The Relationship between Diabetes and Oxidative Stress, Inflammation, and Liver Surgery

Marc Donath*, Maria Catalina

Clinic of Endocrinology, Diabetes and Metabolism, University Hospital Basel 4031, Switzerland.

Corresponding Author*

Marc Donath,

Clinic of Endocrinology, Diabetes and Metabolism, University Hospital Basel 4031, Switzerland;

Phone: +414713209436

E-mail: donath@marc.org

Copyright: © 2022 Donath M, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Received: 28-Sep-2022, Manuscript No. jdm-22-20192; **Editor assigned:** 01-Oct-2022, PreQC No: jdm-22-20192(PQ); **Reviewed:** 08-Oct-2022, QC No. jdm-22-20192; **Revised:** 22-Oct-2022, Manuscript No jdm-22-20192(R); **Published:** 31-Oct-2022, DOI: 10.35248/2155-6156.1000961

Abstract

Hyperglycemia and increased morbidity are hallmarks of diabetes mellitus (DM), a metabolic condition that affects people all over the world. Increased oxidative stress (OS) response and increased inflammatory response are two of hyperglycemia's harmful effects. DM impairs the liver's capacity to regenerate and is particularly linked to a poor prognosis after an injury caused by ischaemia-reperfusion (I/R). This review aims to present recent publications addressing the effects of DM (hyperglycaemia) on OS and the inflammatory process, which play a crucial role in I/R injury and impaired hepatic regeneration after liver surgery, in light of the growing need for knowledge of the impact of DM on the liver following a surgical procedure.

Keywords: Hepatocellular carcinoma; Oxidative stress; Liver surgery; Hyperglycemia; Diabetes

Introduction

The blood flow to the liver must be stopped in order to remove a macroscopic lesion or perform a transplant in order to prevent the hemorrhagic process. Despite the safety of surgical treatments that require cutting off the liver's blood supply (ischaemia), this interruption causes tissue damage that is amplified by blood flow restoration (reperfusion). Ischemia-reperfusion (I/R) damage is a condition linked to oxidative stress and inflammation (OS). Diabetes mellitus (DM) is a metabolic illness caused by inadequate insulin secretion and/or action. This results in hyperglycemia (high blood glucose), which not only worsens the clinical circumstances of DM but also causes oxidative damage and activates inflammatory signalling cascades. The goal of the current study is to offer latest evidence regarding the effects of DM (hyperglycemia) on OS and the inflammatory process in light of the growing demand for understanding about the impact of DM on livers undergoing surgical procedures [1].

Diabetes mellitus (DM) causes significant morbidity and mortality as a result of issues with the macro- and microvascular system. Insulin resistance, with or without an insulin deficit that results in organ failure, is a hallmark of type 2 diabetes, Reactive oxygen species (ROS) and nitrosative species (RNS), both of which are thought to be crucial components of DM macro- and microvascular problems, are produced as a result of persistent hyperglycemia in this condition. Endothelial dysfunction, insulin resistance, and DM problems are all known to be brought on by a decrease in the activity of antioxidant enzymes in addition to the overproduction of ROS and RNS. Additionally, uncoupling protein 2 (UCP-2) activation by oxidative stress decreases the adenosine triphosphate (ATP)/adenosine diphosphate (ADP) ratio, suppresses insulin secretion in pancreatic -cells, and inhibits the insulin-secretory response [2].

The structural abnormalities of lipids, nucleic acids, proteins, and carbohydrates are brought on by ROS and RNS. The activation of many signalling pathways by these free radicals results in transcriptional genes linked to diabetes problems; nuclear factor kappa B activation induces proinflammatory proteins, which are also seen in diabetic polyneuropathy (DPN). We wanted to describe how the inflammatory response, oxidative stress, and mitochondrial function behave in type 2 DM DPN in this review.

