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Research Article

ROLE OF OXIDATIVE STRESS AND ANITOXIDANT CAPACITY IN TYPE 2 DIABETES MELLITUS WITH REFERENCE TO ALCOHOL

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ABSTRACT

Type 2 diabetes is a chronic condition in which body does not use insulin properly. The increased oxidative stress is a consequences of several abnormalities, including insulin resistance, hyperglycemia, dyslipidemia and many more. Alcohol consumption is unfavorable to many metabolic pathways. Alcohol abuse is said to influence many process by production of free radical leading to multiple damages. The present study is thereby undertaken to evaluate the role of oxidative stress, which seems to be one of the probable cause of insulin resistance along with the influence with alcohol abuse. In the present study attempts have been made to evaluate the levels of Serum Lipid peroxide as malondialdehyde (MDA), Nitric oxide (NO), total antioxidant capacity (TAC) and Blood glucose with reference to alcohol. 400 patients were divided to 2 groups – Group I – 100 non-alcoholic healthy controls, 100- alcoholic healthy controls and Group II – 100 newly diagnosed non-alcoholic diabetic subjects, 100 newly diagnosed alcoholic diabetic subjects, both from the age group of 35-55 years. Depleted levels of TAC was observed when compared to the healthy subjects. Highly significant ($p < 0.0001$) values of MDA and NO were observed in the study group when compared with the healthy controls. Strong co-relation was observed among alcohol abuse, decrease in the TCA, increased oxidative stress and diabetic progression.

INTRODUCTION

Oxidation is accustomed and requisite procedure that takes place in our body. On the contrary, oxidative stress (OS) is an imbalance between antioxidants and free radicals in the body [1]. Free radicals are toxic repercussion of oxygen-containing molecules metabolism that may cause significant damage to the cells and tissues [2]. Oxidative stress is a rudimentary cause for conditions like cardiovascular diseases (CVD), dyslipidemia, type 2 diabetes mellitus (T2D), etc. T2D is due to the impaired glucose tolerance, the underlying reason for which is β- cell dysfunction leading to insulin resistance which is predominantly due to increased OS [3]. Consumption of substantial amount of alcohol is also proven to be one of the major factor to cause T2D [4].

In T2D population the effect of OS is said to be intensified by the inactivation of endothelial nitric oxide (NO) [5]. NO is generated practically by almost all types of cell in the human body. It is presumed to be very important molecule in the blood vessel. NO serves as a vasodilator. It has significant effect on smooth muscle tissue. It also acts as neurotransmitter and also involved in wide range of functions. (Fig. 1)

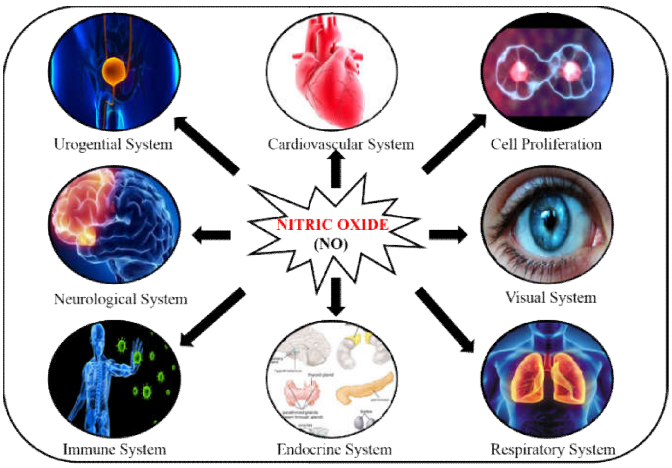

Figure 1 Functions of Nitric Oxide

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Insulin is the hormone which controls the activation of NO synthase (NOS) and this NO metabolic regulation is exceptionally important in T2D [6]. The OS pathways comprises the uncoupling of the endothelial NO synthase (eNOS) (under conditions of substrate deficiency) which in turn produces both NO and superoxide dismutase [7]. DM fundamentally hinder the characteristic feature of the endothelium- vasodilating which assists endothelial dysfunction. OS is said to instigate many event like mitochondrial dysfunction, lipid peroxidation, production of inflammasomes etc., which triggers the process of inflammation by increasing certain cytokines i.e. IL-1, IL-6, etc. Now the increase in the cytokines is further associated with insulin resistance, proinflammatory cytokines and β-cell dysfunction, all this contributes to T2D. [3] (fig. 2)

Diversified results of NO have been noted in diabetic patients, however the results revealed are controversial. Some studies reported increased level of NO in diabetic patients [8, 9, 10], whereas some reported contrast results [11, 12].

