

The Importance of Insulin-Like Growth Factor and the Relevance of its Research

Abduganiev Abdurauf Sodiqzhonovich

MSc in Pharmaceuticals, Lab engineer, Pharmaceutical Technical University, Tashkent.

Nazarov Sherzod Zokirzhonovich

MSc in pharmaceuticals, Senior Officer on Analytics, Pharmaceutical Technical University, Tashkent

Abstract: It is known that growth hormone is a pleiotropic hormone that causes the growth of all organs by coordinating many physiological processes, including its effect on the nervous system, bones, muscles and fat. Metabolically, growth hormone promotes anabolic action in most tissues except adipose tissue, and its catabolic effect leads to the breakdown of accumulated triglycerides into free fatty acids. On the other hand, insulin-like growth hormone is a hormone that serves to indirectly exercise its activity by stimulating this aforementioned growth hormone. Due to its diverse activity and effectiveness, it encourages consideration of the possibility of its use for diagnostic and therapeutic purposes. In many pathologies of the nervous system, cardiovascular and other organs, its amount may shift to one degree or another, and in this regard, the possibilities of inclusion in diagnostic measures are being considered, based on the magnitude of this shift. However, when treating with insulin-like growth factor, it is very important to regulate its amount, since an overdose when using it or vice versa can lead to a violation of hormonal interaction in the body. This leads to various serious disorders in the body. For this reason, substitution or substitution therapy also requires strict caution when using it when considering the prospects of its use in certain oncological diseases. However, given that the level of IGF-1 expression varies depending on a number of clinical conditions, constant maintenance of IGF-I levels within the normal range allows you to avoid side effects caused by its use, as well as to obtain important promising treatment results.

Keywords: IGF-I, IGF-II, growth hormones, growth factors, replacement therapy.

Annotation. Insulin-like growth factors (IGF-I and IGF-II) and their receptors, which perform important functions for the body, begin to be widely expressed in nervous tissue from the earliest embryonic period of human life. There is sufficient convincing evidence that IGF-I and IGF-II play a key role in the development and functioning of the nervous system, since they pass through the blood-brain barrier through active transport, therefore their regulation as an endocrine factor differs from other tissues. In the brain, IGFs acquire a paracrine and autocrine nature in accordance with their action, and they are modulated by IGF-binding proteins, as well as interact with other signaling pathways of growth factors [1, 2, 3]. However, it has been recognized that a deficiency of these hormones can cause quite serious changes and disorders for the body. In particular, there is strong evidence of a link between IGF-I deficiency and metabolic syndrome, which requires focusing on the metabolic effects of IGF-I, the concept of metabolic syndrome and its clinical manifestations, including conditions such as lipid profile disorders, insulin resistance, elevated glucose levels, obesity and cardiovascular diseases. Similarly, it was found that a decrease in serum IGF-1 levels in a population with various diseases or a severe history is associated with an increase in markers of inflammation and fibrin with age. This, in turn, helps explain the association between lower serum IGF-1 levels and an increased risk of cardiovascular disease. From the data obtained as a result of Broligan's studies, it can be understood that serum IGF-1 levels are a clinically significant marker of cardiovascular risk, especially in men [4, 5, 6]. Based on observations and research conducted by reputable scientists over the past 50 years, a plan has been developed to search specifically for IGF-1

and its significance for metabolism, carbohydrates, lipids, proteins, amino acids, metabolic syndrome, cardiovascular diseases, diabetes and other pathologies. At the same time, studies were conducted on the studied animals and humans, which, in turn, allowed us to discuss such important issues as the effect of IGF-I on metabolism and the effect of IGF-I deficiency on the development of metabolic syndrome.

Including a lot of *in vitro* and *in vivo* studies have shown that there is a connection between IGF-I deficiency and lipid metabolism disorders, cardiovascular diseases and changes in the metabolic profile in patients with diabetes. This, in turn, suggests based on these data that IGF-1 is a key hormone in the pathophysiology of metabolic syndrome. The findings, on the other hand, mean that it is possible to discuss the prospects of using IGF-1 replacement therapy for the treatment of widespread diseases around the world and even obtain effective treatment through its use [7, 8, 9, 10]. In this regard, this presented manuscript provides a brief literary analysis of the role of insulin-like growth factors in the performance of normal functions in the body in order to further study them.

