International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(REVIEW ARTICLE)

Check for updates

Diabetes mellitus and anti-oxidative stress

Elshad Abuzar Novruzov [1,*], Dilara Magsood Aliyeva [2], Sabina Anvar Mashadiyeva-Bayramova [3], and Adil Allahyar Bayramov [2]

[1] *Biochemistry Department, Azerbaijan Medical University, Azerbaijan.*
[2] *Normal Physiology Department, Azerbaijan Medical University, Azerbaijan.*
[3] *İnternal Medicine Department, Azerbaijan Medical University, Azerbaijan.*

International Journal of Science and Research Archive, 2023, 09(01), 390–393

Publication history: Received on 20 April 2023; revised on 02 June 2023; accepted on 05 June 2023

Article DOI: https://doi.org/10.30574/ijsra.2023.9.1.0425

Abstract

The development of diabetes complications, both microvascular and cardiovascular, is significantly influenced by oxidative stress. Diabetes-related metabolic problems lead to an overproduction of mitochondrial superoxide in the heart, small and large vascular endothelial cells, and both. Five key pathways implicated in the pathophysiology of problems are activated as a result of the increased superoxide generation. The purpose of this review is to highlight new insights into the processes through which hyperglycemia produces oxygen free radicals.

Keywords: Diabetes mellitus; Insulin deficiency; Antioxidative stress; Hyperglycaemia

1. Introduction

Diabetes mellitus (DM) is a diverse metabolic condition characterized by hyperglycaemia caused by inadequate insulin production, insulin resistance, or both (1). Type 1 diabetes is caused by an autoimmune-mediated death of pancreatic -cells, which results in insulin insufficiency. Patients must be given insulin to live. Insulin resistance and relative, rather than total, insulin insufficiency characterizes type 2 diabetes. Obese people are more likely to develop type 2 diabetes, which is related to hypertension and dyslipidaemia. Nutrients' ability to increase insulin production from pancreatic-cells reflects their ability to boost oxidative fluxes in islet cells (2). Furthermore, oxidative stress, which is linked to insulin resistance and non-insulin-dependent diabetes (3,4), contributes to impaired insulin action (5-7). Thus, the treatment tries to decrease insulin resistance (through diet, exercise, and pharmacological therapy) while increasing insulin secretion. In diabetes, oxidative stress appears to be caused primarily by an increase in free radical generation and/or a rapid decrease in antioxidant defences (8-14). Free radicals produced from oxygen have been linked to the pathogenesis of several diseases, including diabetes mellitus (13). The primary radical produced by the reduction of molecular oxygen is generally acknowledged to be the superoxide anion, which can give birth to secondary radicals or reactive oxygen species (ROS) such as hydrogen peroxide and hydroxyl radical (15,16). Furthermore, Jang et al. (17) discovered that elevated oxidative stress has been implicated in the development and progression of diabetic tissue damage. Diabetes, on the other hand, appears to alter the activity of antioxidant enzymes in a variety of tissues (9). Diabetes mellitus is characterized by a rise in glycoxidation products, which is associated with advanced oxidative stress (18). Higher concentrations of glucose or glycated protein promote lipid peroxidation (19), and lipid peroxides may increase the number of advanced glycation end-products (20).

Free radicals produced during the autoxidation of glucose were assumed to be the cause of oxidative stress in diabetes mellitus (21). Most recently, evidence was presented for the accumulation of oxidation products before the onset of diabetes (23), and increased levels of ROS in type 2 DM were implicated in contributing to a hypercoagulable condition

* Corresponding author: Elshad Abuzar Novruzov

(22). Hyperglycaemia (24) and hyperinsulinemia (25) are the main contributors to increased free radical generation. Consequently, the following will discuss the multiple mechanisms of ROS against DM.

2. Mechanisms of oxygen free radicals' production by hyperglycaemia:

Hyperglycaemia is a widely known cause of enhanced plasma free radical concentrations (24). Increased glycolysis (26), intercellular activation of the sorbitol (polyol) pathway (27), autooxidation of glucose (28), and non-enzymatic protein glycation (29) are the four main ways that hyperglycaemia can produce free radicals.

Increased glucose metabolism to lactate is associated with an increase in NADH/NAD+ ratio (27). Under this condition of markedly accelerated glycolysis, oxidation of glyceraldehyde 3-phosphate (GAP) to 1,3-biphosphoglycerate (1,3-DPG) by glyceraldehyde 3-phosphate dehydrogenase appears to become the rate-limiting step in glycolysis (30), this reaction is coupled to the reduction of NAD+ to NADH. In the cytosol, NADH is oxidized to NAD+ by lactate dehydrogenase (LDH), coupled with a reduction of pyruvate to lactate. Thus, the increase in the ratio of NADH/NAD+ will reflect an increased lactate/pyruvate ratio (27). A mismatch between the rate of oxidation of GAP to 1,3-DPG and the rate of reduction of pyruvate appears to be the mechanism by which a higher rate of glycolysis raises free cytosolic NADH / NAD+ ratio (redox imbalance) (30). This finding suggests that poor oxidation of NADH to NAD+ results in a higher NADH/NAD+ ratio, which is strongly related to increased glycolysis as a result of hyperglycaemia.