A biochemical imbalance known as oxidative stress (OxS) is caused by an excessive synthesis of reactive oxygen and nitrogen species. These species cause oxidative damage to biomolecules and cannot be prevented by antioxidative systems. This is a significant element that accelerates ageing and the onset of a number of illnesses, such as type 2 diabetes mellitus (T2DM). It has been established for many years that the chronic inflammatory process and OxS contribute to the physiopathological processes of T2DM. In this way, the chronic hyperglycemia in T2DM stimulates a number of unusual metabolic pathways in living things, including the sorbitol pathway (or that of aldose reductase), no enzymatic protein glycosylation, glucose autoxidation, modification of protein kinase C activity, pseudo hypoxia, lipoprotein-altered metabolism, and cytokine-associated alteration. All of these mechanisms result in the production of OxS and reactive oxygen species (ROS). Similar to this, numerous studies have demonstrated that T2DM and/or ageing increase the production and release of cytokines such free radicals, tumour necrosis factor-alpha (TNF-alpha), and interleukin 6 (IL-6). All of them are understood to be risk factors for disease-related complications. In this regard, our research team demonstrated that ageing in the presence of diabetes causes inflammation and an increase in OxS production [3].

Due to this, a number of therapeutic supplements have been suggested, including vitamins A, C, and E, omega 3 and 6 fatty acids, coenzyme Q10, melatonin, and alpha-lipoic acid. These supplements have antioxidant and anti-inflammatory characteristics. The enzyme lipoic acid synthase catalyses processes that result in the production of alpha-lipoic acid (ALA), an amphipathic chemical that is produced in the mitochondria of both plants and animals from octanoic acid and cysteine as a sulphur donor. It is crucial that ALA participate in oxidative metabolism. Since it attaches to the amino group of the lysine residues via an amide bond, only the R isoform of ALA functions as a cofactor in the oxidant metabolism. ALA is chemically present in both the R and S forms. The enzymes pyruvate dehydrogenase and -ketoglutarate dehydrogenase can then form a lipoamide as a result.

Studies have shown that ALA has anti-inflammatory, antioxidant, and hypoglycemic properties. Additionally, it has been demonstrated that ALA has a favourable impact on the OxS associated with ageing. The purpose of the current study was to ascertain the impact of 600 mg/day of ALA on various OxS and inflammatory markers as well as RAGE in older persons with T2DM [4].

Materials and Methods

Each participant was independent, had been given a type 2 diabetes mellitus diagnosis for one to three years without any problems or co-morbidities, and was receiving treatment in a public hospital: I ; (ii) medications: all patients taking two tablets of glibenclamide/metformin (5/500 mg) per day as a hypoglycemic treatment and abstaining from antioxidant supplements (vitamins or minerals) or anti-inflammatory drugs for at least 6 months prior to the start of or during the study; (iii) habits: no smoking, no frequent alcohol consumption (less than two drinks or beers per week), and no drug addictions (marijuana 200 senior citizens who were being treated for type 2 diabetes

mellitus in a public hospital in Mexico City were invited. Because they lacked the time for the follow-up meetings held every four weeks for the delivery of the medication, self-report of health status, registration of secondary reactions, and encouragement for therapeutic adherence, 47 patients did not meet the inclusion criteria in this regard, and 18 did not consent to participate in the study.

We gave a summary of the investigation in Figure 1. The following research groups were given to all participants: I the experimental group (EG), which consisted of 50 people; (ii) the placebo group (PG), which also consisted of 50 people; and (iii) the control group (CG), which consisted of just 35 people. The EG and PG were assigned in a random order. Two capsules containing 300 mg of racemic alpha-lipoic acid were given to EG each day. Two capsules containing 295 mg of microcrystalline cellulose and 5 mg of magnesium stearate were given to PG. CG did not receive any medication. Capsules containing alpha-lipoic acid and a placebo were created by ProductosMedix®. A control group (CG) of 35 participants was also introduced with the intention of evaluating the placebo effect [5].

Discussion

The body creates alpha-lipoic acid (ALA) from scratch using small amounts of cysteine and fatty acids. In order to have a therapeutic impact, it is crucial to eat external sources of ALA. In this context, it has been demonstrated that ALA is widely distributed throughout animal tissues, primarily in the viscera, including the heart, liver, and kidneys. However, vegetables including broccoli, spinach, tomatoes, peas, potatoes, and rice bran all contain significant amounts of it. However, a racemic mixture that may be taken as capsules was created from a commercial product offered by ProductosMedix® in order to fully utilise its antioxidant, anti-inflammatory, and hypoglycemic qualities. Since there is a greater absorption of the compound if it is administered 30 minutes before or 2 hours after food intake, it has been shown that the timing of ingestion affects the gastrointestinal absorption of ALA. Additionally, since the R isoform of ALA is absorbed more effectively than the S, it has been demonstrated that ALA absorption is enantioselective [6].