The main purpose of the presented analytical work is to conduct a brief review of the literature on the physiological significance of insulin-dependent growth hormone, its role in the occurrence of diseases and the prospects for its use for medicinal purposes

The main physiological functions of insulin-dependent growth factor. Insulin-like growth factor I is a polypeptide hormone that is mainly produced by the liver in response to the endocrine stimulus of growth hormone, but is also secreted by many tissues for autocrine/paracrine purposes. IGF-I is partially responsible for the systemic activity of growth hormone, although it has unique properties such as anabolic, antioxidant, anti-inflammatory and cytoprotective effects. Insulin-like growth factor-1 is important for stimulating cell growth and differentiation in childhood and is the main mediator of growth hormone, and then has an anabolic effect in adults. IGF-1 is part of an extensive network of growth factors, their receptors, and binding proteins that are involved in cell proliferation, differentiation, and apoptosis. In addition, IGF-1 is a well-known and popular doping agent in sports, and the increased level of it in many cases of high doping in recent years also confirms this claim. However, the presence of IGFBP significantly reduces the levels of immunoreactive IGF-1 in samples, which requires several processing steps, which reduces reproducibility and makes it difficult to interpret the results of IGF-1 analysis. The IGF system. The presence of significant evidence for the specific role of the IGF system in some neurodegenerative diseases of the nervous system indicates that this system plays an important role in the development and maintenance of the nervous system [10, 11, 12, 13].

The diagnostic value of insulin-dependent growth hormone. Changes in this hormone develop to one degree or another in the body either when various pathologies occur, or because of its activity and deficiency. In particular, growth hormone deficiency is a clinical syndrome that can manifest itself with certain symptoms and is usually associated with an additional deficiency of pituitary hormones. Thus, cases of IGF-I deficiency, like any other hormone, cause effects that end in well-known syndromes with significant clinical consequences. To date, the most well-known cases of IGF-I deficiency are: lemon syndrome in children; cirrhosis of the liver in adults; and cardiovascular and neurological diseases associated with aging, including aging. Recently, intrauterine growth retardation has manifested itself as another case of IGF-I deficiency. In these four cases, substitution therapy can have a logically positive effect. In addition, it has recently been suggested that many other diseases are the result or cause of systemic and partial IGF-I deficiency, but more in-depth research is needed to correctly characterize these potential new IGF-I deficiency cases and their future clinical prospects [11-15].

The role of substitution therapy in the elimination or prevention of various diseases. The above-mentioned diagnostic value can be crucial for the diagnosis of diseases, as well as for understanding and even treating the pathological process that has arisen. During treatment, there is mainly a deficiency of this hormone, special attention is paid to maintaining its amount in moderation and carefully adjusting the available IGF-I levels. Summarizing the list of the growing roles of IGF-I in

physiological and pathological conditions, its potential therapeutic possibilities should be provided with treatment taking into account confirmed cases of local or systemic IGF-I deficiency and not exceeding its level above normal. Given the importance of influencing the nervous system for its normal functioning, the neuroprotective effect of it makes this system the main target for new therapeutic approaches [14, 15, 16]. Finally, concerns about the potential link between IGF-I and cancer present a complex problem that may require a more in-depth approach, and studies have shown that low doses of IGF-I are a cytoprotective factor that provides effective mitochondrial protection, anti-inflammatory and antioxidant activity, acting in the early stages of these pathogenic mechanisms. preventing oncogenesis and the development of cancer. In addition, despite constant suspicions of cancer and IGF-I, there is currently no evidence indicating a malignant transformation of a normal cell associated with IGF-I. When developing new treatments, it is necessary to take into account the interaction of IGF-binding proteins and other signaling pathways of growth factors. This evidence will be reviewed, knowledge gaps identified, and recommendations made for future research. Thus, its logical therapeutic use seems to be limited to restoring the physiological level of circulating blood in order to eliminate the clinical consequences of IGF-I deficiency. Despite constant controversy over these conditions, IGF-I treatment has never been associated with oncogenesis. Currently, the most studied cases of IGF-I deficiency are lemon syndrome in children; cirrhosis of the liver in adults; aging, including age-related cardiovascular and neurological diseases; and more recently, intrauterine development delay [11-17].

