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Effect of Novel Biomarkers like Asprosin, Visfatin, and Subfatin in Cases of Metabolic Syndrome: A Systematic Review

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ABSTRACT

Metabolic Syndrome (MetS) is a group of conditions that increases the risk of type 2 diabetes mellitus (T2DM),stroke and cardiovascular diseases.It is characterized by insulin resistance, abdominal obesity, hypertension, and dyslipidemia. In 1999 World Health Organization (WHO) tried to explain MetS.It was later addressed by organizations such as the National Cholesterol Education Program (NCEP) and the International Diabetes Federation (IDF). MetS can cause other health related problems as well as atherosclerosis and in due course of time the organ failure occurs. Conditions like increased abdominal girth, hypercholesterolemia, high blood pressure and raised blood sugar may suggest for metabolic syndrome and this is seen as a red flag sign to one's detoriating health conditions. The main factors which are contributing to MetS or insulin resistance, obesity, PCOS and fatty liver. Now recent works on novel biomarkers like Asprosin, Visfatin and Subfatin offer a great inside into MetS. Asprosin is a protein hormone secreted by white adipose tissues and was discovered in 2016. It has a role in glucose and lipid metabolism. It is also linked to insulin resistance and also helps in improving insulin sensitivity. Visfatin is produced by visceral fat which also known as nicotinamide phosphoribosyl transferase (NAMPT).It regulates glucose and fat metabolism. It increases insulin sensitivity and promotes angiogenesis. Subfatin is produce by subcutaneous fat tissues it also known as C19ORF10 and controls sugar and fat metabolism.It is found in lower amount in persons having T2DM and in pre-diabetic persons thus it has a role in metabolism of glucose and fat.These hormones contribute to the pathophysiology of MetS and obesity, and measuring their levels can provide valuable insights into disease development. Further Research are needed to understand the mechanism of action of these biomarkers and finding their clinical potentials. Understanding these hormones could lead to better diagnosis and treatment of MetS and related conditions like dyslipidemia and fatty liver. This standardized understanding of MetS has facilitated research, clinical management, and public health interventions targeting its prevention and treatment.

Keywords: Insulin Resistance, Metabolic Syndrome, Obesity

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INTRODUCTION

Metabolic syndrome (MetS), a constellation of interconnected metabolic abnormalities, has garnered significant attention in recent decades due to its association with increased risk of cardiovascular disease and diabetes. However, the roots of MetS trace back nearly a century, with various descriptions and labels highlighting its dysmetabolic phenotype. This article provides a historical overview of MetS, beginning with early observations by physicians such as Eskil Kylin and Jean Vague, who identified associations between obesity, diabetes, hyperglycemia, and cardiovascular risk factors. The term "metabolic syndrome" was introduced by Haller, Singer, and later by Gerald Reaven, who emphasized the role of insulin resistance in the syndrome's pathophysiology. With the global rise in obesity prevalence, the burden of MetS has increased substantially, contributing significantly to the burden of diabetes and cardiovascular disease worldwide. Understanding the historical context and evolution of MetS is crucial for addressing its contemporary challenges and developing effective prevention and management strategies. Here we are reviewing the effect of new biomarkers like Asprosin, Visfatin and Subfatin in obesity and metabolic syndrome.

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Effect of Asprosin

Asprosin appears to be a crucial regulator of hepatic glucose release, particularly during fasting states. Here's a breakdown of the key characteristics and implications of Asprosin as described in the provided text:

***Origin and Secretion*:**Asprosin is derived from the C-terminal cleavage of profibrillin, a protein found in white adipose tissue. It is secreted into the bloodstream, where it circulates at nanomolar levels.

***Target Organ*:**Asprosin primarily targets the liver, where it exerts its effects on glucose release.

***Mechanism of Action*:** Upon reaching the liver, Asprosin activates the G protein-cAMP-PKA pathway. This activation leads to the rapid release of glucose into the bloodstream from hepatic stores.

***Pathological Role*:** Elevated levels of plasma Asprosin are observed in humans and mice with insulin resistance. This suggests a potential link between Asprosin and metabolic disorders such as type II diabetes and metabolic syndrome.