The administration of ALA, on the other hand, has been found to reduce body weight and, as a result, the BMI in both humans and animals. In this context, it has been proposed that ALA takes part in the control of several pathways that are involved in energy balance, the production and oxidation of lipids, and the removal of cholesterol through the liver; however the precise processes remain unknown. Adenosine monophosphate activates a protein kinase in one of these routes (AMPK). It is understood that AMPK plays a functional role in behaviour that is related to food intake and energy expenditure by integrating hormonal and nutrient signals in the hypothalamus. Similar to this, it's been claimed that ALA has an anorectic effect that becomes more pronounced during the first two weeks of supplementation and then fades away over time. In contrast to previously published findings, which revealed that the administration of ALA causes a modest loss of body weight and a statistically significant decrease in BMI, no statistically significant alterations were seen in the BMI after treatment with ALA in our investigation. However, greater ALA doses (1200 mg/day and 1800 mg/day) than the 600 mg/day used in our study were used to observe this effect. It's also vital to note that time plays a role in this equation because, as was noted previously, the anorectic effect only lasts for the first few weeks [7].

Regarding ALA's impact on lipid metabolism, it has been noted that it decreases lipogenesis at the peripheral level by boosting fatty acid -oxidation and enhancing overall body energy expenditure. This indicates that the administration of ALA at a dose of 600 mg/day has an effect on HDL that is equivalent to placebo because a statistically significant rise in blood HDL concentration was shown in the EG after treatment in our trial, even though this increase was also seen in the PG. Similar results in this regard were reported. Was a research that involved giving ALA 600 mg/day for eight weeks to patients with renal failure? Additionally, obese adults who ingested 1200 and 1800 mg/day of ALA for 20 weeks did not show statistically significant differences in HDL blood concentration from the placebo group. These findings contrast with the statistically significant rise in HDL levels seen by Zhang et al. in obese patients who received 600 mg/day of ALA for two weeks as compared to a control group. Because of this, the effect of ALA on the lipid profile is still debatable, making its recommendation unjustified for these uses [8].

By stimulating the translocation of glucose transporters (GLUT 1 and GLUT 4) from the Golgi complex to the cell membrane, ALA, on the other hand, has been demonstrated to have a hypoglycemic impact because it enhances the absorption and utilisation of glucose by fat cells and skeletal muscle. Likewise, ALA increases the activity of phosphoinositol-3-kinase (PI3K), the insulin receptor, and its substrates (IR and IRS1), boosting tyrosine phosphorylation in the IR and enhancing PI3K-dependent glucose absorption. The ALA can reduce the concentration of circulating glucose and prevent it from reacting with proteins with a prolonged half-life, which subsequently decreases the expression of genes involved in the formation of advanced glycation end products [9].

It has been noted that ALA is a potent redox pair with the ability to neutralise various ROS, which is relevant to its antioxidant properties. Additionally, it can improve the plasma uptake of cystine to subsequently reduce it to cysteine, which is the precursor to glutathione, increasing the synthesis of glutathione or restoring the reduced/oxidized glutathione ratio (GSH/GSSG) by either transferring electrons directly to the GSSG for reduction or increasing the synthesis of glutathione. Additionally, ALA has the power to restore other antioxidants like vitamins C and E that have been decreased. Additionally, ALA has a tremendous amount of antioxidant capacity due to its capacity to chelate ionic metals and counteract their oxidising effects [10].

The treatment of ALA at doses of 300–1200 mg per day for a period of three to six months has been shown to have a favourable impact on a number of oxidative stress indicators, including MDA, SOD, GPx, PGF2-isoprostane, and 8–hydroxy-2–deoxyguanosine. Negative outcomes have also been noted, as seen in the research below: In a study done on patients with renal failure, who were given 600 mg/day of ALA for eight weeks, Sola et al. did not find statistically significant differences in the concentration of 8-isoprostane in adult patients with metabolic syndrome after treatment with 300 mg of ALA for four weeks compared with the placebo group, found no changes in the levels of MDA, SOD, GPx, or catalase after giving healthy adults 600 mg/day of ALA for seven days. It also found no statistically significant changes in MDA and total antioxidant status levels. It also found no changes in MDA after giving hemodialysis patients 600 mg/day of ALA for two months. In our investigation, there were no statistically significant differences between the EG and PG's blood concentrations of 8-isoprostane. However, after treatment, EG did not exhibit any statistically significant differences in GPx, SOD, or SOD/GPx compared to PG. Given that our population consisted of older adults and that diabetes mellitus is associated with an accelerated ageing process, it may be because of the dose of ALA and/or the length of the treatment's follow-up period [11].

