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Review Article

Biomarkers in epilepsy- Rising role of serum asprosin levels: A comprehensive review

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ABSTRACT:
A class of long-term neurological conditions known as epilepsy is defined by frequent, unpredictable, and spontaneous seizures. Tens of millions of people worldwide are afflicted by this prevalent neurological condition. The intricacy of epileptogenesis, in which immunological processes, epigenetic modifications, and structural alterations in neural tissues have been recognized as playing a vital role, has been disclosed by comprehensive investigations on epilepsy conducted in recent decades. Asprosin presents a promising option for both innovative pharmacological treatment approaches and diagnostic instruments; nonetheless, further comprehension of its operation and signaling pathways is still required.
Key words: Epilepsy, Asprosin

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INTRODUCTION

Paroxysmal spells may indicate events resulting from disorders of the central nervous system, heart problems, psychological issues, or other etiologies. The differential diagnosis of a transient event with movements includes syncope, convulsive concussion, convulsive syncope, rigors, movement disorders, sleep-related events, and psychogenic nonepileptic seizures. Paralyzing seizures are one kind of paroxysmal occurrence.[1- 3]

The brain or specific brain regions that are hyperactive and send too many messages are associated with epilepsy. This leads to epileptic fits, which are seizures. Although a few muscles may twitch during a seizure, they can also force your entire body to spasm, or shake uncontrollably, and cause you to lose consciousness. Any age can get epilepsy. Some people have already experienced their first seizure as children, while others do not experience seizures until they are older. Between seizures, there are typically no outward signs. However, a lot of people are concerned about having another seizure. Both seizure prevention and preserving a high quality of life are made possible by medication. Sadly, it isn't always beneficial: Three out of ten persons still experience seizures on a regular basis.. This makes it particularly difficult for them to live with epilepsy.[4- 6]

Epilepsy has been identified by the World Health Organization (WHO) and its collaborators as a significant public health issue. Hyperexcitability and an imbalance between excitation and inhibition are the causes of epilepsy, which results in seizures1. The World Health Organization estimates that fifty million individuals worldwide suffer with epilepsy, making it one of the most prevalent neurological conditions in the world. Epilepsy is a neurological condition marked by recurring seizures brought on by an abrupt spike in the brain's electrical activity. This results from synchronized hyperexcitability of neurons or aberrant neuronal discharges. But each person experiences these seizures at a different rate.[6]

DEFINITION

One must be completely conversant in the official vocabulary and nomenclature used to describe seizures and epilepsy in order to comprehend seizures and epilepsy. Seizures are defined as abnormal electrical perturbations resulting from a network of neurons, according to the International League Against Epilepsy (ILAE), the primary regulatory

organization for terminology and nomenclature related to seizures and epilepsy (Berg et al. 2010). The definition of epilepsy was updated in 2014 by an ILAE working team (Fisher et al. 2005, 2014).

In the event that an individual fulfills any of the subsequent criteria, they are diagnosed with epilepsy:[7- 9]

At least two unprovoked or reflex seizures occurring >24 hours apart.

- One unprovoked or reflex seizure and a probability of further seizures similar to the general recurrence risk of at least 60% after two unprovoked seizures occurring over the next 10 years.
- A diagnosis of an epilepsy syndrome.
- As such, it is possible that someone can have the diagnosis of epilepsy after having one seizure depending on the etiology and the electroclinical syndrome.

When a person with an age-dependent epilepsy syndrome reaches adulthood and has not taken medication for seizures for the previous five years, or when they have not experienced a seizure in the last ten years, their condition is deemed resolved. In line with other heterogeneous disorders like cancer and heart disease, which are also referred to as illnesses to emphasize the gravity of the condition to lay audiences, epilepsy is now referred to as a disease rather than a disorder under this new definition.[7- 9]

BLOOD BIOMARKERS IN EPILEPSY

There is hope in the epilepsy sector due to our growing understanding of how biochemical indicators can represent brain dysfunction. The utility of such techniques for larger patient groups is limited by cost and impracticality, despite the fact that there is a lot of fascinating research employing connectivity/resting state imaging to detect epilepsy and devices ranging from smart watches to implantable EEG to quantify seizure load. A more scalable solution would be blood testing that could detect epilepsy and seizure burden.

Though it is not impossible, diagnosing epilepsy with blood testing is a significant difficulty. Patients who experience their first seizure are an enriched, high-risk group that frequently interacts with healthcare providers. This makes it possible to acquire blood samples for analysis using high-throughput screening techniques. Pilot research has shown feasibility. Examining individuals who have a recent brain injury and a high risk of developing symptomatic epilepsy is an additional strategy. One advantage of this strategy is that possible epileptogenesis has a defined starting date. The EpiBios4Rx project for posttraumatic epilepsy and the testing of biomarkers panels in acute stroke are two examples of this methodology in action.

