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Mini Review

Myostatin Serum Related to Sarcopenia Among Elderly Population

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Abstract
Background Sarcopenia is a decrease in muscle mass accompanied by a decrease in muscle strength and performance. Sarcopenia arises from a disturbance of the complex balance between anabolic and catabolic factors. Myostatin strongly influences the inhibition of muscle growth by increasing muscle catabolism. Increased myostatin will atrophy in skeletal muscle. In the aging process, there will be an increase in the hormone myostatin plays an active role in the process of sarcopenia. The cause of the increase in myostatin hormone is a chronic inflammatory process that occurs in the aging process.
Methods The writing of this paper is a literature review of the role of myostatin in sarcopenia that occurs due to the aging process.
Results The incidence of sarcopenia in the elderly was 45 people (64.3%). The results of the analysis were a significant difference between myostatin levels in sarcopenia (47.59 ng/mL) and non-sarcopenia (39.7 ng/mL) subjects. The limit of myostatin levels that can cause an increase in muscle catabolic processes is 48.91 ng/mL. The prevalence ratio of the incidence of sarcopenia based on myostatin levels in the elderly was 3.84, while based on the combined risk of age and myostatin levels was 9.75.
Conclusion From the literature review, it was found that there was a significant difference in myostatin levels between the elderly with and without sarcopenia. The prevalence of high myostatin levels in the elderly is almost 4 times higher than in young adults. This will lead to the progression of sarcopenia.
KEYWORDS myostatin, katabolic sarcopenia, elderly

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Sarcopenia in Aging Process

Sarcopenia is a muscle disorder characterized by reduced strength and muscle mass and decreased physical performance. Condition sarcopenia in an aging process makes decreased muscle mass and strength associated with aging. Sarcopenia is a condition characterized by loss of muscle mass and function. Sarcopenia is a syndrome characterized by a progressive and comprehensive loss of skeletal muscle mass and strength and is closely associated with a physical disability, quality of life, and death. Risk factors for sarcopenia include age, gender, and level of physical activity. In aging, lean body mass is lost while fat mass can be maintained or even increased. Loss of muscle mass may be associated with an increase in body fat so that even if the weight is normal, there is marked weakness. There is an important correlation between inactivity and loss of

muscle mass and strength as well as an increase in fat mass.[1,2]

Decreased muscle mass does occur in people who are not physically active. Decreased muscle strength usually begins at the age of 40 years and the process will accelerate after the age of 75 years. [2]

Sarcopenia, in an aging process, are loss of mass and strength of the muscle. Loss of muscle mass in sarcopenia patients is caused by progressive muscle atrophy, loss of type 2 muscle fibers and motor neurons, and fat cell infiltration. The process of muscle loss itself is multifactorial and can be caused by the influence of lifestyle, activation of inflammatory pathways, degeneration of the neuromuscular system, and changes in hormone levels and sensitivity.[5]

Researchers from The Columbia University Medical Center found that the decline in muscle strength with aging occurs due to leakage of calcium from protein groups in muscle cells called ryanodine which then triggers a series of events that limit muscle fiber contraction.[3] Decreased available calcium, contributes to decreased muscle contractions causing the muscles to become weak.[4]

In addition, there is also a loss of muscle strength in sarcopenia. Early diagnosis of sarcopenia in the elderly is very important because it will determine the management strategy and prognosis of the patient's disability. The three main components in the diagnosis of sarcopenia are an objective measurement of muscle mass, measurement of muscle strength, and analysis of physical performance.[6]

The two most important components in the management of sarcopenia are nutrition and physical exercise. Nutrition mainly maintains adequate protein intake and aims to prevent the further mass loss, as well as support mass gain in patients who are given physical exercise. While physical exercise in the elderly aims to increase mass and muscle and improve muscle performance to reduce disability.[5,6]

Role of Hormone in Sarcopenia

In the aging process, there will be changes in body composition that include a gradual decrease in skeletal muscle mass along with a decrease in muscle strength.[7] One of the causes of decreased muscle mass is the endocrine changes associated with aging. During the aging process, there is often a decrease in the secretion of key hormones that stimulate muscle mass and function. skeletal system (growth hormone, insulin-like growth factor 1 (IGFI), testosterone, and estradiol). On the other hand, changes in IGF-I signaling along with decreased insulin sensitivity also have an important impact on myogenesis.[8,9] In addition, catabolic hormones such as cortisol and angiotensin II can accelerate aging-induced muscle atrophy, as they are involved in muscle wasting and their levels increase with age. The role played by these hormones is considered a therapeutic tool to treat sarcopenia.[10]