***Impact of Loss of Function*:** Studies indicate that reducing Asprosin levels, either through immunological or genetic means, results in decreased hepatic glucose release. This, in turn, leads to lower levels of glucose and insulin in the bloodstream.

***Therapeutic Potential*:** Given its role as a glucogenic protein hormone, targeting Asprosin therapeutically could offer benefits in managing conditions like type II diabetes and metabolic syndrome. Strategies to modulate Asprosin levels could potentially help regulate glucose metabolism and improve insulin sensitivity.

Overall, Asprosin represents a promising target for therapeutic intervention in metabolic disorders characterized by dysregulated glucose metabolism. Further research into its precise mechanisms of action and potential therapeutic strategies is needed to explore its expended clinical utility.The discovery of Asprosin adds to the understanding of the complex hormonal regulation of glucose homeostasis.

Consequences of Dysregulation of Asprosin

Perturbations in the hormonal regulation of glucose, including alterations in Asprosin levels, can have pathological consequences. Dysregulation of Asprosin may contribute to metabolic disorders such as lipodystrophy and abnormalities in insulin and glucose levels, highlighting its importance in maintaining metabolic health.

Overall, the discovery of Asprosin sheds light on the intricate network of hormones involved in glucose regulation and highlights its potential as a therapeutic target for managing metabolic disorders. Further research into the mechanisms of action and physiological effects of Asprosin is necessary to fully understand its role in glucose homeostasis and its therapeutic implicationsin metabolic response to physical activity. Specifically, exercise has been shown to influence the secretion of various hormones and signaling molecules involved in metabolism, including Asprosin.

Several studies have explored the impact of exercise on Asprosin levels. For example, a study by Gonzalez-Gil and Elizondo-Montemayor in 2020 investigated the effect of exercise on Asprosin release and its potential implications for metabolic disorders. They found that exercise can modulate the secretion of Asprosin, suggesting a potential role for physical activity in regulating Asprosin levels and, consequently on metabolic function.

Moreover, given the association between Asprosin and metabolic disorders such as insulin resistance and obesity, understanding the impact of exercise on Asprosin release could have significant clinical implications. Exercise-induced changes in Asprosin levels may contribute to the beneficial effects of physical activity on metabolism,including improved glucose regulation, reduced inflammation, and enhanced energy substrate utilization.

Further research is needed to elucidate the precise mechanisms underlying the relationship between exercise and Asprosin regulation. Additionally, exploring how different types, intensities, and durations of exercise influence Asprosin secretion could provide valuable insights into optimizing exercise interventions for the prevention and management of metabolic-related diseases.

Effect of Visfatin

The role of Visfatin, an adipocytokine, in obesity and related metabolic disorders. Here's a breakdown of the main points:

***Visfatin Production*:** Initially thought to be produced only by visceral adipose tissue, it's now known that Visfatin is produced widely in various tissues throughout the body, including immune cells like macrophages. This broad distribution implicates its potential role beyond just adipose tissue.

***Source of Visfatin*:** While adipocytes and macrophages, particularly those in visceral fat, are considered major sources of Visfatin, the stromal vascular fraction of adipose tissue expresses significantly more Visfatin than adipocytes. This suggests that adipocytes may not be the primary source in adipose tissue.

***Differences in Production*:** In obese individuals, visceral fat becomes a more potent producer of Visfatin, while subcutaneous fat may either diminish or maintain its production. This raises questions about whether changes in Visfatin production are solely due to adipocytes or if macrophages play a significant role, especially in the context of obesity.

***Gender Influence*:**Visfatin plasma concentrations have been negatively correlated with BMI only in men in some studies, but the interpretation of these findings is complicated by conflicting results from other studies and the known differences in adiposity distribution between genders.

***Association with BMI and Lipid Metabolism*:** Visfatin mRNA expression in adipose tissue is associated with BMI, with a negative correlation observed in subcutaneous fat and a positive correlation in visceral fat. Visfatin plasma levels show varying associations with lipid metabolism markers such as HDL-cholesterol and triglycerides, with conflicting results across different studies.