Macromolecules' oxidative modification (including lipoproteins and proteins) Nonradical oxidants like hydrogen peroxide, hypochlorous acid, or singlet oxygen, as well as radical oxygen species like superoxide anion and hydroxyl radicals, can cause oxidative damage to physiologically significant macromolecules.

Lipid peroxides are produced when these oxidants attack the double bonds in unsaturated fatty acids. The instability of the peroxidation products and the difficulty of the tests, however, make lipid peroxidation study difficult. Oxygen radicals, particularly the very aggressive hydroxyl radical, can also oxidize apolipoproteins and other plasma proteins, the products of which are much more stable than lipid peroxides. The decrease in the concentration of total proteins in the serum of diabetic rats can be attributed to 1) decreased amino acid uptake (31), 2) greatly decreased concentration of a variety of essential amino acids (32), 3) increased glycogenic amino acid conversion rate to C02 and H20 (33) and 4) reduction in protein synthesis secondary to a decrease in the amount and availability of mRNA. Furthermore, Wanke and Wong attributed the decrease in albumin concentration in experimental diabetes to the presence of inhibitor(s) of albumin promotor activity in the liver.

3. Conclusion

Numerous studies have shown that oxidative stress plays a significant role in the development of diabetes, including the impairment of insulin action and the elevation of the risk of complications. Antioxidants have already demonstrated promise in the management of both type 1 and type 2 diabetes. Increased oxygen and nitrogen free radical levels (ROS/RNS) have been associated with lipid peroxidation, non-enzymatic protein glycation, and glucose oxidation, all of which are factors in diabetes mellitus and its consequences. The majority of research have demonstrated a link between oxidative stress and diabetes, as well as its heart, liver, kidney, and eye consequences. Therefore, it appears that oxidative stress is particularly concerning in metabolic disorders, especially diabetes type 2.

Compliance with ethical standards

Disclosure of conflict of interest

There is no conflict of interest.

References

[1] Gavin III JR, Alberti KGMM, Davidson MB, DeFronzo RA, Drash A, Gabbe SG, Genuth S, Harris MI, Kahn R, Keen H, Knowler WC, Lebovitz H, Maclaren NK, Palmer JP, Raskin P, Rizza RA, Stem MP: Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care, 20:1183-1197, 1997.

[2] Malaisse WJ: Diab Metab, 9:313-320, 1983.

[3] Gopaul NK, Änggård EE, Mallet AI, Betteridge DJ, Wolff SP, Nourooz-Zadeh J: Plasma 8-epi-prostaglandin F2α levels are elevated in individuals with non-insulin dependent diabetes mellitus. FEBS Lett, 368:225-229, 1995.

[4] Nourooz-Zadeh J, Tajaddini-Sarmadi J, McCarthy S, Betteridge DJ, Wolff SP: Elevated levels of authentic plasma hydroperoxides in NIDDM. Diabetes, 44:1054-1058, 1995

[5] Paolisso G, D'Amore A, Volpe C, Balbi V, Saccomanno F, Galzerano D, Giugliano D, Varricchio M, D'Onofrio F: Evidence for a relationship between oxidative stress and insulin action in non-insulin-dependent (type II) diabetic patients. Metabolism 43:1426-1429, 1994.

[6] Faure P, Rossini E, Lafond JL, Richard MJ, Favier A, Halimi S: Vitamin E improves the free radical defence system potential and insulin sensitivity of rats fed high fructose diet. J Nutr, 127:103-107, 1997.

[7] Rudich M, Kozlovsky N, Potashnik R, Bashan N: Oxidant stress reduces insulin responsiveness in 3T3-L1 adipocytes. Am J Physiol, 272:E935-E940, 1997.

[8] Cross CE, Halliwell B, Borish ET: Oxygen radicals and human disease. Ann Intern Med, 107:526-545, 1987.

[9] Oberley LW: Free radicals and diabetes. Free Radical Biol Med, 5:113-124, 1988.

[10] Hunt JV, Bottoms MA, Mitchinson MJ: Ascorbic acid oxidation: A potential cause of the elevated severity of altherosclerosis in diabetes mellitus. FEBS Lett, 311:161-164, 1992.

[11] Young IS, Torney JJ, Trimble ER: The effect of ascorbate supplementation on oxidative stress in the streptozotocin diabetic rat. Free Rad Biol Med, 13:41-46, 1992.

