DOES CIGARETTE SMOKING HAVE ANY RELATIONSHIP WITH OXIDATIVE STRESS AND ANTIOXIDANTS?

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Abstract

An attempted has been made is in this study to show if there is any relationship between cigarette smoking and diabetes mellitus and its comelation with enzymatic antioxidant in response to free radical producation. The results shows that cigarette contains on extremely high concentration of various free radicals and a good relationship with diabetes to generate a situation to effect the enzymatic and nonenzymatic antioxidant .

Introduction

Diabetes mellitus is a very complex chronic disease with syndrome of hyperglycemia (Zhao, 2001). The symptoms of worked hyperglycemia include polyuria. Polydipsia, weight loss, high glucose in urine, increased appetite, ketoacidosis, acid / base imbalance, and diabetic coma.

Long – term complications of diabetes include blindness, neuropathy, kidney failure, lower extremity amputations, cardiovascular complication and pregnancy complication (Bishop ***et al .,*** 2000).

In 1979, the National Diabetes Data Group (NDDG) developed a classification and diagnosis scheme for diabetes mellitus . This scheme provides dividing diabetes into two broad categories : type I, insulin dependency diabetes mellitus (IDDM), and type Π, non-insulin – dependent diabetes mellitus (NIDDM) . In correlation of DM with free radicals, the free radicals can be defined as an atom or molecule that contains one or more unpaired electrons in its outer orbit (Oberley, 1988) .

In addition to internal sources of free radicals one of the external generated sources of free radicals is Cigarette smoke (Bagchi & Puri, 1998)which reduce the activity of antioxidant system, this may lead to imbalance between oxidant– antioxidant in favor of the prooxidant leading to potential damage and dominant risk

factor of many disease (Michiels ***et al .,*** 1994) .

Effect of smoke nicotine on the function of human polymorphnuclear (PMN) leukocytes was the inhibition of microbial function of PMN through inhibition of O_2^- production and release of lysosomal enzymes, but nicotine has no effect on migration of PMN to inflammatory sites . However oxidative damage may also results from RSO· Generated by the increased and activated phagocytes following cigarette smoking (Chow, 1993) and associated with significant increase in circulating nutrophils count and phagocytes derived ROS (Sharma ***et al .,*** 1997) .The aim of this study is to show the effect of smoking on oxidative stress status in Diabetic patients.

Material and Methods

Material

All materials used in this study have been used without any farther purification .

Methods

Place of work

This research was conducted in Al – diwaniya general hospital ; Dept.of Biochemistry, College of medicine, AL- Nahrain University, and Dept.of chemistry, College of Science, Baghdad University .

Subjects

Samples included 50 patients suffering from type Π of diabetes (28 male and 22 female) , aged between 35 and 65 years and 50 patients with type I (32 male and 18 female) aged between B and 65 years with controlled 50 healthy individuals (38 male and 12 female) aged between 15 and 65 years. All tests were performed on serum for detection of variable in this study .

Determination of serum Malondialdehyde, Selenium , chromium, zinc, and glutathione using the methods described by (Burtis & Ashwood, 1999) .

Determination of serum to homoysteine using the method described by (Pastor ***et al .,*** 1988, Shaushel ***et al .,*** 2003) .

Statistical Analysis

The data were analyzed by using student's T – test taking $P \leq 0.05$ as the lowest limit of significant of difference and simple linear correlation between two quantitative parameters and correlation considered significant at $P \leq 0.05$.

Results and Discussion:

Effect of Smoking on Oxidative Stress Status in Diabetics

Evidence for increased oxidation in smokers compared with non-smokers were proved by the presence of increased prooxidant products in blood and urine (Morrow ***et al.***, 1995; Mezzetti ***et al.***, 1995).

In this work, the results reported no

significant difference in levels of serum MDA, tHcy, Cu, Fe, Zn, Se, Cr, GSH, vitamin C, and GST, Ec-Cu/Zn SOD, CK, CAT activities in serum of smokers with type 1, and 2 DM than diabetic non-smokers as well as in levels of serum vitamin E of smokers with type 1 DM, and levels of serum vitamin A of smokers with type 2 DM than that of diabetic non-smokers, table (1).

But there was a significant decrease in level of vitamin A in serum of smokers with type 1 DM, $P \leq 0.05$, figure (1) , and vitamin C in serum of smokers with type 2 DM, $P \leq 0.05$, figure (2) , than diabetic nonsmokers.

