Mini Review

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2024.56.008844

Research Progress on Insulin-Like Growth Factor 1 in Pain

Xiang Qi[1,2], Xin Zhao[1,2] and Jie Wu[2]*

[1]*Changzhi Medical College, China*

[2]*Changzhi People's Hospital affiliated to Changzhi Medical College, China*

***Corresponding author:** Jie Wu, Changzhi People's Hospital affiliated to Changzhi Medical College, China

ARTICLE INFO

Received: April 22, 2024

Published: April 29, 2024

Citation: Xiang Qi, Xin Zhao and Jie Wu. Research Progress on Insulin-Like Growth Factor 1 in Pain. Biomed J Sci & Tech Res 56(3)-2024. BJSTR. MS.ID.008844.

ABSTRACT

Insulin-like growth factor (IGF) has a chemical structure that is similar to proinsulin, which is a single-chain polypeptide. They have same source and be synthesized primarily in liver cells but are also produced in small amounts in other tissues and cells. In recent years, an increasing body of research has found a certain correlation between IGF and pain. However, there is a lack of comprehensive reviews and evaluations of such studies in the world. This article introduces the research progress on IGF-1 in pain, aiming to contribute to further studies in this field.

Keywords: Pain; Insulin-Like Growth Factor 1; Research Progress

Introduction

The 2020 revised definition of pain by the International Association for the Study of Pain (IASP) characterizes it as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Pain is a specific physiological response to noxious stimuli and it is also considered a disease in itself, categorized by its etiology into traumatic pain, inflammatory pain, neuropathic pain, cancer pain and psychological pain. When the body experiences noxious stimuli, pain receptors detect signals generated by tissue damage. Action potentials are then generated and transmitted via nerve fibers to the central nervous system, resulting in the perception of pain. Insulin-Like Growth Factor (IGF) is a polypeptide that exerts physiological effects when it binds to its receptors. While it plays a significant role in various physiological processes such as cell proliferation, growth, metabolism and so on, there are a limited number of reviews and reports on the role of IGF in pain. This article briefly summarizes existing research on IGF-1 in pain-related conditions, providing potential insights for future pain diagnosis and treatment.

IGF Family

Discovered in 1957, the IGF family comprises IGF-1, IGF-2, IGF-1 receptors (IGF-1R), IGF-2 receptors (IGF-2R), and insulin-like growth factor binding proteins (IGFBPs). Due to its high genetic similarity to insulin and similar functions, the IGF was named "insulin-like growth factor." The primary ligands for IGF are IGF-1 and IGF-2, which exert physiological effects by binding to their respective receptors. IGF1 is synthesized in multiple tissues including liver, skeletal muscle, bone and cartilage. The changes in blood concentrations of IGF1 reflect changes in its synthesis and secretion from the liver, which accounts for 80% of the total serum IGF1 in experimental animals. The remainder of the IGF1 is synthesized in the periphery, usually by connective tissue cell types, such as stromal cells that are present in most tissues [1]. IGF-1 is a member of the insulin gene family. It is a 70 amino acid long growth factor hormone with potent anabolic effects during development. The hypothesis that IGF-1 is not only implicated in the regulation of cell growth, differentiation, and apoptosis, but it is also a potential and useful marker of malnutrition status, by defect or by excess, is supported by the U-shape relationship existing between IGF-1 serum concentrations and body mass index. [2,3].

The liver is the main source of circulating insulin-Like Growth Factor-1 (IGF-1) (more than 75%). The variety of IGF-1 activities can be partly summarized as cell proliferation and differentiation; tissue growth and development; insulin-like activity; anti-inflammatory; and antioxidant, mitochondrial protection, and prosuivival/antiaging. On the other hand, a specific and not well-understood IGF-1 activity might consist of contributing to cell polarity, acting on cytoskeleton [4,5]. As a key cytokine in the nervous system, IGF-1 produced in the tissue in response to injury sensitizes the primary afferent neurons via IGF1R and produces tissue injury-induced pain hypersensitivity [6,7]. Several studies have suggested that IGF-1 enhances T-type channel currents through the activation of IGF-1R that is coupled to a G protein–dependent PKCα pathway, thereby increasing the excitability of DRG neurons and the sensitivity to pain [8]. The research findings by Lin and colleagues provided morphological evidence that T-type Cav3.2 channel, at least partially, mediates the pain facilitation of IGF-1/IGF-1R signaling in chronic inflammatory pain condition [9].