***Visfatin in Children*:** In children, plasma Visfatin levels may positively correlate with BMI and increase in obese children, potentially indicating a link between Visfatin and metabolic syndrome components.

Overall, the complexity of Visfatin's role in obesity and related metabolic disorders, involving interactions between adipocytes, macrophages, and various tissues, as well as potential gender differences and its associations with lipid metabolism.

Effect of Subfatin

Subfatin, a newly discovered secretory protein identified through advanced bioinformatic techniques, exhibits induction by exercise in skeletal muscle and cold stimulation in adipocytes. Its role in promoting white adipose tissue browning, enhancing thermogenesis, accelerating adipose tissue decomposition, and improving insulin resistance suggests its potential significance in metabolic syndrome (MS). Consequently, it holds promise as a therapeutic target for MS. However, despite these promising attributes, the precise mechanisms underlying its interaction with various signaling pathways remain largely unknown, hindering its immediate clinical application. Additionally, the relationship between Subfatin and fatty liver has yet to be explored, indicating further avenues for research to expand our understanding of Subfatin's impact on MS, particularly through its correlation with fatty liver.

The study investigated the serum levels of Subfatin, an adipokine with insulin-sensitizing properties, in patients with type-2 diabetes mellitus (T2DM), prediabetes subjects, and controls. Additionally, it examined the levels of adhesion molecules and their association with Subfatin levels in these groups.

Here's a breakdown of the key findings:

Subfatin Levels in T2DM and Prediabetes Groups: The study found that serum levels of Subfatin were lower in both the T2DM group and the prediabetes group compared to the control group. This suggests a potential association between decreased Subfatin levels and the development of diabetes.

***Adhesion Molecule Levels*:** The serum levels of adhesion molecules were higher in the T2DM group. Adhesion molecules involves in endothelial dysfunction, which is commonly associated with diabetes and its complications.

***Comparison in Obese vs. Lean T2DM Patients*:** Among T2DM patients, serum Subfatin levels were lower in obese patients compared to lean patients. This suggests that obesity may further decrease Subfatin levels in individuals with T2DM.

***Association with Vascular Adhesion Molecules*:** The study found a negative association between Subfatin levels and vascular adhesion molecules (such as ICAM-1, VCAM-1, and E-selectin) in both prediabetes subjects and the T2DM group. This suggests that lower Subfatin levels may be associated with increased endothelial dysfunction, as indicated by higher levels of adhesion molecules.

Overall, the findings suggest that decreased serum levels of Subfatin may be implicated in the pathogenesis of diabetes and endothelial dysfunction. Further research is needed to understand the role of Subfatin in these conditions and its potential as a therapeutic target for managing diabetes and related vascular complications.

DISCUSSION

Metabolic Syndrome (MetS) has evolved from early observations into a formally recognized constellation of metabolic abnormalities associated with increased risk of cardiovascular disease and diabetes. Its history traces back to the late 20thcentury, marked by formalization efforts such as those by the WHO and subsequent discussions by medical organizations like EGIR, AACE, and NCEP/ATPIII. The consensus on MetS components, including obesity, impaired glucose metabolism, hypertension, and atherogenic dyslipidemia, has facilitated research and clinical interventions.

One crucial regulator of glucose release, particularly during fasting, is Asprosin. Derived from profibrillin cleavage in white adipose tissue, Asprosin targets the liver and activates the G protein-cAMP-PKA pathway to release glucose into the bloodstream. Elevated plasma Asprosin levels are linked to insulin resistance and metabolic disorders, suggesting therapeutic potential in managing conditions like type II diabetes and MetS.Exercise influences the secretion of various metabolic hormones, including Asprosin. Studies indicate that exercise can modulate Asprosin secretion, potentially contributing to improved glucose regulation and metabolic function. Further research is needed to understand the mechanisms underlying exercise-induced changes in Asprosin levels fully.

