

PARAMETERS OF OXIDATIVE STRESS IN PATIENTS WITH DIABETES

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Abstract

Patients with diabetes show an increase in oxidative stress, the more pronounced, the more metabolic imbalance is greater. Oxidative stress is an imbalance between the antioxidant and prooxidative reactions, the balance is tilted in favor of prooxidative. Oxidative stress is more marked in diabetic patients who show a poor metabolic control. This will lead in time to a worsening in proteins, lipids and carbohydrates structures, generating a series of pathophysiological processes that will contribute to the emergence and rapid evolution of chronic degenerative complications of diabetes.

keywords: *oxidative stress, diabetes, metabolic control*

Introduction

Oxidative stress is the disruption of redox homeostasis or all oxidative damages produced by an overproduction of reactive species (RS) or a reduction in capacity of antioxidative systems (AO) in the cell or in whole organism [1, 3].

Essentially, there is a prooxidant/antioxidant balance disorder in favor of prooxidants and against antioxidants.

Oxide radicals exercise two types of effects: beneficial and harmful [2, 4, 5]:

Beneficial effects:

- bactericide in the phagocytosis
- stimulate cell activity
- control of vascular tone

- stimulating growth and proliferation of cells

- stimulating secretion of erythropoietin.

Harmful effects:

- destructive/damage cellular structures
- malignant cell transformation
- aging cell.

Effects on genetic material and on different metabolic pathways:

1. Effects on **DNA**: nucleolus fragmentation, activation of oncogenes, inactivation of tumor suppressor genes.

2. Effects on **lipids**: lipid peroxidation, loss of fluidity and the function of cell membranes.

3. Effects on **proteins**: activation/inactivation of enzymes, cross-linking,

fragmentation of protein structures, modification of body immune function.

4. Effects on **carbohydrates**: cross-linking.

Working hypothesis

This research started from the growing interest that is given to the involvement of oxidative stress in diabetes complications. The intense prooxidant activity in diabetic patients compared with nondiabetics will lead to micro and macrovascular changes that will lead to early and accelerated appearance of complication of diabetes.

Objectives

The study of oxidative stress parameters: ceruloplasmin, malondialdehyde, carbonyl proteins, carbohydrate parameters (basal blood glucose, Hb A1c).

Material and methods

We included in the study a number of 120 patients with diabetes and a control plot of 60 patients without diabetes, without changes in glucose tolerance and without other diseases. People in the control plot were performed the same investigations as those in the diabetic plot.

The study protocol of patients with diabetes plot included the following data: patient age, gender, environment of origin, duration of disease progression, the type of therapy administered, the degree of metabolic control, microvascular complications of diabetes, carbohydrate and lipid metabolism parameters.

Parameters studied: at both diabetic patients and control plot were determined

parameters of oxidative stress: malondialdehyde, ceruloplasmin, carbonyl proteins.

To establish the diagnosis of diabetes mellitus and stage of disease progression and to assess the presence of chronic complications, we conducted rigorous and comprehensive clinical examination that added laboratory investigations and specialized consults: ophthalmic, nephrology. Data on disease duration and development were obtained from patient history and record sheet from the Clinic Center for Diabetes Oradea.

For each patient with diabetes have recorded: age of disease, degree of metabolic control has been assessed by several parameters: fasting blood glucose, 2-hour postprandial glucose, glycemic profile, glycosylated hemoglobin.

In terms of **distribution according to sex**, there were no statistically significant differences between the two plots, the ratio men/women nearly 1:1 to both plots.

Distribution according to environment of origin

39,4% of diabetic patients came from rural areas and a percentage of 60.6% came from urban areas. Nondiabetics plot was composed of 38,6% patients in rural and 61,4% patients in urban areas.

Neither in terms of distribution according to the environment do not differ significantly between the two plots, predominantly urban patients ($p>0,05$).

Distribution of cases according to age of patients

Patients studied were aged 21-70 years for both the diabetic patient plot and the control plot.

The largest number of patients ranged in age group 51-60 years (36,1% respectively 41,4%) .

