physiologically, it enhances glucose-dependent insulin secretion, suppresses glucagon release, delays gastric emptying, and promotes satiety through central nervous system mechanisms [22]. However, endogenous GLP-1 has a very short half-life; therefore, synthetic analogues-GLP-1 receptor agonists (GLP-1 RAs)-have been developed to provide prolonged activity and greater enzymatic stability [13,22].

Endogenous GLP-1 secretion is also influenced by lifestyle factors. Population studies have shown that regular physical activity is associated with a more favorable postprandial GLP-1 response, highlighting the role of the gut-metabolic axis in the regulation of glucose homeostasis [8].

GLP-1 receptor agonists bind to GLP-1 receptors expressed in the pancreas, central nervous system, adipose tissue, skeletal muscle, and other organs. Activation of these receptors increases intracellular cyclic adenosine monophosphate (cAMP) levels, leading to enhanced glucose-dependent insulin secretion and improved insulin sensitivity [22]. At the same time, glucagon secretion is suppressed, contributing to improved glycemic control and reduced hyperinsulinemia-a key mechanism underlying ovulatory dysfunction in obesity and PCOS [10,19].

Another important mechanism of GLP-1 RA action is their effect on appetite regulation and energy balance. By acting on hypothalamic centers, particularly the arcuate nucleus, these agents reduce hunger and enhance satiety, resulting in decreased caloric intake and significant weight loss [5,13,22].

Clinical studies have demonstrated that newer agents, such as semaglutide and tirzepatide, can achieve weight reductions of approximately 15-25% of initial body weight, approaching the effectiveness observed with bariatric surgery [5,17].

Beyond their metabolic effects, increasing attention has been given to the potential influence of GLP-1 RAs on inflammatory processes and endothelial function. These agents exhibit anti-inflammatory properties, reduce levels of pro-inflammatory cytokines, and may modulate immune responses, which could influence endometrial receptivity and embryo implantation [31]. Experimental models also suggest that activation of the GLP-1 receptor may affect the hypothalamic-pituitary-gonadal axis through modulation of GnRH and gonadotropin secretion, although these mechanisms have not yet been clearly confirmed in humans [28].

In the context of reproductive health, the effects of GLP-1 receptor agonists therefore include both indirect mechanisms-such as weight reduction and improved insulin sensitivity-and potential direct effects on the hormonal and immunometabolic environment of the female reproductive system [18,19,31]. This multidirectional mechanism of action underlies the growing interest in the use of these agents in the preconception period among women with obesity and PCOS.

4. Metabolic Effects Relevant to Fertility

Obesity and its associated metabolic disturbances play a key role in the pathogenesis of female infertility. A central component of these disturbances is insulin resistance and secondary hyperinsulinemia, which lead to dysregulation of the hypothalamic-pituitary-ovarian (HPO) axis, excessive androgen production, and impaired ovarian follicle maturation [4,10,19]. Hyperinsulinemia stimulates androgen synthesis in ovarian theca cells and reduces the concentration of sex hormone-binding globulin (SHBG), thereby increasing the pool of free androgens and promoting anovulation [10,19,30].

Even modest weight reduction (approximately 5-7% of initial body weight) can significantly improve insulin sensitivity, restore ovulation, and increase the likelihood of spontaneous pregnancy [11,30]. In this context, GLP-1 receptor agonists (GLP-1 RAs) are of particular interest, as they simultaneously improve glycemic control, reduce hyperinsulinemia, and induce substantial weight loss [13,17,19]. Clinical studies in women with PCOS have demonstrated that treatment with GLP-1 RAs is associated with reduced testosterone levels, increased SHBG concentrations, and improved menstrual cycle regularity and ovulation rates [15,16,19].

Another important mechanism linking obesity with impaired fertility is chronic low-grade inflammation. Excess adipose tissue, particularly visceral fat, leads to increased production of pro-inflammatory cytokines such as TNF-α and IL-6, which negatively affect oocyte quality, endometrial receptivity, and embryo implantation [18,31]. GLP-1 receptor agonists exhibit anti-inflammatory properties and may modulate immune responses, thereby contributing to a more favorable implantation environment [31].

In addition, obesity is associated with dyslipidemia, oxidative stress, and endothelial dysfunction, which may impair ovarian and endometrial perfusion [25]. GLP-1 receptor agonists have been shown to reduce triglyceride levels, improve the lipid profile, and decrease visceral adipose tissue mass [15,19]. In a meta-analysis including women with PCOS, treatment with GLP-1 RAs resulted in significant reductions in BMI, waist circumference, triglycerides, and total testosterone compared with placebo [15].