OS is determined by the overall capacity of antioxidant. A depletion of TAC is strongly associated with higher incidence of diabetic complications. TAC is the measure of the amount of free radicals scavenged by a test solution, being used to evaluate the antioxidant capacity of biological samples [13, 14, 15]. The advantage of TAC estimation over measuring individual antioxidant assay is reduction in time and labor and cost effective [16].

Many studies express that alcohol increases lipid peroxidation as well as the modification of proteins. Nevertheless it is not always clear if these changes are the causes rather than consequences of alcohol –induced tissue injury. The acetaldehyde produced during metabolism of alcohol is said to damage the cell membrane by generation of free radical which is produced by the interaction of acetaldehyde with proteins and lipid molecules [17, 18]. These changes in the protein and lipid molecules leads to many disorders, one of the major disorder is various cardiac diseases [19]. Alcohol nurtures the causation of ROS release in the liver, hefty drinking minimizes the body's sensitivity to insulin, which may provoke T2D. Chronic pancreatitis is one of the common disease caused due to large alcohol intake. Oxidative stress is induced due to increase in cytokines and inflammatory compounds which is said to be the attributes by alcohol misuse [20]. Therefore the present study was performed to accomplish the association between alcohol abuse, oxidative stress and type 2 diabetes mellitus.

MATERIAL & METHODS

This study was conducted in Grant Govt. Medical College & Sir JJ Group of Hospitals, in the department of Biochemistry, on the participants having Type 2 Diabetes alcoholics and non-alcoholics, within the age group of 35-55 years having no other systemic diseases like Type 1 DM, HIV, cancer etc. were chosen as study group. Other 200– age and sex-matched apparently with no history of diabetes or other metabolic disorders were taken as controls non- alcoholics and alcoholics respectively.

The diagnosis of diabetes mellitus was based on the WHO criteria [21]. The subjects were well informed about the sample collection procedure and were told to maintain 13-14 hours of fasting before collection. 7ml of fasting blood sample was collected in a heparinized tube and the plasma was allowed to separate. The samples were stored at 4°C if required. The collected samples were later used for biochemical estimations of Nitric oxide by Cadmium reduction method [22] and MDA as a marker of lipid peroxidation by Kei Satoh's method [23]. 2ml blood was collected in fluoride blub for glucose estimation and estimation was done using GOD-POD method colorimetrically. The TAC was determined by the spectrophotometric Ferric Reducing Ability of Plasma (FRAP) method [24]. All results were summarized as mean ± standard deviation (±SD) and the comparison between cases and control was done using students 't' test. P value ≤ 0.0001 was considered as statistically significant.

RESULT & DISCUSSION

The study was conducted among 100 newly diagnosed T2D subjects non - alcoholic, 100 newly diagnosed T2D subject alcoholics and 100 healthy controls non - alcoholic and 100 healthy alcoholic controls respectively. The blood glucose values – between study group and control group significantly differed.

In oxidative stress the cells and tissues undergo changes which may harm them as they are unable to cope up with the free radical generation. The MDA and the NO generated in the course of free radical production leads to many biological changes in the body. Serum MDA levels were found to be significantly higher in diabetic patients as compared to the healthy controls. Among diabetics, alcoholic patients showed significantly high values ($p < 0.0001$) when compared with the non-alcoholic diabetic subjects. Our results are at par to many studies where the MDA levels are seen to be increased significantly in alcoholics [25, 26]. The free radicals are generated through various mechanisms, the cell proteins and the lipids are then prone to cellular damage there by resulting in the increase of serum MDA levels [27] which then leads to various alternative mechanisms deforming to increase in the systemic inflammation, insulin resistance, beta cell dysfunction and thereby T2D (fig. 2).

