STUDY ON THIOBARBITURIC ACID ACTIVITY IN PLASMA OF DIABETIC PATIENTS – A Review

Mohammad Chand Jamali[(1)], Mohammad Qasim[(2)]

1. **Senior Clinical Scientist- Department of Health & Medical Sciences, Zayed Military Hospital, Al Ain, Abu Dhabi, UAE**
2. **Principal- Al Shaheen Paramedical College & Hospital, College of Health & Medical Sc, UAE University, Al Ain, UAE**

ABSTRACT

Several studies have demonstrated that endothelial dysfunction plays a central role in diabetic mortality and that the prooxidative effect of postprandial hyperglycemia may actively contribute to atherogenesis. Thus, we investigated the possible effect of short-acting (repaglinide) and long-acting (glibenclamide) insulin secretagogues on endothelial function in type 2 diabetic patients.

Key Words: Thio Barbituric Acid, Pro-oxidative effect, Glibenclamide

No:of References: 9

Corresponding Author: Mohammad Chand Jamali, Department of Health & Medical Sciences, Khawarizmi International College, 25669, Abu Dhabi, United Arab Emirates, E-mail: mjamali68@gmail.com

INTRODUCTION

The prevalence of diabetes mellitus has increased in recent years, particularly type 2 diabetes, which is related to obesity and sedentary lifestyle. The total number of people globally affected by diabetes was reported to be 171 million in 2000 and is projected to be 366 million by 2030, and the vast majority of these cases will be of type 2 diabetes. Free radical production has been reported to be increased in patients with diabetes mellitus and hyperglycemia appears to be the contributing factor for the generation of reactive oxygen species (ROS) which lower the concentrations of antioxidant enzymes. Oxidative stress induced by a high glucose concentration plays a central role in complications of diabetes. Oxidative stress induces the production of highly reactive oxygen radicals that are toxic to cells and has been attributed to protein glycation and/or glucose auto-oxidation owing to a hyperglycemic environment. Oxygen radicals also interact with the lipid bilayer and produce lipid peroxides particularly in cell membranes. Lipid peroxidation of cellular structures is thought to play an important role in complications of diabetes.

Alcoholic beverages are used universally and alcohol is the world's most widely used psychoactive drug, but chronic, excessive alcohol consumption leads to permanent organ damage or death. Alcohol is rapidly oxidized in the liver tissue to acetaldehyde and acetate by alcohol dehydrogenase (ADH) and acetaldehyde dehydrogenase (ALDH), respectively. Further alcohol consumption and diabetes disturb the balance between the pro- and antioxidant systems of the organism, thereby leading to the oxidative stress by generating free radicals or ROS, which results in liver and kidney injury.

There are limited reports on the influence of alcohol on a diabetic state. A J-shaped relationship between alcohol consumption and diabetes has been reported by Hoffmeister *et al*. Chronic excessive consumption of alcohol may lead to deleterious effects upon many organs and metabolism. Diabetogenic effects of alcohol include its contribution to obesity, induction of pancreatitis, and disturbance of carbohydrate and glucose metabolism. However, the harmful effects of alcohol abuse on the functions of liver, kidney, heart, immune system, and central and peripheral neural system are not yet known.

There are no reports on the effect of alcohol on antioxidant enzymes and blood glucose in diabetic rats. The purpose of this study was to investigate the effect of alcohol in streptozotocin (STZ)-induced diabetic rats by measuring blood glucose levels and assaying the antioxidant enzymes activities in liver and kidney tissues.

Discussion

In the diabetic group, the body weight was decreased. Weight loss during diabetes is mainly related to urinary glucose excretion because cells use glucose for many functions. Another factor could be the osmotic diuresis resulting in hyperosmotic dehydration. With alcohol treatment in diabetic rats, we observed significantly ($P < 0.001$) lower body weights compared to diabetic rats. This was due to the dehydration, excess utilization of proteins for the energy. So, in alcohol-treated diabetic rats, decreased body weight was observed.

SOD scavenges the superoxide radical by converting it to H_2O_2 and oxygen. In the present study, the SOD activity was decreased in the diabetic group. Pari and Latha also reported that the SOD activity was decreased in diabetic rats. The decrease in the SOD activity in diabetic rats could result from the inefficient scavenging of ROS, which might be implicated in the oxidative inactivation of enzymes and especially the deleterious effects due to the accumulation of superoxide radicals, or by glycosylation of the enzymes, which have been reported to occur in diabetes. In the current investigation, we observed a decreased activity of SOD in the alcohol-treated group. Shanmugam *et al*. and Mallikarjuna *et al*. reported that alcohol administration depleted the SOD activity in the kidney and liver tissues of albino rats. Several studies have reported that alcohol consumption decreases the SOD activity in the liver, heart, brain, kidney muscle, and serum. The reduced activity of SOD in the presence of alcohol may cause the accumulation of $O2^{\bullet-}$, H_2O_2, or the products of its decomposition. However, in the combination treatment group, i.e., alcohol-treated diabetic rats (D + At), the SOD activity was significantly ($P < 0.001$) decreased compared to that of the alcohol-treated group and diabetic control group. This may be due to the excessive production of free radicals and superoxide radicals, so the SOD activity was decreased to counter the same.