Given the association of IGF-1 with pain, numerous studies have been conducted both domestically and internationally. Miura et al. proposed that IGF-1 produced in the tissue in response to injury sensitizes the primary afferent neurons via IGF1R and produces tissue injury-induced pain hypersensitivity [10]. Some studies have indicated a relationship between the hypothalamus-pituitary-target organ secretion axis and pain generation. Bálint et al. found that retrograde endocannabinoid is involved in the effect of IGF-1, the endocannabinoid 2-AG, tonically secreted from the GnRH neuron, decreases the excitatory GABA release from the presynaptic axon terminals and thus, suppression of the endocannabinoid production results in an increased GABA release and fine-tuning the hypothalamus-pituitary-gonadal axis [11]. In conclusion, IGF-1 is closely associated with neuropathic pain, inflammatory pain, and cancer pain.

IGF Family and Pain

IGF Family and Neuropathic Pain: Neuropathic pain refers to pain caused by nerve damage and lesions occurring anywhere in the nervous system, including peripheral nerves and the central nervous system. Chen et al. found that IGF1 (derived from astrocytes) in the lumbar cord increased along with the neuropathic pain induced by CCI. IGF1R was predominantly expressed on neurons. IGF1R antagonism or IGF1 neutralization attenuated pain behaviors induced by CCI, relieved mTOR-related suppression of autophagy, and mitigated neuroinflammation in the spinal cord. These findings reveal that the abnormal IGF1/IGF1R signaling contributes to neuropathic pain by exacerbating autophagy dysfunction and neuroinflammation [12]. Elevated IGF-1 expression is closely related to neuropathic pain, and it enhances T-type channel currents through the activation of IGF-1R that is coupled to a G protein–dependent PKCα pathway, thereby increasing the excitability of DRG neurons and the sensitivity to pain [13]. Several studies provide practical evidence for the treatment of neuropathic pain with IGF-1R antagonists.

IGF Family and Inflammatory Pain: Inflammatory pain results from biological or chemical inflammation in peripheral tissues, eliciting discomfort associated with sensory receptors and signaling pathways. There has been extensive research on inflammatory pain, both domestically and internationally, focusing on receptors, ion channels, growth factors, neurotrophic factors, prostaglandins, and more. Mayumi Miura suggested that increased tissue IGF-1 production sensitizes primary afferent neurons via the IGF1R/Akt pathway to facilitate pain hypersensitivity after tissue damage [14].

IGF Family and Cancer Pain: Cancer pain arises from tumor-induced tissue ischemia, tumor infiltration of surrounding organs, or nerve compression. It has a severe impact on patients' daily life, self-care abilities, and overall quality of life. Tas et al. found that elevated serum level of IGF-1 is associated with favorable progression-free and overall survivals in EOC patients [15]. In breast cancer, the adjuvant hormonal treatment of choice for postmenopausal estrogen-receptor-positive breast cancer, and (原文 although) the pain is usually attributed to the estrogen depletion associated with Ais. Gallicchio et al. suggested the IGF axis in the development of AI-associated musculoskeletal pain, a first step in developing effective interventions [16]. In cancer-related bone pain, Wan proposed that when the cancer cells metastasized into bone marrow, the elevated endogenous formaldehyde induced bone cancer pain through activation on the transient receptor potential vanilloid subfamily member 1 (TRPV1) in the peripheral nerve fibers. More interestingly, TRPV1 expressions in the peripheral fibers were upregulated by the local insulin-like growth factor I (IGF-I) produced by the activated osteoblasts [17]. Similarly, in a rat breast cancer model, Li and colleagues found that TRPV1 current density was significantly increased in the acutely isolated DRG neurons from bone cancer pain rats. At the same time, there was an increase in the expression of insulin-like growth factor 1 (IGF-1) in the tibial cavity [18]. This suggests that in cancer pain, IGF-1 production is mediated through the expression of TRPV1.

Conclusion and Outlook

As the fifth vital sign, pain is increasingly receiving attention and insulin-like growth factor 1 (IGF-1) plays a crucial role in the development and manifestation of pain. Given the significant impact of pain on patients' quality of life, further elucidating the mechanisms and pathophysiological processes of IGF-1 in pain is crucial. Exploring therapeutic approaches targeting the mechanisms of IGF-1 in pain management will be a focal point in research, with the aim of improving the quality of life for individuals experiencing pain.

References

1. Clemmons DR (2007) Modifying IGF1 activity: An approach to treat endocrine disorders, atherosclerosis, and cancer. Nat Rev Drug Discov 6(10): 821-833.
2. Marcello Maggio, Francesca De Vita, Fulvio Lauretani, Valeria Buttò, Giuliana Bondi, et al. (2013) IGF-1, the Cross Road of the Nutritional, Inflammatory and Hormonal Pathways to Frailty. Nutrients 5(10): 4184-4205.