Myostatin as a target for skeletal muscle anabolic hormones

Myostatin is a selective cytokine that has the potential to inhibit myogenesis. Mechanism of the anabolic action of growth hormone (GH) on skeletal muscle growth, influenced by inhibition of myostatin mRNA expression. [11] The inhibitory effect of growth hormone on myostatin is associated with an increase in lean body mass. This will lead to a decrease in skeletal muscle myotubes due to the effect of myostatin as a potential key target for GH-induced anabolism. Elderly people with myostatin levels ≥48.91 pg/mL have a prevalence of sarcopenia almost 4 times higher than elderly with myostatin levels. [12] The performance of myostatin in sarcopenia can be through the myostatin-smad

pathway which will inhibit mTOR in response to growth-supporting signals (such as insulin and IGF-1). [13] Under normal circumstances, IGF-1 and insulin stimulate protein synthesis through activation of the Akt/mTOR/P70s6k pathway and at the same time inhibit forkhead box O (FoxO) via phosphorylation. [14,15] Under pathological conditions, phosphorylation does not inhibit FoxO, resulting in the accumulation of FoxO in the nucleus which then binds to DNA. This binding will induce the transcription of E3 ubiquitin ligase. Through this pathway, myostatin is involved in the proliferation and differentiation of skeletal muscle precursor cells, and the degradation pathways of myofiber maturation proteins[16]

Myostatin also plays a role in regulating muscle-to-fat cross-talk, further exacerbating metabolic dysfunction in the elderly.[17]

So myostatin signals function to regulate muscle mass and strength. Myostatin is a superfamily of TGF- which is secreted only in skeletal muscle. Its cellular effects are mediated through an autocrine/paracrine process by binding to activin type II A and B receptors (ActRIIA and ActRIIB). [18,19] This stimulates the phosphorylation of Smad2 and Smad3, which combines with Smad4 to form the Smad2/3/4 complex that triggers gene transcription. [20,21] Thus Myostatin is a major regulator of skeletal muscle growth where its overexpression induces muscle atrophy. Myostatin expression has been reported to be increased in several human diseases associated with skeletal muscle wasting, such as cancer cachexia, AIDS, heart failure, and sarcopenia in the aging process. [22]

Currently being developed to treat aging-associated muscle loss with myostatin inhibitor therapy, a negative regulator of skeletal muscle mass. Knockout mouse studies have shown that myostatin also affects adiposity and changes in glucose levels. Lower serum insulin and glucose levels in rats. Clinical intervention can inhibit the loss of skeletal muscle mass with aging and can have beneficial effects on other organ systems as well.[23] In skeletal muscle, the most important inhibitor of muscle growth is a member of the TGFβ family known as myostatin, also called growth differentiation factor 8 (GDF8). Myostatin/GDF8 inhibits muscle differentiation and causes differentiated myotubes to atrophy. Loss of myostatin function increases muscle mass (Figure 1).[24]

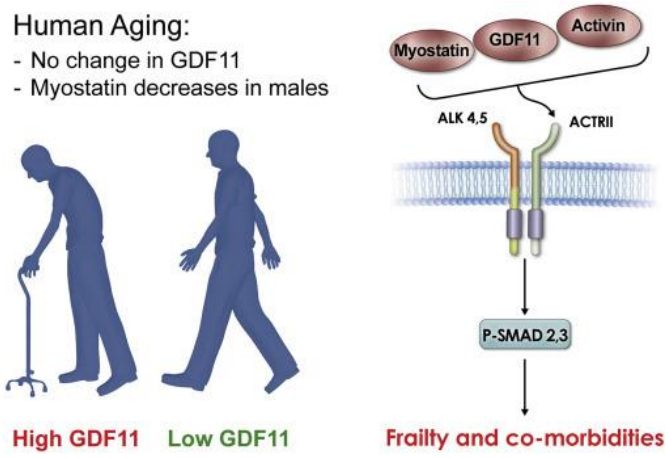

Figure 1. GDF11. Total Protein Levels and Mechanisms

Signaling myostatin, GDF11, and activin via the ActRII/Alk4,5 complex induces SMAD2 and SMAD3 phosphorylation. The induction of phosphorylation will decrease skeletal muscle growth. In humans, GDF11 is not regulated by age, whereas myostatin is decreased in men.[25] Myostatin and Activin A were shown to function via the type II (IIa or IIb) activin receptor complex, which then induces activation of ALK4 or ALK5 type I receptors. ALK activation induces phosphorylation and activation of the transcription factors SMAD2 and SMAD3, which translocate to the nucleus upon phosphorylation, suppressing genes required for muscle differentiation. Myostatin signaling pattern can induce myotube atrophy and inhibit differentiation.[26]

Conclusion

Myostatin is a protein that is the target of anabolic hormones, where myostatin protein can be considered to be used for early detection in the process of sarcopenia.

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