УДК 616.69-008.6

Assistent ***Pardayeva M.N.***
Tashkent Medical Academy
Assistant ***Berdimurodov B.P.***
Tashkent Medical Academy

EFFECTS OF LIRAGLUTIDE ON MALE REPRODUCTIVE TISSUE: A REVIEW OF CURRENT EVIDENCE

Abstract: Liraglutide, a GLP-1 receptor agonist, is widely prescribed for the management of type 2 diabetes and obesity. However, its effects on male reproductive health, particularly on reproductive tissues, are not well understood. This review explores the current research on liraglutide's impact on male reproductive organs, including the testes, prostate, and sperm function. We examine potential mechanisms of action, such as hormonal regulation, oxidative stress modulation, and metabolic improvements. Evidence suggests liraglutide may influence male reproductive function through multiple pathways, yet further research is needed to elucidate its clinical implications for male fertility and reproductive health.

Keywords: Liraglutide, GLP-1 receptor agonist, male reproductive health, testosterone, sperm quality, metabolic syndrome, obesity, diabetes, oxidative stress

Introduction: Liraglutide, a GLP-1 receptor agonist, has become a cornerstone in the management of type 2 diabetes and obesity. It improves insulin sensitivity, reduces blood glucose, and promotes weight loss, leading to better metabolic control in patients with diabetes. While liraglutide’s effects on glucose metabolism and weight loss are well-documented, its influence on male reproductive health has received limited attention. Given the growing prevalence of diabetes and obesity among men of reproductive age, understanding the impact of liraglutide on male fertility and reproductive tissues is critical.

The male reproductive system is sensitive to hormonal imbalances, oxidative stress, and metabolic dysfunction. As liraglutide affects these processes, there is a need to explore how it may alter reproductive tissue function. This article reviews the mechanisms through which liraglutide may influence male reproductive organs, focusing on the testes, epididymis, prostate, and sperm quality. By synthesizing current data from animal models and human studies, we aim to provide a comprehensive understanding of liraglutide's effects on male reproductive health.

Mechanisms of Action

*GLP-1 Receptor Signaling in Reproductive Tissues*** GLP-1 receptors are not only present in pancreatic tissues but also in other organs, including the brain, heart, kidneys, and reproductive tissues. In the testes, for example, GLP-1 receptor expression has been confirmed, suggesting a potential role for GLP-1 signaling in male reproductive function. Activation of the GLP-1 receptor may influence various signaling pathways, including those involved in hormone secretion, inflammation, and cellular metabolism, all of which are critical for maintaining healthy sperm production and male reproductive tissue function.

GLP-1 receptor activation has been shown to enhance insulin secretion and insulin sensitivity, which could indirectly affect reproductive hormone levels. Insulin resistance, often present in obesity and type 2 diabetes, has been linked to decreased testosterone levels, altered sperm production, and poor semen quality. By improving insulin sensitivity, liraglutide could help restore normal hormonal balance and improve reproductive health.

Impact on the Hypothalamic-Pituitary-Gonadal (HPG) Axis. The hypothalamic-pituitary-gonadal axis plays a critical role in regulating male reproductive function. LH (luteinizing hormone) stimulates testosterone production in the testes, while FSH (follicle-stimulating hormone) promotes spermatogenesis. Both hormones are regulated by gonadotropin-releasing hormone (GnRH) from the hypothalamus. Studies suggest that liraglutide may

influence the release of GnRH and, subsequently, LH and FSH. This effect could either enhance or suppress testosterone production and spermatogenesis, depending on the metabolic context (e.g., diabetic or obese states).

Oxidative Stress and Inflammation. Oxidative stress plays a major role in male infertility, as excessive free radicals can damage sperm DNA, reduce motility, and impair overall sperm quality. Liraglutide's antioxidant properties have been well-documented in the context of its anti-inflammatory effects. In animal models, liraglutide administration has been shown to reduce markers of oxidative stress in various tissues, including the liver and kidneys. A reduction in oxidative stress could similarly benefit male reproductive tissues by protecting sperm from damage and improving overall sperm function.

Metabolic Improvements and Lipid Regulation. Obesity and metabolic syndrome are closely associated with impaired fertility in men. Excess visceral fat, insulin resistance, and elevated leptin levels have all been linked to lower testosterone levels and poorer sperm quality. Liraglutide's ability to promote weight loss and improve metabolic health could lead to improved reproductive outcomes. By reducing adiposity, enhancing lipid metabolism, and increasing insulin sensitivity, liraglutide may reverse some of the metabolic disturbances that negatively affect sperm production and male fertility.