Discussion. Insulin-dependent growth hormone performs many important functions for the body, and this system is phylogenetically related to insulin and its receptors, and the insulin system is value-conservative. Insulin-dependent growth hormones penetrate the blood-brain barrier and play an important role in the performance of endocrine activity in the brain. They bind to a family of IGF-binding proteins with high affinity, which regulates the availability of IGF to interact with their receptors. It is known that the effects of each IGF and the effect resulting from this effect are specific to cells and tissues [1-4]. Understanding the importance and basic functions of IGFs in nervous tissue is considered important for understanding the paracrine or autocrine role, as well as the effect of endocrine IGFs on normal physiology and diseases of the nervous system. In particular, nowadays, when the prevalence of neurodegenerative diseases is increasing, and knowledge of the IGF system may be important for finding therapeutic goals [5, 6]. In addition, given the numerous physiological features of IGF-I, it is possible to develop their valuable therapeutic perspectives by considering the basic concepts of its importance. Thus, IGF-I is a closed regulatory hormone, the therapeutic use of which, in principle, should be limited to restoring the physiological level, but in endocrinological diseases such as hypothyroidism, diabetes, it is necessary to pay attention to the fact that it does not exceed the normal range, as usual [7-11]. In conditions of IGF-I deficiency, exogenous administration of IGF-I is usually a response to an attempt to use its anti-inflammatory, hematopoietic, antioxidant, metabolic or anabolic properties. However, despite the limited results of these strategies, they can pose certain risks. At best, these strategies require careful and short-term treatment, as with corticotherapy. Low doses of IGF-I are able to restore the level of this hormone in the blood without side effects, including hypoglycemia without side effects. IGF-I replacement therapy led to the restoration of the altered GH/IGF-I axis by reducing the level of circulating growth hormone and improving somatostatinergic tone [12, 13, 14, 15]. It is important to remember that substitution therapy should be carried out only to restore physiological levels, but in no case should it exceed physiological limits, cause no side effects and be useful for patients [16-21].

Conclusions. Thus, the physiological value of insulin-like growth hormone and its significance for diagnosis are also related to its prospects for use in treatment. Based on the available data and despite existing limitations in this regard, IGF-i therapy can only be developed to restore its physiological level as a replacement therapy. However, given that the level of IGF-1 expression varies depending on a number of clinical conditions, constant maintenance of IGF-I levels within the normal range allows you to avoid side effects caused by its use, as well as to obtain important promising treatment results.

References.