Risk Factors	GROUP I		GROUP II	
	Control-Non-Alc	Control-Alc	Newly diagnosed Diabetic subjects): Non-Alc	Newly diagnosed Diabetic subjects: Alc
Blood glucose (mg/dl)	83.26±4.8	92 ± 5.1	174.35±9.9$^{\$}$	192.67±10.73*$^{\$}$
Serum MDA (mmol/l)	1.13±0.3	2.32±0.7	2.93±0.91$^{\$}$	3.62±0.9*$^{\$}$
Serum NO (mmol/l)	8.33±1.8	11.23±1.9	12.42±2.3$^{\$}$	14.1±3.2*$^{\$}$
Serum TAC (mmol/l)	1.10 ± 0.12	1.96 ± 0.14	1.03 ± 0.18$^{\$}$	0.84 ± 0.21*$^{\$}$

(Alcoholic compared to alcoholic group & Non-alcoholic compared to non-alcoholic group and alcoholic)$^{\#}$Data reported as mean ± SD
Paired t test: *p<0.0001 compared to Group II (Newly diagnosed)
Unpaired t test: $^{\$}$ p<0.0001 Compared to Group I (Control)

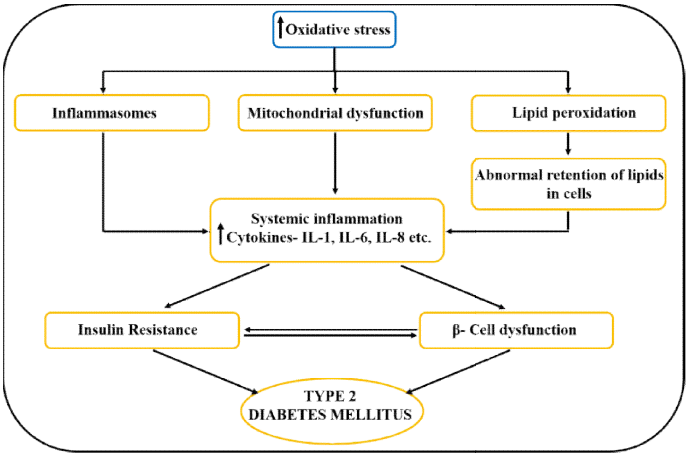

Figure 2 Relation of Oxidative stress& Diabetes

Serum NO levels were noted significantly high in diabetic patients as compared to the healthy controls. Among the study group the alcoholic diabetics showed notable significance when compared to the non-alcoholic diabetic patients. Liver undergoes endotoxic shock due to alcohol. The production of NO and its adverse effects are accelerated by alcohol. Alcohol consumption leads to endothelial OS and mis-regulation of NO production [28]. There is a strong accordance that impairment of NO production is observed in prolonged DM leading to further complications [29, 30]. Our study is at par with many researchers where chronic hyperglycemia leads to hindered NO production leading to progression of atherosclerosis, stroke, thrombosis etc. [31, 32, 33]

Serum TAC levels were strikingly lowered in diabetic patients as compared to the healthy controls. The decreased TAC levels is an outcome of increased lipid peroxidation and thereby its utilization in the scavenging the free radicals, which plays a crucial role in the pathogenesis of the disease [34, 35, 36]. Many investigators have shown that alcohol decreases the activity of various antioxidant enzymes which results in the decreased TAC [37, 38, 39]

CONCLUSION

In conclusion, our study emphasizes on how the commonly and socially consumed alcohol has influence on the quality of life. The hefty consumption of alcohol evidently affects the function of liver as NO is said to be an important mediator pathophysiologically. Oxidative stress triggered by increased concentration of glucose has a crucial contribution in complications related to diabetes. The increased NO and MDA concentration are related to untimely clinical occurrence, such as endothelial dysfunction, pancreatic cell dysfunction and thereby insulin resistance. The decreased TAC levels may be the significant cause of increased levels of serum NO, and MDA or vice-versa. Additionally alcohol consumption in diabetes disturbs the balance of antioxidants thereby leading to oxidative stress resulting in liver and kidney damage. However, there is future opportunity for research as the harmful effects and mechanism by alcohol abuse on the liver, kidney, central nervous system, immune system etc. are not yet clear.