Novel cardiometabolic indices, such as the cardiometabolic index (CMI) and the weight-adjusted waist index (WWI), are also noteworthy, as they appear to correlate more strongly with infertility risk than BMI alone [24,27]. Improvements in metabolic parameters achieved through anti-obesity treatment may therefore translate into a reduction in overall reproductive risk.

In summary, the metabolic effects of GLP-1 receptor agonists-including weight reduction, improved insulin sensitivity, normalization of the androgen profile, anti-inflammatory activity, and improvement of lipid parameters-provide a biologically plausible rationale for their consideration in preconception therapy among women with obesity and PCOS [13,19,30,31]. Despite promising results, further studies are required to evaluate whether these improvements translate into hard clinical outcomes, such as live birth rate.

5. Effects of GLP-1 Receptor Agonists in Polycystic Ovary Syndrome (PCOS)

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age and one of the leading causes of anovulatory infertility [10,19]. The pathophysiology of PCOS involves complex interactions between insulin resistance, hyperinsulinemia, hyperandrogenism, and dysregulation of the hypothalamic-pituitary-ovarian (HPO) axis. Approximately 40-70% of women with PCOS present with overweight or obesity, which further exacerbates both metabolic and reproductive disturbances [10,19].

Insulin resistance plays a central role in the development of PCOS. Hyperinsulinemia stimulates ovarian theca cells to increase androgen production and reduces hepatic synthesis of sex hormone-binding globulin (SHBG), resulting in higher levels of circulating free androgens and impaired ovulation [10,19,30]. Consequently, improving insulin sensitivity represents a key therapeutic target in this population.

GLP-1 receptor agonists (GLP-1 RAs) have demonstrated beneficial effects on both metabolic and hormonal parameters in women with PCOS. Clinical studies have reported significant reductions in body weight, waist circumference, and glycemic parameters compared with placebo or metformin [15,16,19]. In a meta-analysis involving women with PCOS, GLP-1 RA therapy was associated with significant decreases in BMI, triglyceride levels, total testosterone, and waist circumference [15]. In some studies, combination therapy with GLP-1 RAs and metformin resulted in greater weight reduction and more favorable changes in androgen profiles compared with monotherapy [16,19].

Experimental data also suggest that GLP-1 RAs may exert direct effects on ovarian function. In animal models, treatment with GLP-1 RAs has been associated with improved ovarian morphology, a reduction in cystic follicles, and decreased hyperandrogenemia [18]. These effects may result not only from weight reduction but also from modulation of the hypothalamic-pituitary-gonadal axis and anti-inflammatory activity [18,31].

Effects on Ovulation and Hormonal Profile

Normal ovulation depends on a precisely regulated hypothalamic-pituitary-ovarian axis and appropriate metabolic-hormonal balance. Obesity and insulin resistance disrupt pulsatile GnRH secretion, leading to altered LH/FSH ratios, hyperandrogenism, and anovulation [4,10,19]. Hyperinsulinemia further increases ovarian androgen production and decreases SHBG levels, thereby increasing the fraction of free testosterone and worsening menstrual cycle disturbances [10,30].

Weight reduction, even modest (approximately 5-7% of initial body weight), is associated with improved ovulation and a higher rate of spontaneous pregnancies [11,30]. Through improving insulin sensitivity and inducing significant weight loss, GLP-1 receptor agonists may positively influence the regulation of the HPO axis. Clinical studies in women with PCOS have demonstrated that GLP-1 RA therapy leads to reductions in total and free testosterone levels, increases in SHBG concentrations, and improved menstrual cycle regularity [15,16,19].

Randomized trials have also reported increased ovulation rates in women treated with GLP-1 RAs compared with placebo or metformin, particularly when therapy was combined with lifestyle modification [16,19]. Some studies have additionally shown improvements in the free androgen index (FAI) and reductions in clinical hyperandrogenism, including hirsutism [19].

Experimental evidence further suggests that activation of GLP-1 receptors may influence the hypothalamic-pituitary-gonadal axis through modulation of GnRH and gonadotropin secretion, potentially supporting the restoration of normal ovulatory rhythms [18,28]. However, these mechanisms have not yet been fully confirmed in human studies.

In the context of infertility treatment, improvements in hormonal parameters may also enhance the effectiveness of ovulation induction and assisted reproductive technologies (ART). Although data on the impact of GLP-1 RAs on live birth rates remain limited, the observed improvements in ovulation and hormonal profiles provide a biologically plausible rationale for their use in the preconception period in selected patients [15,19,30].