Quantifying seizure burden is an important use of blood biomarkers in epilepsy. At the moment, the clinical response—the lack of overt seizures—is used to determine how much ASM to take. Management would be substantially aided by biomarkers of disease activity, such as HBA1c for diabetes or NT-proBNP for heart failure. To enable interventions such as sleep therapy or adjustment of ASM therapy prior to a clinical seizure, the marker or markers should ideally be responsive to slight quantities of subclinical seizure activity. From a conceptual standpoint, seizures do leave physiological traces, such as momentarily elevated lactate levels.[10-12]

Prognostic biomarkers

"Identify likelihood of a clinical event, disease recurrence or progression in patients who have the disease or medical condition of interest" is the purpose of prognostic biomarkers. For instance, predictive biomarkers for the development of epilepsy following a particular type of brain injury include neural specific enolase, NSE, S100B, serum metalloproteinase 9, IL-6, IL-8, IL-17a, IL-1b, IL-1Ra, IL-10, IL-17a, TNF-α, and sTNFr2. Prognostic biomarkers that indicate the onset of cognitive damage following an epilepsy diagnosis are another example. Prognostic biomarkers are applied to populations that already have a condition, whether or not medicine is being taken. This is how they vary from susceptibility or risk biomarkers. Crucially, the kind of drug (such as AEDs) may affect the prognostic biomarkers' ability to distinguish between outcomes in terms of sensitivity and specificity. [13]

Pharmacodynamic/response biomarkers

"A biomarker used to show that a biological response has occurred in an individual who has been exposed to a medical product or an environmental agent" is what is meant to be understood by pharmacodynamic/response biomarkers. A shift in the level of pharmacodynamic/response biomarkers (small plasma molecules, for example) in response to treatment exposure can mean that a treatment is engaging its target, offer early proof-of-concept evidence that it is biologically active and/or affecting a clinical endpoint, offer guidance on how to vary the dosage and duration of a novel treatment, or raise potential safety concerns. Pharmacodynamic/response biomarkers are frequently classified as monitoring biomarkers due to the serial nature of their examination.[13]

Asprosin as biomarker

Adipokines, or adipose-derived secreted factors, are a class of bioactive mediators with both pro- and anti-inflammatory properties that are produced by adipose tissue, which functions as a major energy storage endocrine organ. Adipocytes, which are lipid-rich cells found in white adipose tissue, the major kind of fat in mammals, are the primary producers of adipokines, albeit they are not the only ones. They can quickly enter the systemic circulation and use the autocrine, paracrine, and endocrine networks of intercellular communication to carry out their

activities. Additionally, they preserve the control of a number of normal metabolic processes in the human body, such as insulin sensitivity, inflammatory response, and glucose and lipid homeostasis. [14]

Asprosin is a new glucose sensor that plays a variety of peripheral or central metabolic activities. It is mostly secreted by white adipose tissue during fasting. The FBN1 gene's 3' truncated mutation decreases the maintenance of healthy fat tissue and results in inadequate asprosin expression. According to its expressed protein asprosin, the FBN1 gene may have distinct effects on both healthy and pathological states. Asprosin stimulates the hypothalamic nuclei ARH and PVN, which in turn cause sympathetic flow and appetite stimulation, respectively. Peripherally, asprosin causes enhanced insulin resistance, inflammation, and endoplasmic reticulum stress due to its direct impact on insulin signaling. Asprosin's discovery has led to new understandings in clinical diagnostic practice, especially with regard to chronic diseases with increased frequency, such type 2 diabetes and obesity.[14]

Yaryari AM, et al. measured the serum concentrations of asprosin, a new glucogenic adipokine generated from white adipose tissue, in patients with epilepsy receiving valproic acid treatment. Three groups of sixty-six individuals with idiopathic tonic-clonic generalized epilepsy were identified: twenty-two patients who were newly diagnosed or untreated, valproic acid treatment (n = 22), and lamotrigine treatment (n = 22). Twenty-two healthy volunteers with a similar age and gender distribution made up the control groupFor both the patient and control groups, measurements of body mass index (BMI), fasting serum levels of asprosin, glucose, insulin, glycohemoglobin (HbA1c), and lipid profile were made. For the groups under investigation, the homeostasis model assessment for insulin resistance (HOMA-IR) was also computed. participants treated with valproic acid had significantly higher mean BMI values and fasting blood levels of glucose, insulin, HbA1c, total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides than participants in the other study groups. In addition, more research participants in the valproic acid group met the insulin resistance criterion (defined as HOMA-IR > 2.5) than in the other groups. The valproic acid group had a significantly greater mean fasting serum asprosin concentration in comparison to the other study groups. At the same time, the lamotrigine, healthy, and untreated groups all had similar study parameter values. According to their research, increased asprosin levels may be one of the pathogenic processes underlying the emergence of obesity, insulin resistance, and metabolic problems associated with valproic acid therapy.[15]

CONCLUSION

The identification and appropriate validation of epileptic biomarkers may aid in the following tasks: tracking the progression of the disease after a diagnosis is made; determining the presence and extent of tissue that may induce spontaneous seizures; and evaluating pharmacoresistant situations. Discovering reliable biomarkers may also shed light on underlying mechanisms that could be targeted therapeutically to develop cutting-edge antiepileptogenic and antiseizure medications.

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