Distribution of cases according to the degree of metabolic control in diabetic patients

Diabetic patients had various degrees of metabolic control. This was assessed by glycemic values and by glycosylated hemoglobin.

- 41,1% -good metabolic control
- 42,2% -mild metabolic control
- 16,7% -poor metabolic balance.

Assessment of metabolic control level was made according to criteria: fasting blood glucose, 2-hours postprandial glucose and Hb A1c (figure 1).

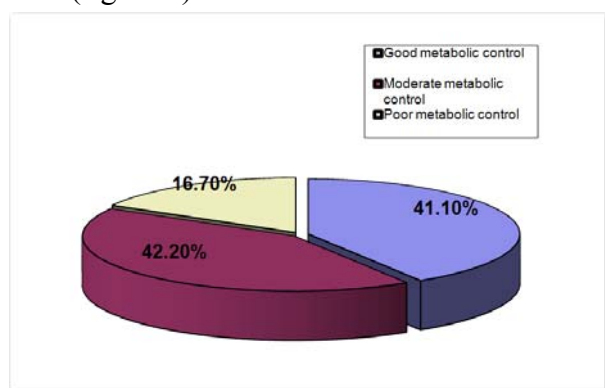


Figure 1. Distribution according to degree of metabolic control

Distribution of cases by type of hypoglycemic therapy in diabetic patients

In terms of antidiabetic therapy, diabetic patients were undergoing igieno-dietary regime and/or treated with oral agents, insulin or combination therapy (insulin plus oral agents). A small percentage (8,9%) of patients

followed exclusively igieno-dietary regime, the rest of them following in about equal percentages insulin therapy (31,1%), insulin associated with oral agents (32,2%) and only oral agents (27,8%). All diabetic patients followed igieno-dietary regime and to all were made education therapy to optimize lifestyle (figure 2).

Distribution of cases according to duration of disease progression in diabetic patients

Patients with diabetes had a known disease duration of evolution from a few months to 15 years (figure 3).

Almost 50% of diabetics had a period of evolution of diabetes of 6-10 years and over ¼ of patients are diagnosed with diabetes for 2-5 years.

Study of oxidative stress parameters

- o Evaluation of oxidative stress was done by determining the parameters,
- o Malondialdehyde (lipid peroxidation product)- tiobarbituric acid method,
- o Carbonyl proteins: result from oxidation of proteins – spectrophotometric method,
- o Ceruloplasmin: antioxidant – caused by reaction Ravin.

Malondialdehyde values

Mean malondialdehyde determined in mmol/mg:

Control plot	1,89+/-0,42
Type 1 DM	4,7+/-0,83
Type 2 DM	3,54+/-0,46

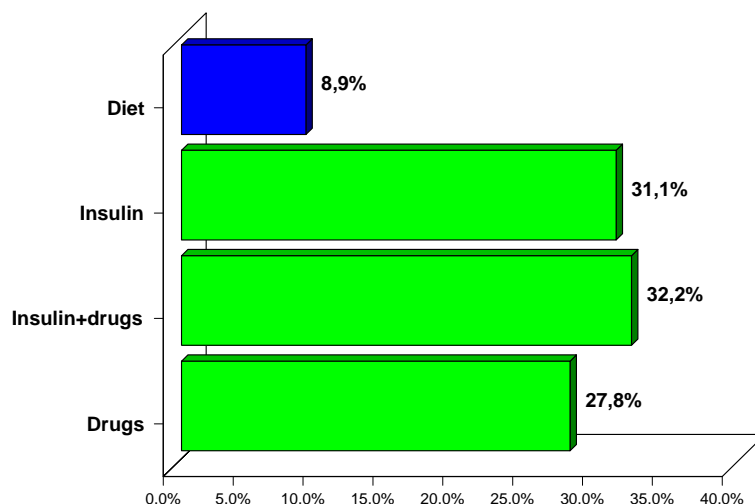


Figure 2. Distribution according to type of antidiabetic therapy

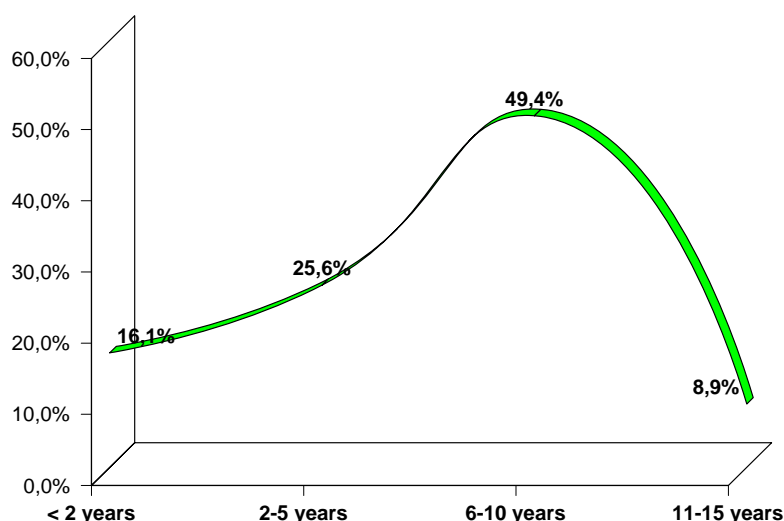


Figure 3. Distribution of cases according to duration of disease progression.

Carbonyl proteins values

Mean carbonyl proteins determined in mmol/mg:

Control plot	1,34+/-0,12
Type 1 DM	2,45+/-0,11
Type 2 DM	1,92+/-0,09

Ceruloplasmin values

Mean ceruloplasmin determined in mg%:

Control plot	34,14+/-1,22
Type 1 DM	24,5+/-0,95
Type 2 DM	29,4+/-0,87

The correlation between the degree of metabolic control and intensity of oxidative stress

Through the analysis of oxidative stress parameters was found that there was an increase in oxidative stress in (figure 4):

- 65% of metabolic uncontrolled diabetes,
- 44% of patients with moderate metabolic control,
- 18% of patients with good metabolic control.

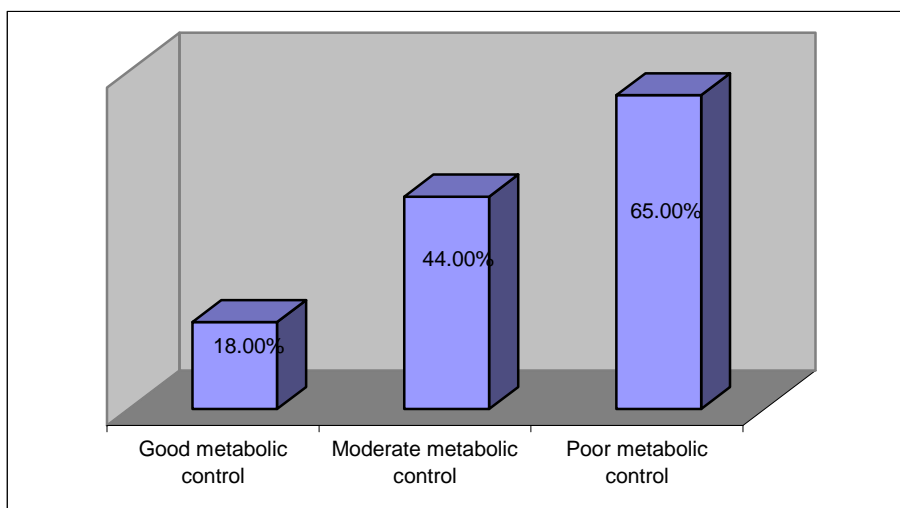


Figure 4. The correlation between oxidative stress and metabolic control level.

Conclusions

The appearance of oxidative stress is breaking the existing balance between the oxidizing agents and antioxidants.

Indirect methods of determining free radicals on various structures are the dosage: malondialdehyde (MDA), lipid peroxidation products, carbonyl proteins.

Body antioxidant capacity can be assessed by assays of antioxidant substances such as: ceruloplasmin.

Oxidative stress is more marked in diabetic patients who show increased metabolic imbalance.

Making a good metabolic control by appropriate therapy leads to reduction of oxidative stress with beneficial effects on body.

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