These results may probably be due to the following:

1. Smoking may be enhance oxidative stress through the production of free radicals and weaken antioxidant defense mechanism (Maragnon et al, 1998; Zhao & Yu, 1998; James et al, 2000; Al-Meshhadani, 2003). Therefore, smoking slightly increases level of MDA in serum of diabetic smokers than diabetic non-smokers.

2. Some toxic components of tobacco smoke could interact with thiol rich compounds leading to structural and functional changes of these molecules (Zappacosta et al., 2002). Therefore, smoking could be slightly depletion level of GSH and accumulation of tHcy in serum of diabetic smokers than diabetic non-smokers, or decreased level of GSH may be due to increase GSH utilization in neutralizing smoking induced free radicals.

3. Cigarette smoke contains an extremely high concentration of various free radicals, which are increased susceptibility of -SH groups of CK enzyme to be oxidized and inhibition or probably due to the interaction between smoke aldehydes and -SH groups; the active sites of enzyme molecules and reduced its activity, therefore smoking could be slightly decreased level of CK activity in serum of diabetic smokers than diabetic non-smokers (Zappacosta et al., 2002).

4. Smoke contains $O2^{\cdot -}$ and in response to the increase amounts of substrate of O2.- this results in an increase in Ec-Cu/Zn SOD activity probably through induction. In addition nicotine (5 X 10-6 to 5 X 10-11 M) in cigarette was found to inhibit of $O2^{\cdot -}$ production from polymorphonuclear cells (Sasagawa et al., 1985). But because $O2^{\cdot -}$ considered as a stimulant to increase synthesis of SOD (Lunec et al., 1981), therefore this explanation could be the cause behind the slight decrease in Ec-Cu/Zn SOD level in diabetic smokers, also lead (Pb) and cyanide is considered as a component of cigarette smoke (Mawin-Mateo et al., 1997) and the coppro zinc enzymes are inhibited by cyanide

(Borders & Fridovich, 1985), while Pb causes non-competitive inhibition of a covalent bond at the enzyme and decrease in Vmax of enzyme reaction (Mawin-Mateo et al., 1997).

5. Increased CAT enzyme utilization in neutralizing smoking induced free radicals (Muhlhauser et al., 1996; Ritzetal., 1996) lead to slightly decreased levels of CAT activity in serum of diabetic smokers than diabetic non-smokers.

6. Presence of toxic compounds in the cigarette smoke such as semiquinones (Kasai & Nishimura, 1986) induced accumulation of GST enzyme by increase its synthesis to play a protective role, therefore smoking may be slightly increases level of GST activity in serum of diabetic smokers than diabetic non-smokers.

7. Utilizing high level of vitamin C in diabetic smokers to neutralize free radicals generation through smoking results in slightly reduced levels of vitamin C in serum of diabetic smokers than non-smokers, while vitamin A levels were slightly reduced in serum of smokers with type 2 DM than diabetic non-smokers, but is reduced significantly in serum of smokers with type 1 DM, these results are due to that gas phase of cigarette smoke is a complex oxidizing milieu processing an array of free radical species including peroxy radicals (ROO.), and O2.- (Pryor & Ston, 1993), which has been shown to deplete lipid phase. Furthermore, vitamin E levels were slightly reduced in serum of smokers with type 1 DM than diabetic non-smokers, while are reduced significantly in serum of smokers with type 2 DM. This may be due to increase production of catecholamine hormone in smokers with type 2 DM and act as an antagonist to insulin action (Targher, 1997), thus increase free radicals production under hyperglycemia that require high level of vitamin E to be neutralization.

8. Smoking is increasing oxidative stress and weakening defense system, therefore it increases disturbance in trace elements levels in diabetic smokers than diabetic non-smokers, thus there was a slightly increase in levels of copper and iron and slightly decrease in levels of zinc, selenium and chromium in serum of diabetic smokers than diabetic non-smokers.

Table (1): Effect of smoking on the levels of some biochemical markers related to oxidative stress syndrome in diabetics.