Overall, GLP-1 receptor agonists appear to promote the restoration of ovulation through reductions in hyperinsulinemia, normalization of androgen levels, and improvement of hormonal balance. These effects seem particularly relevant in women with PCOS and obesity; however, further long-term studies evaluating clinically relevant endpoints are required.

6. GLP-1 Receptor Agonists and Pregnancy Outcomes

The use of GLP-1 receptor agonists (GLP-1 RAs) in the periconception period has attracted increasing attention, as these agents significantly improve metabolic parameters such as body weight, insulin resistance, and glycemic control-key risk factors for obstetric complications in women with obesity and/or type 2 diabetes [14,28]. However, GLP-1 RAs remain contraindicated during pregnancy due to limited safety data and findings from animal studies [28,29].

6.1. Safety of Early Pregnancy Exposure

Animal studies consistently indicate a risk of embryotoxicity and teratogenicity at supratherapeutic doses, including fetal growth restriction and skeletal abnormalities. Some of these effects may be secondary to maternal weight loss and energy deficit rather than direct drug toxicity [28].

In contrast, available human data-although limited and largely observational-are more reassuring. In the largest prospective cohort including 168 pregnancies with first-trimester exposure, no increased risk of congenital malformations or pregnancy loss was observed [28].

Registry analyses including approximately 900 exposures have reported similar findings, although wide confidence intervals and limited statistical power were noted [28]. A review focusing on preconception and early pregnancy exposure likewise did not demonstrate adverse obstetric outcomes but emphasized the limited number of high-quality clinical studies [29].

6.2. Placental Transfer and Mechanisms

Direct human data on placental transfer of GLP-1 RAs are lacking. Due to their relatively large molecular size, passive placental diffusion appears unlikely, and animal models suggest minimal fetal exposure [28]. Nevertheless, indirect effects through changes in maternal weight, glycemia, or nutritional status cannot be excluded.

6.3. Preconception Exposure and Obstetric Outcomes

Recent studies have also explored whether preconception treatment with GLP-1 RAs may reduce pregnancy complications by improving metabolic status. A retrospective nationwide database analysis showed that women prescribed GLP-1 RAs within 24 months prior to pregnancy had a lower risk of gestational diabetes, hypertensive disorders of pregnancy, preterm birth, and cesarean delivery compared with unexposed women [20]. However, these findings should be interpreted cautiously because exposure was defined by prescription rather than confirmed drug use, and data on dosage and duration were unavailable [20].

6.4. Clinical Implications

Given the uncertainty regarding safety, planned discontinuation of GLP-1 RAs before conception is recommended. Suggested minimum wash-out periods depend on pharmacokinetics: semaglutide ≥35 days, tirzepatide 25-35 days, and liraglutide ≥3 days [28]. Other reviews suggest that a practical minimum wash-out period of at least four weeks may be reasonable, although robust evidence for a universal recommendation is lacking [29]. Clinical decisions should consider the specific drug used, the rate of weight loss, and the potential risk of rapid weight regain after treatment cessation [17,28].

6.5. Weight Regain After Discontinuation

An additional concern is weight regain following discontinuation of GLP-1 RAs. Studies suggest that a substantial proportion of lost weight may be regained after therapy cessation, increasing the risk of “weight cycling” in the periconception period [17]. This may contribute to excessive gestational weight gain and metabolic complications. Therefore, discontinuation of GLP-1 RAs should be accompanied by strategies aimed at maintaining metabolic benefits, including lifestyle interventions, psychological support, and in some cases transition to alternative therapy such as metformin [17,28].

6.6. Summary

Current evidence suggests that unintentional early-pregnancy exposure to GLP-1 RAs is not clearly associated with an increased risk of congenital malformations or pregnancy loss, although available data remain limited and largely observational [28,29]. Preconception use of GLP-1 RAs may potentially reduce obstetric complications through metabolic improvement, but these findings require confirmation in prospective studies [20]. Therefore, GLP-1 RAs should be considered a tool for optimizing preconception metabolic health, with planned discontinuation before conception and strategies to prevent rapid weight regain after treatment cessation [3,17].

7. Immunomodulatory Mechanisms and Recurrent Pregnancy Loss (RPL)

Obesity promotes chronic low-grade inflammation that disrupts maternal–fetal immune tolerance and may increase the risk of implantation failure and recurrent pregnancy loss (RPL) [31]. Excess production of proinflammatory cytokines, increased activity of natural killer (NK) cells, and impaired function of regulatory T lymphocytes (Treg) contribute to an abnormal immune response to the embryo [31].

GLP-1 receptor agonists (GLP-1 RAs) exhibit anti-inflammatory and immunomodulatory properties. Experimental studies have shown macrophage polarization toward an anti-inflammatory M2 phenotype, reduced levels of proinflammatory cytokines, and improved immune balance [31]. These agents may also improve endothelial function and microcirculation, potentially supporting proper implantation [31].