[12] Thompson KH, Lee M: Effects of manganese and vitamin E deficiencies on antioxidant enzymes in streptozotocin diabetic rats. J Nutr Biochem, 4:476-481, 1993.

[13] Giugliano D, Ceriello A, Paolisso G: Oxidative stress and diabetic vascular complications. Diabetes Care, 19:257-267, 1996.

[14] Low PA, Nickander KK, Tritschler HJ: The roles of oxidative stress and antioxidant treatment in experimental diabetic neuropathy. Diabetes, 46:S38-S42, 1997.

[15] Grisham MB, McCord JM: Chemistry and cytotoxicity of reactive oxygen metabolites. In: Physiology of oxygen radicals. Ed by Taylor AE, Matalon S, Ward P. Bethesda MD: American Physiology Society, pp 1-19, 1986.

[16] Katusic ZS: Superoxide anion and endothelial regulation of arterial tone. Free Radic Biol Med, 20:443-446, 1996.

[17] Jang YY, Song JH, Shin YK, Han ES, Lee CS: Protective effect of boldine on oxidative mitochondrial damage in streptozotocin-induced diabetic rats. Pharmacological Res, 42:361-371, 2000.

[18] Mullarkey CJ, Edelstein D, Brownlee M: Free radical generation by early glycation products: a mechanism for accelerated atherogenesis in diabetes. Biochem, Biophys Res, Commun, 173:932-939, 1990.

[19] Kawamura M, Heinecke JW, Chait A: Pathophysiological concentrations of glucose promote oxidative modification of low density lipoprotein by a superoxide dependent pathway. J Clin Invest, 94:771-778, 1994.

[20] Hicks M, Delbridge L, Yue DK, Reeve TS: Increase in crosslinking of nonenzymatically glycosylated collagen induced by products of lipid peroxidation. Arch Biochem Biophys, 268:249- 254, 1989.

[21] Miyata T, van Ypersele de Strihou C, Kurokawa K, Baynes JW: Origin and significance of carbonyl stress in longterm uremic complications. Kidney International, 55:389-399, 1999.

[22] Collier A, Rumley A, Rumley AG, Paterson JR, Leach JP, Lowe GDO, Small M: Free radical activity and hemostatic fatcors in NIDDM patients with and without microalbuminuria. Diabetes, 41:909-913, 1992.

[23] Matteucci E, Giampietro O: Oxidative stress in families of type 1 diabetic patients. Diabetes Care, 23:1182-1186, 2000.

[24] Hammes HB, Bartmann A, Engi L, Wulforth P: Antioxidant treatment of experimental diabetic retinopathy in rats with nicanartine. Diabetologia, 40:629-634, 1997.

[25] Paolisso G, Giugliano D: Oxidative stress and insulin action: is there a relationship? Diabetologia, 39:357-363, 1996.

[26] Vaag A, Dmsbo P, Hother-Nielsen O, Beck-Nielsen H: Hyperglycemia compensates for the defects in insulin mediated glucose metabolism and in the activation of glycogen synthase in the skeletal muscle of patients with type 2 (non-insulin dependent) diabetes mellitus. Diabetologia, 35:80-88, 1992.

[27] Williamson JR, Chang K, Frangos M, Hassan KS, Kawamura T, Nyengaard JR, Van Den EM, Kilo C, Tilton RG: Hyperglycemic pseudohypoxia and diabetic complications. Diabetes, 42:801-813, 1993.

[28] Wolff SP, Jiang ZY, Hunt JV: Protein glycation and oxidative stress in diabetes mellitus and ageing. Free Rad Biol Med 10:339-352, 1991.

[29] Ceriello A, Quatraro A, Giugliano D: New insights on non-enzymatic glycosylation may lead to therapeutic approaches for the prevention of diabetic complications. Diabet Med, 9:297- 299, 1992.

[30] Kobayashi K, Neely JR: Control of maximum rates of glycolysis in rat cardiac muscle. Circ Res, 44:166-175, 1979. 124. Gutterridge JMC, Halliwell B: The measurement and mechanism of lipid peroxidation in biological systems. Trends in Biochemical Science, 15:129-135, 1990.

[31] Garber AJ: The impact of streptozotocin-induced diabetes mellitus on cyclic nucleotide regulation of skeletal muscle amino acid metabolism in the rat. J Clin Invest, 65:478-487, 1980.

[32] Brosnan JT, Man KC, Hall HE, Clobourne SA, Brosnan ME: Interorgan metabolism of amino acids in streptozotocin-diabetic rat. Am J Physiol, 244:E151-E158, 1984.

[33] Mortimore GE, Mandon CE: Inhibition of insulin of valine turnover in liver. J Biol Chem, 245:2375-2383, 1970