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A Review Article on the Different Relationships between Hyperglycemia and its Effects on the Neurological System

Puja Kumari[1], Dr. Sarika[2], Ranjana Kumari[3]

[1,3]Research Scholar, University Department of Zoology, T. M. B. U., Bhagalpur, Bihar, India
[2]Associate Professor, S. M. College, Bhagalpur, Bihar, India

ABSTRACT

Diabetes is gradually turning into an epidemic, and because of its numerous complications, the clinical burden is rising quickly. This review focuses on the neuronal alterations brought on by diabetes, including the effects of hyperglycemia on brain structure and function, its correlation with a number of neurological conditions, and a few peripheral neuropathic changes brought on by the disease. Since the majority of current treatment choices are concentrated on improving glycemic control, an attempt has been made to summarise the pertinent literature about the neuronal effects of diabetes mellitus. However, more study is still required to identify novel therapy options that can stop or slow the course of neuronal abnormalities.

Keywords: *Blood glucose control, Cognition, Diabetes complications, Nervous system, "Diabetes mellitus"*

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INTRODUCTION

Glucose is the energy source that the brain needs to function at its best, from neurotransmitter production to cellular upkeep. About 20% of the body's glucose levels, which are primarily controlled by the hypothalamus's integration with various hormones that influence food intake, energy expenditure, insulin secretion, hepatic glucose production, and glucose/fatty acid metabolism in adipose tissue and muscle tissue in the skeleton, make up 2% of the human total body weight (Nimgampalle M,et al., 2021).

Diabetes mellitus (DM) is a metabolic disease that is characterised by inadequate blood glucose regulation, primarily a long-term state of hyperglycemia, as well as frequent episodes of hypoglycemia. The disease is classified primarily into type 1 and type 2, although there are other subtypes that can be caused by endocrinopathies, medications, infections, immunologic, genetic, or pancreatic factors. These metabolic dysregulations are the primary cause of death and can result in a number of problems that influence the heart, kidneys, blood vessels, eyes, and neurological system, hence lowering quality of life.

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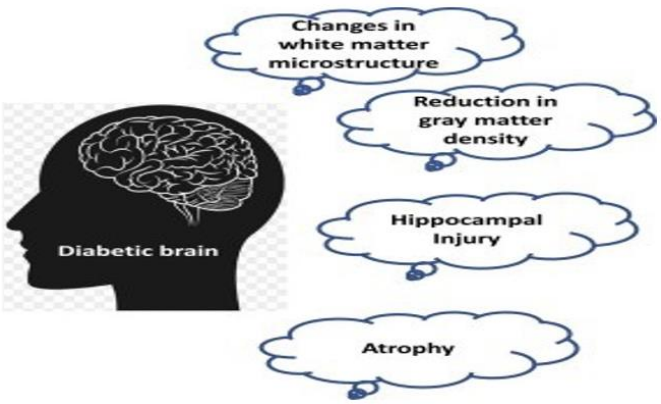
Axonopathies, neurodegenerative illnesses, neurovascular diseases, and general cognitive impairment are among the nervous system problems associated with diabetes mellitus. Not to add that nearly all DM patients have a number of comorbidities related to their arteries, metabolism, and other systems, which compound with high glucose levels to exacerbate neurological problems (Seaquist ER. 2010).

IMPORTANT FACTORS OF DM INCLUDES ON HEALTH OF HUMAN BEINGS



Implications with regard to the autonomic, peripheral, and central nervous systems

A persistently raised blood glucose level is associated with a very significant risk of cognitive impairment and microstructural changes in the white matter tracts. Cognitive impairment in individuals with type 2 diabetes is characterised by insufficient attention that affects work, executive function, mental processing, and memory recall. On the other hand, there are no appreciable changes in the way that simpler tasks like simple response time and immediate memory are performed. Furthermore, diabetic children and adults with type 1 diabetes (Type 1 diabetes) have reduced scores on intellect, scholastic achievement, attention, mental processing, and executive functions. According to a recent meta-analysis, T2DM has the greatest impacts on verbal learning, planning, mental efficiency, and information processing speed (Palta P, et al., 2014).

