OPEN ACCESS Freely available online

ISSN: 2572-5629
Diabetes Case Reports

Short Communication

Impact of Glucolipotoxicity Upon β-Cell Dysfunction and Diabetic Health Management

Pervaiz Delanois*

Department of Medical Technology, Walailak University, Nakhon Si Thammarat, Thailand

DESCRIPTION

Glucolipotoxicity is a term that describes the harmful effects of chronic exposure to high levels of glucose and Free Fatty Acids (FFAs) on various tissues, especially the pancreatic β-cells that produce insulin. Glucolipotoxicity is considered to be one of the major factors that contribute to the progression and worsening of type 2 diabetes, a metabolic disorder characterized by insulin resistance and β-cell dysfunction. Insulin is a hormone that regulates the uptake and utilization of glucose by the cells of the body [1]. In normal conditions, the β-cells sense the rise in blood glucose levels after a meal and secrete insulin accordingly. Insulin then binds to its receptors on the target cells and activates a cascade of signalling pathways that promote glucose transport, glycolysis, glycogen synthesis, and lipid synthesis. Insulin also inhibits the breakdown of glycogen and lipids, and the production of glucose by the liver. Thus, insulin maintains the blood glucose levels within a narrow range and prevents hyperglycemia. However, in type 2 diabetes, the target cells become resistant to the action of insulin, resulting in impaired glucose uptake and utilization [2-4]. This leads to a compensatory increase in insulin secretion by the β-cells, which initially maintains the blood glucose levels within the normal range. However, over time, the β-cells fail to cope with the increased demand for insulin and lose their function and mass. This causes a decline in insulin secretion and a rise in blood glucose levels, leading to overt diabetes.

The exact mechanisms that cause β-cell failure in type 2 diabetes are not fully understood, but several factors have been implicated, such as genetic susceptibility, inflammation, oxidative stress, Endoplasmic Reticulum (ER) stress, mitochondrial dysfunction, and glucolipotoxicity. Glucolipotoxicity refers to the combined effects of elevated glucose and FFAs on the β-cells [5-7]. FFAs are derived from the diet or from the breakdown of adipose tissue. In normal conditions, FFAs are an important source of energy for the β-cells and also potentiate glucose-stimulated insulin secretion. However, in the context of insulin resistance and hyperglycemia,FFAs accumulate in the β-cells and interfere with their function and survival. Glucolipotoxicity affects many aspects of β-cell biology, such as glucose sensing, insulin synthesis and secretion, gene expression, cell cycle, apoptosis, and autophagy.

Increased production of Reactive Oxygen Species (ROS) and oxidative stress, which damage the β-cell components and impair the insulin signalling pathways [8]. Increased ER stress, which results from the accumulation of misfolded proteins in the ER and activates the Unfolded Protein Response (UPR), a cellular defense mechanism that aims to restore the ER homeostasis. However, prolonged and severe ER stress can trigger apoptosis. Impaired mitochondrial function, which reduces the ATP production and the coupling efficiency of glucose metabolism and insulin secretion. Mitochondrial dysfunction also increases the ROS generation and the release of pro-apoptotic factors. Altered lipid metabolism, which leads to the accumulation of toxic lipid intermediates, such as Diacylglycerol (DAG), ceramide, and sphingolipids, in the β-cells [9,10]. These lipids activate various signalling pathways that inhibit insulin secretion, induce inflammation, and promote apoptosis.

CONCLUSION

Reduced autophagy, which is a process that degrades and recycles the damaged or unnecessary cellular components. Autophagy is essential for the maintenance of β-cell quality and function, but glucolipotoxicity impairs the autophagic flux and causes the accumulation of dysfunctional organelles and aggregates. Glucolipotoxicity is a therapeutic target in type 2 diabetes, as several drugs can modulate the underlying stress responses in the β-cells and improve their function and survival. For example, some drugs can enhance the antioxidant capacity, reduce the ER stress, improve the mitochondrial function, or restore the autophagy in the β-cells. Moreover, lifestyle interventions, such as diet and exercise, can lower the blood glucose and FFA levels and reduce the glucolipotoxic burden on the β-cells. Glucolipotoxicity affects multiple aspects of β-cell biology and involves various

Correspondence to: Pervaiz Delanois, Department of Medical Technology, Walailak University, Nakhon Si Thammarat, Thailand, E-mail: delano@thanm.com

Received: 02-Jan-2024, Manuscript No. DCRS-24-24864; **Editor assigned:** 05-Jan-2024, PreQC No. DCRS-24-24864 (PQ); **Reviewed:** 19-Jan-2024, QC No DCRS-24-24864; **Revised:** 26-Jan-2024, Manuscript No. DCRS-24-24864 (R); **Published:** 05-Feb-2024, DOI: 10.35841/2572-5629.24.9.195

Citation: Delanois P (2024) Impact of Glucolipotoxicity Upon β-Cell Dysfunction and Diabetic Health Management. Diabetes Case Rep. 9:195.

molecular mechanisms that impair the insulin production and secretion. Glucolipotoxicity is a potential target for the prevention and treatment of type 2 diabetes.

REFERENCES

1. Ohkubo Y, Kishikawa H, Araki E, Miyata T, Isami S, Motoyoshi S, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. Diabetes Res Clin Pract. 1995;28(2):103-117.
2. MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008;358(24): 2560-2572.
3. Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008;358(24):2545-2559.
4. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2016;375(4):311-322.
5. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jodar E, Leiter LA, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2016;375:1834-1844.
6. Gerstein HC, Colhoun HM, Dagenais GR, Diaz R, Lakshmanan M, Pais P, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. Lancet. 2019;394(10193):121-130.
7. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2020. Diabetes Care. 2020;43(1):S98-S110.
8. Buckley ST, Bækdal TA, Vegge A, Maarbjerg SJ, Pyke C, Ahnfelt-Ronne J, et al. Transcellular stomach absorption of a derivatized glucagon-like peptide-1 receptor agonist. Sci Transl Med. 2018;10(467):7047.
9. Husain M, Birkenfeld AL, Donsmark M, Dungan K, Eliaschewitz FG, Franco DR, et al. Oral semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2019;381(9):841-851.
10. Ninomiya T, Perkovic V, De Galan BE, Zoungas S, Pillai A, Jardine M, et al. Albuminuria and kidney function independently predict cardiovascular and renal outcomes in diabetes. J Am Soc Nephrol. 2009;20(8):1813-1821.