Reference

1. Oxidative stress: definition, effects on the body and prevention. Available at: https://www.healthline.com/health/oxidative-stress Accessed on 24th June 2019
2. Lobo V, Patil A, Phatak A, *et al*. Free radicals, antioxidants and functional foods: impact on human health. Pharmacogn rev. 2010; 4(8): 118-26.
3. Tangvarassittichai S. Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. *World J Diabetes*. 2015; 6(3): 456-80.
4. Wannamethee SG, Shaper AG, Perry IJ, Alberti KG. Alcohol consumption and the incidence of type II diabetes. *J Epidemiol Community Health*. 2002; 56(7):542-8.
5. Folli F, Corradi D, Fanti P, *et al*. The role of oxidative stress in the pathogenesis of type 2 diabetes mellitus micro- and macrovascular complications: avenues for a mechanistic-based therapeutic approach. Curr Diabetes Rev. 2011; 7(5): 313-24.
6. Fisslthaler B, Benzing T, Busse R, Fleming I. Insulin enhances the expression of endothelial nitric oxide synthase in native endothelial cells: a dual role for Akt and Ap-1. Nitric Oxide 2003; 8(4): 253-61.
7. Münzel T, Sinning C, Post F, *et al*. Pathophysiology, diagnosis and prognostic implications of endothelial dysfunction. Ann Med. 2008; 40(3):180-96.
8. R.D. Hoeldtke, K.D. Bryner, D.R. McNeill, *et al*. Oxidative stress and insulin requirements in patients with recent-onset type 1 diabetesJ. Clin. Endocrinol. Metab, 2003; 88(4):1624-28.
9. Aydin, H. Orhan, A. Sayal, M. Ozata, *et al*. Oxidative stress and nitric oxide related parameters in type II diabetes mellitus: effects of glycemic control Clin. Biochem., 2001; 34(1): 65-70.
10. R. Adela, S.K. Nethi, P.K. Bagul, A.K. Barui, *et al*. Hyperglycaemia enhances nitric oxide production in diabetes: a study from South Indian patients PloS One, 2015; 10(4): e0125270.
11. M. Krause, J. Rodrigues-Krause, C. O'Hagan, *et al*. Differential nitric oxide levels in the blood and skeletal muscle of type 2 diabetic subjects may be consequence of adiposity: a preliminary study. Metab. Clin. Exp., 2012; 61(11):1528-37.
12. M. Daimon, K. Sugiyama, T. Saitoh, *et al*. Increase in serum ceruloplasmin levels is correlated with a decrease of serum nitric oxide levels in type 2 diabetes. Diabetes Care, 2000; 23(4): 559-60
13. Marues SS, Magalhaes LM, Toth IV, *et al*. Insights on antioxidants assays for biological samples based on the reduction of copper complexes- the importance of analytical conditions. Int J Mol Sci. 2014; 115: 11387-402.
14. Bartosz G. Non-enzymatic antioxidant capacity assays: limitations of use in biomedicine. Free Radic Res. 2010: 44: 711-20.
15. Pinchuk I, Shoval H, Dotan Y, Linhtenberg D. Evaluation of antioxidants: scope, limitations and relevance of assays.Chem Phys. 2012; 165: 638-47.
16. Erel O. A novel automated direct measurement method for totsl antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem. 2004; 37:277-85.