Another adipocytokine, Visfatin, plays a complex role in obesity and metabolic disorders. While initially associated with visceral adipose tissue, Visfatin is produced in various tissues, implicating broader physiological roles. Its production in obese individuals, particularly in visceral fat, underscores its potential involvement in metabolic dysregulation. Gender differences and associations with BMI and lipid metabolism further highlight the complexity of Visfatin's role in metabolic health.

Subfatin, a newly discovered adipokine, shows promise in promoting white adipose tissue browning, enhancing thermogenesis, and improving insulin resistance, suggesting therapeutic potential for MetS. However, its mechanisms of action and relationship with fatty liver require further investigation for clinical application.A recent study examined Subfatin levels in T2DM and prediabetes groups, revealing lower serum levels in both compared to controls. Higher levels of adhesion molecules in the T2DM group, along with a negative association between Subfatin levels and vascular adhesion molecules, suggest implications for diabetes pathogenesis and endothelial dysfunction. Understanding Subfatin's role could offer insights into managing diabetes and related vascular complications.

In summary, MetS has undergone formalization over time, leading to consensus on its components and facilitating research and clinical interventions. Asprosin, Visfatin, and Subfatin represent emerging targets for understanding and managing MetS. Exercise modulation of Asprosin secretion and the complex roles of Visfatin and Subfatin in metabolic health underscore the need for further research to elucidate their mechanisms and therapeutic potential. Understanding the intricate interplay between these regulatory molecules and metabolic pathways is crucial for developing effective strategies to prevent and manage MetS and associated complications.

CONCLUSION

Metabolic Syndrome (MetS) stands as a significant health challenge in contemporary society, marked by a constellation of metabolic abnormalities that predispose individuals to cardiovascular disease and diabetes. Its journey from early observations to formal recognition reflects a nuanced understanding of its components and implications. This article has provided an in-depth historical overview of MetS, tracing its formalization process initiated by organizations like the WHO and subsequent discussions by medical groups such as EGIR, AACE, and NCEP/ATPIII.

The consensus on MetS components, including obesity, impaired glucose metabolism, hypertension, and atherogenic dyslipidemia, has not only facilitated research but also streamlined clinical interventions and public health initiatives aimed at its prevention and management. However, the complexity of MetS necessitates a deeper understanding of its underlying mechanisms and regulatory factors.

One such factor is Asprosin, a crucial regulator of hepatic glucose release, particularly during fasting. Its discovery and characterization shed light on the intricate hormonal regulation of glucose homeostasis and its potential as a therapeutic target for managing metabolic disorders like type II diabetes and MetS. Furthermore, the influence of exercise on Asprosin secretion underscores the importance of lifestyle interventions in modulating metabolic health.

Visfatin, another adipocytokine, adds to the complexity of MetS with its broad distribution in various tissues and its associations with obesity and lipid metabolism. Its intricate roles underscore the need for further research to elucidate its mechanisms and potential implications for metabolic health.

Similarly, Subfatin, a newly discovered adipokine, holds promise in addressing MetS through its involvement in promoting white adipose tissue browning, enhancing thermogenesis, and improving insulin resistance. Despite its therapeutic potential, the precise mechanisms underlying Subfatin's interaction with signaling pathways require further exploration.

A recent study examining Subfatin levels in T2DM and prediabetes groups revealed lower serum levels in both compared to controls. This finding, coupled with higher levels of adhesion molecules in the T2DM group and the negative association between Subfatin levels and vascular adhesion molecules, suggests implications for diabetes pathogenesis and endothelial dysfunction. Understanding Subfatin's role could offer valuable insights into managing diabetes and related vascular complications.

In conclusion, MetS represents a multifaceted health issue influenced by various genetic, environmental, and lifestyle factors. Its formalization and recognition over time have paved the way for comprehensive research and targeted interventions. The discoveries of regulatory molecules like Asprosin, Visfatin, and Subfatin offer promising avenues for understanding and managing MetS. However, further research is needed to unravel their intricate roles and therapeutic potentials fully. By elucidating the complex interplay between regulatory molecules and metabolic pathways, we can develop more effective strategies for preventing and managing MetS and its associated complications, ultimately improving public health outcomes.

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