1. Lewitt MS, Boyd GW. The Role of Insulin-Like Growth Factors and Insulin-Like Growth Factor-Binding Proteins in the Nervous System. *Biochem Insights*. 2019 Apr 17;12:1178626419842176. doi: 10.1177/1178626419842176
2. Barzilai N, Huffman DM, Muzumdar RH, Bartke A. The critical role of metabolic pathways in aging. *Diabetes*. 2012;61:1315–1322.
3. Daza DO, Sundstrom G, Bergqvist CA, Duan C, Larhammar D. Evolution of the insulin-like growth factor binding protein (IGFBP) family. *Endocrinology*. 2011;152:2278–2289.
4. Puche, J.E., Castilla-Cortázar, I. Human conditions of insulin-like growth factor-I (IGF-I) deficiency. *J Transl Med* 10, 224 (2012). <https://doi.org/10.1186/1479-5876-10-224>
5. Bailes J, Soloviev M. Insulin-Like Growth Factor-1 (IGF-1) and Its Monitoring in Medical Diagnostic and in Sports. *Biomolecules*. 2021 Feb 4;11(2):217. doi: 10.3390/biom11020217
6. Gusscott S., Jenkins C.E., Lam S.H., Giambra V., Pollak M., Weng A.P. IGF1R derived PI3K/AKT signaling maintains growth in a subset of human T-cell acute lymphoblastic leukemias. *PLoS ONE*. 2016;11:e0161158. doi: 10.1371/journal.pone.0161158.
7. Annibalini G., Contarelli S., De Santi M., Saltarelli R., Di Patria L., Guescini M., Villarini A., Brandi G., Stocchi V., Barbieri E. The intrinsically disordered E-domains regulate the IGF-1 prohormones stability, subcellular localisation and secretion. *Sci. Rep.* 2018;8 doi: 10.1038/s41598-018-27233-3
8. Zhang WB, Aleksic S, Gao T, Weiss EF, Demetriou E, Verghese J, Holtzer R, Barzilai N, Milman S. Insulin-like Growth Factor-1 and IGF Binding Proteins Predict All-Cause Mortality and Morbidity in Older Adults. *Cells*. 2020; 9(6):1368. <https://doi.org/10.3390/cells9061368>
9. Backeljauw, P.F., Andrews, M., Bang, P. *et al.* Challenges in the care of individuals with severe primary insulin-like growth factor-I deficiency (SPIGFD): an international, multi-stakeholder perspective. *Orphanet J Rare Dis* 18, 312 (2023). <https://doi.org/10.1186/s13023-023-02928-7>
10. Aguirre, G.A., De Ita, J.R., de la Garza, R.G. *et al.* Insulin-like growth factor-1 deficiency and metabolic syndrome. *J Transl Med* 14, 3 (2016). <https://doi.org/10.1186/s12967-015-0762-z>
11. Harada, K., Hanayama, Y., Obika, M., Itoshima, K., Okada, K., & Otsuka, F. (2020). Clinical relevance of insulin-like growth factor-1 to cardiovascular risk markers. *The Aging Male*, 23(5), 1030–1038. <https://doi.org/10.1080/13685538.2019.1657083>
12. Werner H and Laron Z (2023) Insulin-like growth factors and aging: lessons from Laron syndrome. *Front. Endocrinol.* 14:1291812. doi: 10.3389/fendo.2023.1291812
13. Kubo, H., Sawada, S., Satoh, M. *et al.* Insulin-like growth factor-1 levels are associated with high comorbidity of metabolic disorders in obese subjects; a Japanese single-center, retrospective-study. *Sci Rep* 12, 20130 (2022). <https://doi.org/10.1038/s41598-022-23521-1>
14. Wrigley S, Arafa D and Tropea D (2017) Insulin-Like Growth Factor 1: At the Crossroads of Brain Development and Aging. *Front. Cell. Neurosci.* 11:14. doi: 10.3389/fncel.2017.00014
15. Kasprzak A. Insulin-Like Growth Factor 1 (IGF-1) Signaling in Glucose Metabolism in Colorectal Cancer. *International Journal of Molecular Sciences*. 2021; 22(12):6434. <https://doi.org/10.3390/ijms22126434>
16. Fatani TH. Diagnostic Value of IGF-1 in Growth Hormone-Deficient Children: Is a Second Growth Hormone Stimulation Test Necessary? *J Endocr Soc.* 2023 Jan 31;7(4):bvad018. doi: 10.1210/jendso/bvad018.
17. Yuen, K. C. J., Johannsson, G., Ho, K. K. Y., Miller, B. S., Bergada, I., & Rogol, A. D. (2023). Diagnosis and testing for growth hormone deficiency across the ages: a global view of the

accuracy, caveats, and cut-offs for diagnosis. *Endocrine Connections*, 12(7), e220504. Retrieved Apr 29, 2024, from <https://doi.org/10.1530/EC-22-0504>

18. Shen Y, Zhang J, Zhao Y, et al. Diagnostic value of serum IGF-1 and IGFBP-3 in growth hormone deficiency: a systematic review with meta-analysis. *European Journal of Pediatrics*. 2015 Apr;174(4):419-427. DOI: 10.1007/s00431-014-2406-3.
19. Nielsen J, Jensen RB, Juul A. Growth hormone deficiency in children. *Ugeskr Laeger*. 2014;176(25):V12130706.
20. Grimberg A, DiVall SA, Polychronakos C, et al.. Guidelines for growth hormone and insulin-like growth factor-I treatment in children and adolescents: growth hormone deficiency, idiopathic short stature, and primary insulin-like growth factor-I deficiency. *Horm Res Paediatr*. 2016;86(6):361–397.
21. Sharma R, Kopchick JJ, Puri V, Sharma VM. Effect of growth hormone on insulin signaling. *Mol Cell Endocrinol*. 2020 Dec 1;518:111038. doi: 10.1016/j.mce.2020.111038.