

artículo original

The use of Ozone for Metabolic Disorders Correction in patients with Metabolic Disorder

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Abstract

Metabolic syndrome (MS) is a complex disease caused by a combination of genetic factors with a person's life- style (nutrition characterized by a high content of carbohydrates, hypodinamia, alcohol, smoking, mental and physical strain). The incidence of metabolic syndrome in different countries ranges from 10% to 30%. In Russia about 1,200,000 people die annually as a result of MS complications. MS incidence has been found to be increasing in female patients for the recent 10 years, compared with the one for male patients.

Criteria for metabolic syndrome were elaborated and unified for various ethnic groups; however, there are some discrepancies among MS criteria that have been suggested lately. WHO experts emphasize the role of misbalance in carbohydrate metabolism and insulin resistance. The expert group of the USA National Council in its Third Report on identification, evaluation and treatment of hypercholesterolemia in adult patient's high-lights the role of lipid metabolism misbalance and fatty tissue condition. Inter- national Diabetes Federation worked out approved criteria for the disease.

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INTRODUCTION

Metabolic syndrome (MS) is a complex disease caused by a combination of genetic factors with a person's life-style (nutrition characterized by a high content of carbohydrates, hypodynamia, alcohol, smoking, mental and physical strain). The incidence of metabolic syndrome in different countries ranges from 10% to 30%. In Russia about 1,200,000 people die annually as a result of MS complications. MS incidence has been found to be increasing in female patients for the recent 10 years, compared with the one for male patients.

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Present-day MS criteria are subdivided into principal and additional ones, the principal being central obesity with waist circumference starting from 94cm for male and 80cm for female patients; additional criteria including serum triglyceride starting from 1,7 mmol/L or special treatment of hypertriglyceridemia; Chol-LPHD should be less than 1,03 mmol/L for male and 1,03 mmol/L for female patients or special treatment of hypoalipoproteinemia; systolic pressure being above 130 mm mmHg. and diastolic pressure - above 85 mm Hg or special treatment of arterial hypertension; serum fasting glucose starting from 5,5 mmol/L or Diabetes Mellitus of Type II, diagnosed earlier. MS diagnosis can be made in cases when the principal criterion is accompanied with any of the 2 additional criteria. In addition, insulin resistance plays one of the main roles in development of MS.

So, it's necessary to investigate the level of insulin with the following calculation of HOMA-index (homeostasis model assessment).

The aim of the work is to study biochemical characteristics in the blood of patients with metabolic syndrome under the influence of ozone in low doses and to compare the results in parallel groups.

MATERIAL AND METHODS

Evaluation of pathologic changes and MS complications was done with the use of specially elaborated number system, which allows to define the part of various nosologic forms in the combined clinical picture of each patient. A three-point scale was used to assess the manifestation degree of a disease being the part of metabolic syndrome (DM-II, hypertension, atherosclerosis, obesity, concomitant diseases). Numerical form of a diagnosis was a mathematical sum of a total score made by a doctor. This system allows to make a clinical evaluation of examined patients in accordance with the accepted classifications taking into consideration the stage of the disease being the part of metabolic syndrome complex.

The examined group consisted of 100 patients, average age being 40 – 60, with different nosologic forms of metabolic syndrome manifestations.

Table 1: Correlation of Various Diagnostic Criteria of Patients with Metabolic Syndrom.

Criterion	Number of patients
Visceral Obesity	100%
Arterial Hyper-tension	65%
Hyper-glyceridemia	53%
Hypo-alphalipoproteinemia	57%
Fasting glucose	48%

Metabolic misbalance was corrected with low doses of ozone in the clinic of Nizhny Novgorod Medical Center of Ozone Therapy.

The course of treatment consisted of 6-8 procedures depending on the severity of the disease, the procedures done every second day. Each procedure included intra- venous infusions (200ml) of ozonated physiologic saline (0.9% NaCl) with ozone concentration of 300-400mcg/l. Barbotage of 0,9% NaCl was done simultaneously with intravenous infusions, ozone being generated by “Kvazar” - ozonator, holding European certificate of quality.

Control group consisted of 55 healthy persons, within the same age range, that were included into the group regarding the following criteria: lack of chronic diseases in the stage of exacerbation, no acute respiratory viral dis- eases or alcohol intake within the period of 10 days either before or on the day of analysis.

Level of total cholesterol, free cholesterol, triglycerides, Chol-LPHD, Chol-LPLD, the content of non-etherified fatty acids (NEFA) was measured with Dia Sys test-system (Germany). The level of insulin was analyzed by DRG (Germany). The activity of the basic antioxidant enzymes (SOD, catalase, glutathione-peroxidase, glutathione-reductase) was estimated with the use of Rendox reagents (England). Potential binding capacity of albumin was studied by Al- bumin-Zond1 device with the use of Cintacom-sets (Russia) to define total and effective albumin concentration. The activity of detoxifying enzyme of glutathione-S-transferase was defined according to Karpischenko method (2002).

RESULTS AND DISCUSSION

HOMA-index was increased in 3 times ($5,48 \pm 0,89$) in comparison with healthy people ($1,80 \pm 0,15$). This demonstrated presence of insulin resistance in our patient's tissues. Initial increase of total cholesterol by 26,35% was revealed in 78% patients. It made up $6,57 \pm 0,20$ mmol/L with the recommended level not exceeding 5,2 mmol/L. Free cholesterol, marker of cholesterol reverse transport disorder, was noticed to have high level in 68% patients. TG level was found to be increased only in 33% by 68% exceeding the recommended level and it was by 235% higher than the level in healthy persons ($1,21 \pm 0,12$ mmol/L).