Although clinical data on the direct impact of GLP-1 RAs on recurrent pregnancy loss remain limited, their metabolic and immunomodulatory effects suggest a potential role in preconception care among women with obesity. Further studies are required to confirm their effect on pregnancy maintenance.

8. Safety and Preconception Management

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are contraindicated during pregnancy due to limited clinical data and findings from animal studies suggesting potential embryotoxic effects at high doses [28,29]. Available observational data regarding inadvertent exposure in early pregnancy have not demonstrated a clear increase in the risk of congenital malformations or pregnancy loss; however, the number of studied cases remains small and the quality of evidence is limited [28,29].

For this reason, planned discontinuation of GLP-1 RAs is recommended before attempting conception. The required washout period should be adjusted according to the pharmacokinetic profile of the specific agent. For semaglutide and tirzepatide, a discontinuation period of several weeks is generally recommended, whereas for liraglutide a shorter interval may be sufficient due to its shorter half-life [28].

During the preconception period, a comprehensive approach is essential, including assessment of metabolic status (glucose levels, HbA1c, lipid profile), weight reduction strategies, optimization of insulin resistance treatment, and appropriate nutritional and psychological support [17,28]. It is also important to consider the risk of weight regain following treatment discontinuation and to implement strategies aimed at preventing this effect.
In summary, GLP-1 RAs may represent an effective tool for optimizing metabolic health prior to pregnancy; however, therapy should be discontinued before conception and clinical management should be individualized.

9. Discussion

The increasing prevalence of obesity among women of reproductive age represents a significant challenge for reproductive medicine. Obesity, particularly visceral obesity, through insulin resistance, hyperandrogenism, and chronic low-grade inflammation, significantly impairs the function of the hypothalamic-pituitary-ovarian axis, reduces oocyte quality, disrupts endometrial receptivity, and increases the risk of implantation failure and miscarriage [4,10,25,31]. In this context, effective and safe optimization of metabolic status prior to pregnancy is of major clinical importance.

GLP-1 receptor agonists exert multidirectional effects-they reduce body weight, improve insulin sensitivity, decrease circulating androgen levels, and demonstrate anti-inflammatory properties [13,19,31]. In women with PCOS, improvements in menstrual regularity, increased ovulation rates, and favorable changes in hormonal profiles have been observed [15,16,19]. Importantly, some studies also suggest potential benefits in reducing the risk of obstetric complications following preconception exposure, although the available evidence is largely observational [20].

However, it should be emphasized that most available studies focus on surrogate outcomes such as BMI, testosterone levels, HOMA-IR, and ovulation rates, whereas large randomized trials assessing definitive clinical endpoints, particularly live birth rates, are lacking. Data regarding safety during pregnancy remain limited and are largely based on retrospective analyses and case reports [28,29]. Therefore, these medications should currently be considered as part of a preconception strategy rather than as therapies used during pregnancy.

An additional clinical concern is the risk of weight regain following discontinuation of GLP-1 RA therapy. The "weight regain" effect may partially offset previously achieved metabolic benefits and potentially influence early pregnancy outcomes [17]. This highlights the need for structured transition strategies from pharmacological treatment to lifestyle-based interventions or alternative therapies.

From a broader healthcare perspective, there is an increasing need for integrated models of care that combine preconception counseling, obesity management, psychological support, and individualized infertility treatment. Within such models, GLP-1 receptor agonists may represent an important therapeutic tool, particularly in women with PCOS and coexisting insulin resistance.

10. Conclusions

Obesity and its associated metabolic disorders represent significant, modifiable risk factors for infertility, implantation failure, and pregnancy complications. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) exert multidirectional effects, including weight reduction, improved insulin sensitivity, normalization of the androgen profile, and anti-inflammatory properties, which makes them a promising tool for optimizing preconception health.

Available evidence suggests improvements in ovulation and hormonal parameters, particularly in women with polycystic ovary syndrome (PCOS); however, clear evidence demonstrating an increase in live birth rates is still lacking. Current safety data do not indicate a clear increase in the risk of congenital malformations following inadvertent early pregnancy exposure, but due to the limited number of studies, GLP-1 RAs should be discontinued prior to planned conception.

GLP-1 RAs should therefore be considered as part of a comprehensive strategy for obesity management in the preconception period, including individualized risk assessment, appropriate discontinuation planning, and support aimed at maintaining metabolic benefits. Further prospective studies are required to determine their long-term impact on reproductive and obstetric outcomes.

Disclossure

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