Regarding ALA's anti-inflammatory abilities, it has been demonstrated that it has the power to reduce TNF-, IL-1, and IL-6 production in both animal models and people. ALA inhibits the activation and release of NF-B, as well as its translocation to the nucleus and the subsequent transcription of genes that direct the synthesis of proinflammatory proteins (TNF-, IL-1, and IL-6). It does this by acting at the level of phosphorylation of the factor inhibitor protein B (IKK). In this regard, diabetic patients receiving ALA at doses of 300-600 mg/day for 3–6 months reported a reduction in the markers of chronic inflammation. Comparing the GC to the GE and GP after six months, we found that all proinflammatory parameters (CRP, TNF-, IL-1, IL-6, IL-8, and IL-10) significantly increased in the GC. Our outcomes suggest that the administration of 600 mg/day of ALA has an anti-inflammatory effect that is comparable to placebo, which is consistent with our findings regarding the effect of ALA on the OxS markers [12].

Conclusion

The goal of this review was to discuss the literature on the detrimental impact of diabetes mellitus (DM) on the recovery of the liver following surgery and, in particular, to highlight the need for more research on this topic to help patients with DM who are undergoing surgical procedures, which are becoming more common in clinical practise. The distinctions between the diabetic and nondiabetic livers following surgery still require a lot of investigation. Investigating this topic will make it possible to create novel therapies that will enhance the diabetic liver's ability to heal following surgery.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Acknowledgement

None

References

1. Powner DJ (2004) Factors during donor care that may affect liver transplantation outcome. Progress in Transplantation 14(3):241-249.
2. Serracino-Inglott F, Habib NA, Mathie RT (2001) Hepatic ischemia-reperfusion injury. The American Journal of Surgery 181(2):160-166.
3. Brownlee M (2001) Biochemistry and molecular cell biology of diabetic complications. Nature 414 (6865):813-820.
4. Videla LA, Rodrigo R, Orellana M (2004) Oxidative stress-related parameters in the liver of non-alcoholic fatty liver disease patients. Clinical Science 106(3):261-268.
5. Baynes JW, Thorpe SR (1999) Role of oxidative stress in diabetic complications: a new perspective on an old paradigm. Diabetes. 48(1):1-9.
6. Young IS, Tate S, Lightbody JH, McMaster D, Trimble ER, et al, (1995) The effects of desferrioxamine and ascorbate on oxidative stress in the streptozotocin diabetic rat. Free Radical Biology & Medicine 18(5):833-840.
7. Granger DN, Kvietys PR (2015) Reperfusion injury and reactive oxygen species: the evolution of a concept. Redox Biology 12(6):524-551.
8. Anisimov VN (1998) Ageing and the mechanisms of carcinogenesis: some practical implications. Journal of Experimental & Clinical Cancer Research 17(3):263-268.
9. Malhi H, Gores GJ, Lemasters JJ (2006) Apoptosis and necrosis in the liver: a tale of two deaths? Hepatology 43(1):31-44.
10. Serracino-Inglott F, Habib NA, Mathie RT (2010) Hepatic ischemia-reperfusion injury. The American Journal of Surgery 181(2):160-166.
11. Videla LA, Rodrigo R, Orellana M (2004) Oxidative stress-related parameters in the liver of non-alcoholic fatty liver disease patients. Clinical Science 106(3):261-268.
12. Baynes JW (1991) Role of oxidative stress in development of complications in diabetes. Diabetes 40(4):405-412.

Cite this article: Marc Donath, Maria Catalina. The Relationship between Diabetes and Oxidative Stress, Inflammation, and Liver Surgery. J Diabetes Metab, 2022, 13(10): 961.