Variables	Type 1 DM, No.=50			Type 2 DM, No.=50		
	Smokers No.=11Mean±SE	Smokers No.=39Mean±SE	P-Value	Smokers No.=17Mean±SE	Smokers No.=33Mean±SE	P-Value
Age (Years)	33±3.734	31.82±2.772	NS	48.176±2.054	53.272±1.490	NS
Duration of DM (Years)	9.325±2.217	10.657±1.685	NS	5.284±1.556	5.787±1.017	NS
MDA (µmol/L)	0.966±0.099	0.962±0.034	NS	0.999±0.068	0.848±0.037	NS
tHcy (µmol/L)	20.507±0.810	19.475±0.484	NS	22.451±0.663	21.037±0.481	NS
Ec-SOD (U/ ml)	1.543±0.180	1.585±0.057	NS	1.288±0.096	1.402±0.081	NS
CAT (K/ml)	0.382±0.054	0.387±0.016	NS	0.488±0.031	0.542±0.024	NS
GST (U / l)	4.879±0.504	4.689±0.216	NS	4.172±0.277	3.709±0.210	NS
CK (U / l)	158.09±10.15	171.512±5.897	NS	147.176±6.245	156.787±3.197	NS
GSH (µmol/L)	0.641±0.084	0.694±0.024	NS	0.816±0.060	0.901±0.47	NS
VitaminE(µmol/L)	3.084±0.173	3.429±0.086	NS	2.935±0.171	3.506±0.123	NS
VitaminA(µmol/L)	0.742±0.123	1.345±0.096	S	1.324±0.089	1.41±0.114	S
VitaminC(µmol/L)	3.439±0.233	3.455±0.202	NS	3.618±0.217	3.689±0.232	NS
Iron(µmol/L)	10.2±1.130	8.202±0.323	NS	6.96±0.565	6.653±0.332	NS
Copper (µmol/L)	17.281±1.182	16.96±0.693	NS	15.883±1.083	15.814±0.674	NS
Zinc (µmol/L)	10.387±0.260	10.524±0.137	NS	11.106±0.214	11.136±0.137	NS
Chromium(µmol/L)	0.564±0.018	0.583±0.011	NS	0.566±0.016	0.595±0.008	NS
Selenium(µmol/L)	0.847±0.025	0.857±0.017	NS	0.862±0.019	0.875±0.009	NS

Determination of serum superoxide Dismutase (SOD) using the method described by (Winter boun ***et al.,*** 1975).

Determination the activity of serum creatine kinase, iron, copper, by using commercially available kit (Randox – UK) .

Determination of serum Glutathione –s- Transferase by using the method described by (Habig ***et al .,*** 1974) .

Determination of serum vitamin E,A,C by HPLC Technique (cited in Salman , 2001) .

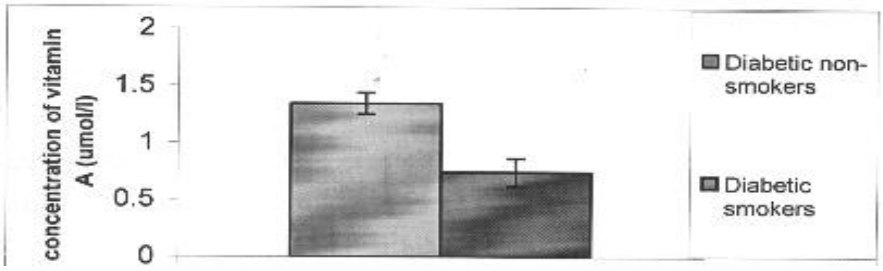

Figure (1) : Level of vitamin A in serum of smokers and non – smokers patients with type 1 diabetes mellitus (DM) disease . The values are the mean ± SE .

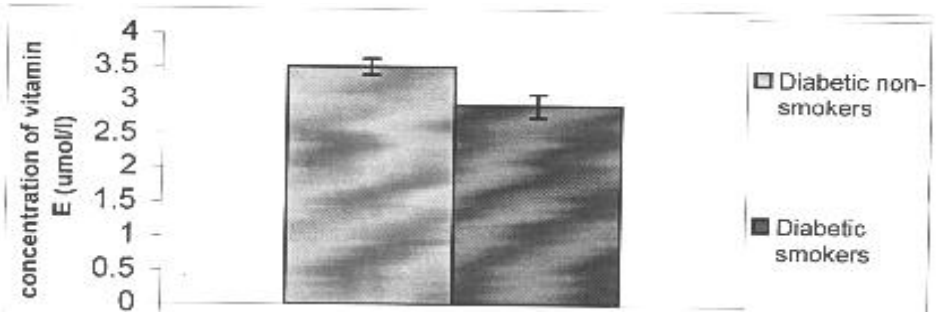

Figure (2) : Levels of vitamin E in serum of smokers and non – smokers patients with type 2 diabetes mellitus (DM) diseases . The values are the mean ± SE

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