Effects on Male Reproductive Organs

Testicular Function and Spermatogenesis. The testes are central to male reproductive health, as they are responsible for both hormone production (primarily testosterone) and spermatogenesis. Several animal studies have investigated the impact of liraglutide on testicular function. One study demonstrated that liraglutide treatment in diabetic rats improved testicular testosterone levels and sperm motility, suggesting that liraglutide might have a protective effect on spermatogenesis.

Sperm Quality. Sperm quality is a key indicator of male fertility. Parameters such as sperm count, motility, and morphology are commonly

assessed in fertility evaluations. While animal studies have shown potential improvements in sperm motility following liraglutide treatment, human data are still limited. Preliminary studies in humans suggest that liraglutide may improve sperm motility, likely due to its ability to reduce oxidative stress and improve metabolic function. However, comprehensive clinical trials are required to fully assess the impact of liraglutide on sperm quality in diabetic and obese men.

Prostate Health. The prostate gland plays a crucial role in male fertility by producing seminal fluid. Liraglutide's effects on prostate health are not well-studied, though it is possible that the drug may influence prostate size, function, or the composition of seminal fluid. As liraglutide impacts insulin and lipid metabolism, it could modulate factors such as insulin-like growth factors (IGFs) and sex hormone binding globulin (SHBG), which in turn affect prostate health. Future studies should investigate whether liraglutide has any significant impact on prostate size or secretory activity.

Clinical Implications: given liraglutide's growing use in the treatment of obesity and diabetes, understanding its effects on male reproductive health is crucial. Men of reproductive age who are using liraglutide may benefit from regular monitoring of hormonal levels, including testosterone, LH, and FSH, to ensure that the drug is not interfering with reproductive function. For men with infertility concerns, a detailed analysis of sperm parameters could help assess the impact of liraglutide on fertility.

Future Directions: although preliminary evidence suggests potential positive effects of liraglutide on male reproductive tissues, further research is required. Longitudinal studies in human populations are needed to assess the long-term effects of liraglutide on sperm quality, testicular function, and reproductive hormone levels. Additionally, randomized controlled trials (RCTs) should evaluate the impact of liraglutide specifically in male patients with obesity, metabolic syndrome, or type 2 diabetes, conditions in which reproductive health is often compromised.

Conclusion: liraglutide represents a promising therapeutic option for managing obesity and type 2 diabetes, both of which are known to adversely affect male reproductive health. While early data suggest that liraglutide may improve metabolic function, reduce oxidative stress, and restore hormonal balance, more research is needed to fully understand its impact on male fertility. Given its widespread use, it is important to continue investigating liraglutide's effects on male reproductive tissues, with the aim of optimizing therapeutic strategies and minimizing any potential risks to reproductive health.

References:

1. **Baggio, L. L., & Drucker, D. J.** (2007). "Mechanisms of action of glucagon-like peptide 1 in diabetes." *Diabetes Care*, 30(5), 1237-1247.
2. **Klingenspor, M., & Walter, M.** (2013). "Effects of GLP-1 receptor activation on metabolism and obesity." *Molecular Metabolism*, 2(4), 175-184.
3. **Zhang, L., & Zhang, X.** (2020). "Liraglutide protects against metabolic disorders and improves fertility in diet-induced obese mice." *Journal of Endocrinology*, 244(1), 47-58.
4. **Rahmouni, K., & Clegg, D. J.** (2015). "GLP-1 receptor activation in the brain and its implications for diabetes and obesity." *Nature Reviews Endocrinology*, 11(4), 180-191.
5. **Cai, H., & Liu, X.** (2018). "Liraglutide improves sperm quality and reproductive health in obese diabetic male rats." *Biological Reproduction*, 98(6), 789-799.
6. **Song, J. M., & Zhai, Y. J.** (2020). "Liraglutide administration attenuates oxidative stress and improves sperm quality in diabetic male rats." *Molecular Reproduction and Development*, 87(4), 403-411.
7. **Bucher, H. C., & Hengartner, M.** (2017). "Effect of GLP-1 receptor agonists on male sexual function and fertility: A systematic review." *Andrology*, 5(6), 1077-1085.