Neuronal damage caused by molecular factors

The known source of the neuronal alterations brought on by hyperglycemia is oxidative stress. Major biochemical pathways involve a number of different molecular components that also play a part. Some pathways include the polyol pathway, advanced glycation end (AGE) products pathway, hexosamine pathway, mitogen-activated protein kinase (MAPK) pathway, nuclear factor-κB (NF-kB) signaling and the role of tumor necrosis factor-α (TNF-α). Below is a discussion of the functions of the few metabolic pathways described above in modifications to neurons. . (Dewanjee S, et al., 2018).

Hexosamine Pathway

Increased fructose-6-phosphate concentration brought on by hyperglycemia leads to the hexosamine pathway, where it is transformed into glucosamine-6-phosphate. Uridine diphosphate N-acetyl glucosamine (UDPGlcNAc) is then produced by glucosamine-6-phosphate amidotransferase. Pancreatic beta (β)-cell dysfunction is caused by oxidative stress induced by N-acetyl glucosamine (GlcNAc). Increased hydrogen peroxide levels cause oxidative stress that affects the neural environment, insulin causes hyperglycemia,and glutamine fructose-6 phosphate aminotransferase overexpression inhibits glucose transporter 2 (GLUT2) (Kaneto H, et al., 2001). GlcNAc levels rise with hyperglycemia, and the gene transcription factor Sp1 is activated (Kolm-Litty V, et al,. 1998).

Polyol Pathway

Through the polyol pathway, aldose reductase (AR) and sorbitol dehydrogenase are key players in the metabolism of glucose. Generally speaking, AR has less affinity for glucose. The polyol route is the mechanism by which extra glucose is metabolised in diabetes mellitus (DM). (Bhattacharjee N, et al., 2016)

Oxidative stress

Oxidative stress is a major factor in diabetic neuropathy and arises when there is an imbalance between free radical scavengers and free radical species (reactive nitrogen, oxygen species). (Low P, and Feldman EL. 2004). Reactive free radical species can harm the lipids in myelinated nerve structures, which can harm the nervous system's microvasculature environment (Casellini CM, Vinik AI. 2006). Neuropathic pain originates as a result of oxidative stress on peripheral nerves leading to hyper-excitability in central neurons and afferent nociceptors triggering spontaneous impulses in axon and dorsal nerve ganglia (Ko SH, and Cha BY. 2012) Oxidative stress brought on by diabetes can alter the potential of the mitochondrial membrane, causing it to expand and become more permeable (Cameron NE, Cotter MA 1994).

Nuclear Factor-kB Pathway

An immunological response, apoptosis, and inflammation are all mediated by nuclear factor-kB (NF-kB), a transcriptional factor. Stimuli causing inflammation trigger NF-kB. Compared to normal control mice, diabetic transgenic mice exhibited enhanced NF-kB activity in their dorsal root ganglia, sciatic nerve, and sural nerve. Additionally, active NF-kB was found in the endoneurium, epineural arteries, and perineurium of sural nerve biopsies from diabetic participants. (Bierhaus A, et al., 2004) An investigation on isolated Schwann cells in high- and low-glucose environments revealed that the hyperglycemic medium upregulated NF-kB. (Suzuki T, et al., 2004). In both acute and chronic inflammatory demyelinating polyneuropathies, the p65 subunit of NF-kB is shown to be overexpressed, suggesting that NF-kB is crucial for inflammatory demyelination (Andorfer B, et al., 2001).

Conclusion

We have therefore compiled the majority of the pertinent literature in order to better understand the different relationships between hyperglycemia and its effects on the neurological system. The clinical

burden of diabetes and diabetes-related complications is ever increasing, with risk factors like obesity, riskof eating junk food and many more reasons are the explosion globally. Recombinant insulin, innovative medications, and improved treatment regimens all contribute to improved glycemic control, which halts or slows the developmentof neuronal alterations in diabetes mellitus. Still, there is room for more study on the subject, particularly in regards to herbal medications that stop and reverse theneurological side effects of diabetes mellitus.

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