17. Haorah J, Ramirez SH, Floreani N, *et al*. Mechanism of alcohol-induced oxidative stress and neuronal injury. Free Radic Biol Med. 2008; 45(11): 1542-50.
18. Defeng Wu, Cederbaum A. Alcohol, oxidative stress and free radical damage. Clinical Trails. National Institute on Alcohol Abuse and alcoholism. Available at : https://pubs.niaaa.nih.gov/publications/arh27-4/277-284.htm Accessed on -8th August 2019
19. Smita Swami, Anuradha Kanhere, Sanjay Swami. Role of lipids in type 2 diabetes mellitus for causation of coronary artery disease. IJCBR. 2018; 5(1): 134-7.
20. Vonlaufen A, Wilson JS, Pirola RC, *et al*. Role of alcohol metabolism in chronic pancreatitis. Alcohol Res Health. 2007; 30(1): 48-54.
21. WHO criteria for Diabetes 2017. Accessed on 13th August 2019. Available at : http://www.who.int/diabetes/action_online/basics/en/index2.html
22. Najwa K Cortas, Nabil W Wakid. Determination of inorganic nitrate in serum and urine by kinetic cadmium reduction method. Clin Chem 1990; Vol.36 (8): 1440-43.
23. Kei Satoh. Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. Clin Chim Acta 1978; Vol.90: 37-43.
24. Singh M, Aggarwal HK, Aggarwal SK. Significance of the glutathione-S-transfeurase activity and total thiols status in chronic alcoholics. *J Clin Diagn Res*. 2012; 6(1): 31-3.
25. Benzie IF, Strain JJ. The ferric reducing ability of plasma (FRAP) as a measure of "antioxidant power" the FRAP assay. Anal Biochem. 1996 Jul 15; 239(1): 70-6.
26. Zhang X, Li S Y, Brown R A, *et al*. Ethonal and acetaldedyde in alcoholic cardiomyopathy: from bad to ugly en route to oxidative stress. Alcohol 2004; 32: 175-86
27. Shinde A, Ganu J, Naik P, *et al*. Oxidative stress and antioxidant status in pateints with alcoholic liver disease. Bio Res. 2012; 23: 105-8
28. Lin Shu-Han, Chung Pei-Hsuan, Wu Ying-Ying, Fung Chang-Phone, *et al*. Inhibition of nitric oxide production reverses diabetes-induced Kupffer cell activation and Klebsilla pneumonia liver translocation. 2017 May. Available at : https://doi.org/10.1371/journal.pone.0177269
29. Pfeilschifter J. Does nitric oxide, an inflammatory mediator of glomerular mesangial cells, have a role in diabetic nephropathy? Kidney Int., 1995; 51: S50-60
30. Avogaro A, Albeiro M, Menegazzo L, *et al*. Endothelial dysfunction in diabetes: the role of reparatory mechanisms. Diabetes Care, 2011; 34(2): S285-90
31. Schmidt HH, Walter U. NO at work. Cell. 1994; 78(6): 919-25
32. Dellamea BS, Leitao CB, Friedman R, *et al*. Nitric oxide system and diabetic nephropathy. Diabetol. MetabSyndro., 2014; 6(1): 17
33. Napoli C, Ignarro LJ. Nitric oxide and pathogenic mechanisms involved in the development of vascular diseases. Arch Pharmacol Res., 2009; 32(8): 1103-08.
34. Reddy S. K, Husian K, Schioff E. C. *et al*. Dose response of ethanol ingestion on antioxidant defense system in ratbrain subcellular fraction. Neurotoxicology. 1999; 20: 977-87
35. Zima T, Flalova L, Metsek O, *et al*. Oxidative stress, metabolism of ethanol and alcohol-related disease. J Biomed Sci. 2001; 8: 59-70
36. Mihallescu I, Mohora M, Dinu V. Preliminary evidence for lipid peroxidation and changes in pro-oxidant status in brain tissue and blood in ethanol intoxicated rats. Revue Roumaine De Physiologie 1991: 28: 137-7.
37. Saravanan R, Rajendra PN, Pugalendi KV. Effect of pipierbetleleaf extract on alcoholic toxicity in the rat brain. J Med Food. 2003; 6: 261-5
38. Bjorneboe GA, Johnsen J, Bjorneboe A. *et al*. Effect of heavy alcohol consumption on serum concentrations of fat-soluble vitamins and selenium. Alco & Alcoholism 1987; 1: 533-7.
39. Bjorneboe GE, Johnsen J, Bjorneboe A, *et al*. Some aspects of antioxidants status in blood from alcoholics. Alcoholism. Clin Exp Res. 1988; 12: 806-10.

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