3. Christa Loth Myhre, Camilla Thygesen, Birgitte Villadsen, Jeanette Vollerup, Laura Ilkjær, et al. (2019) Microglia Express Insulin-Like Growth Factor-1 in the Hippocampus of Aged APPswe/PS1ΔE9 Transgenic Mice. Frontiers in Cellular Neuroscience 13: 308.
4. Lara Diaz V J, I Castilla Cortazar, I Martín Estal, M García Magariño, GA Aguirre, et al. (2017) IGF-1 modulates gene expression of proteins involved in inflammation, cytoskeleton, and liver architecture. Journal of physiology and biochemistry 73(2): 245-258.
5. Salso Angela, Giuseppe Tisone, Laura Tariciotti, Ilaria Lenci, Tommaso Maria Manzia, et al. (2014) Relationship between GH/IGF-1 axis, graft recovery, and early survival in patients undergoing liver transplantation. BioMed research international 2014: 240873.
6. Mayumi Miura, Mika Sasaki, Keiko Mizukoshi, Masayuki Shibasaki, Yuta Izumi, et al. (2011) Peripheral sensitization caused by insulin-like growth factor 1 contributes to pain hypersensitivity after tissue injury. Pain 152(4): 888-895.
7. Li Y, J Cai, Y Han, X Xiao, X L Meng, et al. (2014) Enhanced function of TRPV1 via up-regulation by insulin-like growth factor-1 in a rat model of bone cancer pain. European journal of 18(6): 774-784.
8. Zhang Y, Qin W, Qian Z, Xingjun Liu, Hua Wan, et al. (2014) Peripheral pain is enhanced by insulin-like growth factor 1 through a G protein-mediated stimulation of T-type calcium channels 7(346).
9. Lin SF, Yu XL, Wang B, Ya-Jun Zhang, Yan-Gang Sun, et al. (2016) Colocalization of insulin-like growth factor-1 receptor and T type Cav3.2 channel in dorsal root ganglia in chronic inflammatory pain mouse model. Neuro report 27(10): 737-743.
10. Miura M, Sasaki M, Mizukoshi K, Shimosato G, Amaya F, et al. (2011) Peripheral sensitization caused by insulin-like growth factor 1 contributes to pain hypersensitivity after tissue injury. Pain 152(4): 888-895.
11. Bálint F, Csillag V, Vastagh C, Zsolt Liposits, Imre Farkas, et al. (2021) Insulin-Like Growth Factor 1 Increases GABAergic Neurotransmission to GnRH Neurons via Suppressing the Retrograde Tonic Endocannabinoid Signaling Pathway in Mice. Neuroendocrinology 111(12): 1219-1230.
12. Chen X, Le Y, He WY, Jian He, Yun-Hua Wang, et al. (2021) Abnormal Insulin-like Growth Factor 1 Signaling Regulates Neuropathic Pain by Mediating the Mechanistic Target of Rapamycin-Related Autophagy and Neuroinflammation in Mice. ACS Chem Neurosci 12(15): 2917-2928.
13. Zhang Y, Qin W, Qian Z, Xingjun Liu, Hua Wang, et al. (2014) Peripheral pain is enhanced by insulin-like growth factor 1 through a G protein-mediated stimulation of T-type calcium channels. Sci Signal 7(346): ra94.
14. Miura M, Sasaki M, Mizukoshi K, Masayuki Shibasaki, Yuta Izumi, et al. (2011) Peripheral sensitization caused by insulin-like growth factor 1 contributes to pain hypersensitivity after tissue injury. Pain 152(4): 888-895.
15. Tas F, Karabulut S, Serilmez M, Didem Tastekin, Derya Duranyildiz, et al. (2014) Clinical significance of serum insulin-like growth factor-1 (IGF-1) and insulinlike growth factor binding protein-3 (IGFBP-3) in patients with epithelial ovarian cancer. Tumour Biol 35(4): 3125-3132.
16. Gallicchio L, MacDonald R, Helzlsouer KJ (2013) Insulin-like growth factor 1 and musculoskeletal pain among breast cancer patients on aromatase inhibitor therapy and women without a history of cancer. J Cancer Res Clin Oncol 139(5): 837-843.
17. Wan Y, Zhiqian Tong, Wenhong Luo, Yanqing Wang, Fei Yang, et al. (2016) New Mechanism of Bone Cancer Pain: Tumor Tissue-Derived Endogenous Formaldehyde Induced Bone Cancer Pain via TRPV1 Activation. Adv Exp Med Biol 904: 41-58.
18. Li Y, Cai J, Han Y, X Xiao, X L Meng, et al. (2014) Enhanced function of TRPV1 via up-regulation by insulin-like growth factor-1 in a rat model of bone cancer pain. Eur J Pain 18(6): 774-784.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2024.56.008844

Jie Wu. Biomed J Sci & Tech Res