The increased NEFA content was revealed in serum of 85 % patients with the studied pathology and upon average made up $0,76 \pm 0,06$ mmol/L.

Table 2: The Level of Biochemical Indices in Healthy Persons and Patients with Metabolic Syndrome ($M \pm m$)

Index (mmol/L)	Recommended values	Health persons	MS patients
Triglycerides	less 1,7	$1,21 \pm 0,12$	$2,84 \pm 0,15$ *
Total cholesterol	less 5,2	$4,61 \pm 0,20$	$4,97 \pm 0,22$
Free cholesterol (% from total cholesterol)	22 – 30%	$24,26 \pm 2,78$	$47,30 \pm 2,2$ 3*
Chol-LPHD male female	above 1,03 above 1,30	$1,65 \pm 0,14$	$0,95 \pm 0,03$ *
Glucose	less 5,6	$4,78 \pm 0,20$	$10,25 \pm 0,9$ 4*
NEFA male female	0,10-0,60 0,10-0,45	$0,40 \pm 0,04$	$0,76 \pm 0,06$ *

Significant differences with indices for the normal group

Changes in the indices of lipid metabolism and glucose level after the course of ozone therapy are presented in Table 3.

Table 3: Changes in Lipid Metabolism and Glucose Level after Ozone Procedures

Index (mmol/l)	Group of patients
Triglycerides	Decrease by 35% (p<0,05)
Total cholesterol	Tendency to decrease (5%)
Free cholesterol	Decrease by 33% (p<0,05)
Chol-LPHD	No significant changes revealed
Fasting glucose	Decrease by 9% (p<0,05)

The activity of antioxidant enzymes - SOD and catalase in erythrocytes of MS patients was found to be significantly decreased by 77% and 34%, respectively while the activity of glutathione-peroxidase and of glutathione reductase appeared to be increased by 3 and 2 times, accordingly.

Under the influence of medical ozone used in low doses there was registered normalization of the indices of lipid metabolism (total cholesterol level, free cholesterol level, triglycerides, Chol-LPHD, Chol-LPLD), significant decrease of NEFA by 22% in serum of MS patients.

The described changes seemed to be caused by activation of aerobic processes under the influence of ozone, β -oxidation of excessive NEFA content.

Intravenous ozone therapy was found to facilitate the normalization of antioxidant enzymes balance, increasing SOD and catalase activity and decreasing glutathione-peroxidase and glutathione-reductase.

To evaluate the detoxifying function of the body it was necessary to study the activity and binding capacity of albumin. The levels of albumin total concentration in blood of healthy persons and MS patients were found to be significantly different. Effective concentration of albumin in MS patients upon average was lower by 18,5%, compared with healthy persons. According to the received data, albumin potential capacity in healthy persons is equivalent to $96,10 \pm 1,08\%$. In MS patients APC was significantly lower ($p < 0,05$) and made up $83,09 \pm 1,19$. Informative criteria of albumin detoxifying function point to the decrease in albumin effective concentration and potential binding capacity in blood plasma when metabolic syndrome develops. The study of informative parameters of albumin detoxifying capacity revealed the increase of albumin binding capacity in group 1, where it was $88,01 \pm 1,43$, the normal one being $96,10 \pm 1,08$. It should be noted that total concentration of albumin increased by 8% upon average ($p < 0,05$) in patients who did not have any significant increase, of albumin potential capacity. It testified to the fact, that ozone in low doses produces systemic effect on the liver protein synthesis function.

Evaluation of glutathione-S-transferase activity after the course of ozone therapy revealed the reduction of the activity in 76% of examined patients by 14% ($p < 0,05$), the increased activity of glutathione-S-transferase plasma fraction within the normal limits was found in 15% of patients and in 9% of patients it was increased by 37%.

Glutathione-S-transferase is known to be the enzyme of the second phase of exogenic and endogenic toxins biotransformation. Neutralization of toxic substances is done by their reduction. Glutathione-S-transferase can attach the molecules of reduced glutathione to the substrate or to perform nucleophilic substitution of hydrophobic groups. Conjugation of toxic LP products protein oxidative modification with glutathione results in their ejection. On studying glutathione-S-transferase activity in erythrocytes and in blood plasma there was found the increase of enzyme activity by 89% (up to $14,42 \pm 0,76$ mol//min, with the norm being $7,63 \pm 1,29$ mol//min. The enzyme erythrocytic fraction activity was found to be also increasing by 44% in MS patients, starting from $124,40 \pm 11,55$ mol//min in healthy persons and up to $178,57 \pm 9,92$ mol//min in erythrocytes of patients with metabolic syndrome.

CONCLUSIONS

1. Initially pathologic characteristics of lipid peroxidation (total cholesterol level, free cholesterol level, the levels of triglycerides, Chol-LPHD, Chol-LPLD, NEFA) had a tendency to normalization after the course of ozone therapy.
2. Intravenous administration of Ozonated Saline Solution helps to restore the balance of antioxidant enzymes and to be more precise, it results in increase of catalase and SOD activity and decrease of glutathione-peroxidase and glutathione-reductase.
3. The administration of therapeutic low doses of ozone leads to reduction in the activity of erythrocyte and glutathione-S-transferase plasma fractions in 76% of examined patients ($p < 0,05$) and to increase in albumin binding capacity.