In the present study, the CAT activity was decreased in diabetic rats. The reduced activity of CAT in kidney and liver tissues may result in a number of deleterious effects due to the accumulation of H_2O_2. The CAT activity was also decreased in alcohol-treated (At) rats in the present study. The reduced activity of CAT in the presence of alcohol causes the accumulation of free radicals which are toxic in nature. Balasubramaniyan *et al*. and Mallikarjuna *et al*. reported that the CAT activity in kidney and liver was decreased in the alcohol-treated group. CAT helps to scavenge hydroxyl ions, so the CAT activity was lowered in alcohol-treated rats whereas in the combination treatment (D + At) group, the CAT activity was significantly decreased ($P < 0.001$) compared to the alcohol-treated or diabetic group. This may be due to the excess production and accumulation of hydroxyl radicals. CAT helps in neutralizing these toxic hydroxyl radicals, so the CAT activity was decreased. The additive

effects of alcohol are observed in diabetic animals causing a greater reduction in these two enzymes.

In the current study, MDA levels were increased in diabetic rats. Previous studies have reported an increase in lipid peroxidation in the liver, kidney, and brain of diabetic rats. Lipid peroxide-mediated tissue damage has been observed in type I and type II diabetes. Higher levels of lipid peroxides in plasma urine and renal proximal tubules were observed in diabetic rats. Kakkar *et al*. also reported the same. Ostrowska *et al*. reported a threefold higher concentration of lipid hydroperoxides in alcohol-treated rats compared to the control groups. During alcohol metabolism, potentially dangerous byproducts are generated including ROS which react with membrane lipids and cause lipid peroxidation leading to cell death. In alcohol treated diabetic rats, we observed significantly ($P < 0.001$) higher levels of MDA compared to alcohol and diabetic groups. During combination treatment, more free radicals are produced, hence the MDA level was increased in combination treatment.

The histopathological studies revealed that in the kidney tissue of alcohol-treated rats, tubular degeneration, necrosis of renal cells, and degeneration of Bowman's capsule were observed. In diabetic control rats, severe tubular degeneration, degeneration of glomeruli, focal necrosis of tubules, cystic dilatation of tubules, and fatty infiltration were observed. This might be associated with increased diuresis and renal hypertrophy in diabetic rats. The above-mentioned pathological changes were more severe in alcohol-treated diabetic rats. The dilatation of Bowmen's capsule and hyaline casts were also observed.

The histopathological studies of the alcoholic liver showed the disruption of hepatocytes, sinusoids, and central vein. This proves that free radical production might cause hepatic damage. In the diabetic group, greater damage of hepatocytes, sinusoids, and central vein was observed whereas in the alcohol-treated diabetic group, hepatocytes, sinusoids, and central vein were more severely degenerated. The histological evidence of alcohol-treated diabetic rats suggests that structural alterations at the end of 30 days are due to diabetic stress and alcoholic stress. Thus, in addition to elevated levels of blood glucose, histopathological observations also support the concept that alcohol produced additive effects, and hence renal, hepatic tissue damage in diabetic rats.

REFERENCES

Uzar E, Alp H, Cevik MU, Fırat U, Evliyaoglu O, Tufek A, Altun Y. Ellagic acid attenuates oxidative stress on brain and sciatic nerve and improves histopathology of brain in streptozotocin-induced diabetic rats. Neurol Sci. 2012; 33: 567–574.

Anitha M, Abraham PM, Paulose CS. Striatal dopamine receptors modulate the expression of insulin receptor, IGF-1 and GLUT-3 in diabetic rats: effect of pyridoxine

treatment. Eur J Pharmacol. 2012; 696: 54–61.

Pari L, Latha M. Protective role of Scoparia dulcis plant extract on brain antioxidant status and lipidperoxidation in STZ diabetic male Wistar rats. BMC Complement Alter Med. 2004; 4: 16.

Gipsen WH, Biessels GJ. Cognition and synaptic plasticity in diabetes mellitus. Trends Neurosci. 2000; 23: 542-549.

McCall AL. The impact of diabetes on the CNS. Diabetes. 1992; 41: 557-570.

Li PA, Gisselsson J, Keuker J, Vogel ML, Kuschinsk SW. Hyperglycemia-exaggerated ischemic brain damage following 30 min of middle cerebral artery occlusion is not due to capillary obstruction. Brain Res. 1998; 804: 36-44.

Arlt S, Beisiegel U, Kontush A. Lipid peroxidation in neurodegeneration: new insights into Alzheimer's disease. Curr Opin Lipidol. 2002; 13: 289-294.

Prince PSM, Kumar MR, Selvakumari CJ. Effects of gallic acid on brain lipid peroxide and lipid metabolism in streptozotocin-induced diabetic Wistar rats. J Biochem Mol Toxicol. 2011; 25: 101-107.

Makar TK, Hungund BL, Cook GA, Kashfi K, Cooper AJ. Lipid metabolism and membrane composition are altered in the brains of type II diabetic mice. J Neurochem. 1995; 64: 2159-2168.