The Influence of Body Mass on Blood Nitric Oxide Values in Patients with Metabolic Syndrome

Nino Eloshvili, Manana Koplatadze, David Virsaladze, Eldar Imedidze

Department of Endocrinology, Tbilisi State Medical University, Georgia

ABSTRACT

The redox-system imbalance related to free-radical nitric oxide (NO) data plays a considerable role in the development of cardiovascular diseases. Our aim was to investigate body mass influence on NO values in patients with metabolic syndrome. 86 Patients with metabolic syndrome were investigated. Body mass index (BMI), waist circumference, glycemic and blood pressure (BP) data were determined. Blood NO concentration was estimated using the electronic-paramagnetic resonance (EPR) method by NO EPR signal intensity. The patients were divided into 4 groups: group I – normal body mass (BMI=18,5-24,9 kg/m^2), group II – overweight (BMI=25,0-29,9 kg/m^2), group III – obesity (BMI=30,0-34,9 kg/m^2) and group IV – obesity (BMI ≥ 35,0 kg/m^2). According to our results NO decrease was significant in both groups of obese patients No.3 and No.4 in comparison with normal body mass group I (p_{1-3}=0.009 and p_{1-4}<0.001, respectively). NO EPR-signal significantly differed between groups III and IV (11.7±2.8 и 9.5±2.4 mm/mg, respectively; p=0.008). In all 4 groups NO data were significantly lower in comparison with the control group parameter. In the whole contingent BMI correlated inversely with NO (r=-0.462, p<0.001). The similar relation was found out between waist circumference and NO (r=-0.301, p=0.049). In the groups divided by BMI waist circumference, systolic and diastolic BP were increasing parallel with BMI increase, and were significantly higher than the analogous parameters of the control group.

KEYWORDS: *metabolic syndrome, nitric oxide, obesity, body mass*

Obesity – the problem of excess deposition of fat in the body has spread beyond the bounds of esthetic estimation. Nowadays obesity belongs to the most widespread diseases. By the World Health Organization data 30% of the world population suffers from excess weight [1]. The connection of obesity to dyslipidemia, insulin resistance/hyperinsulinemia, diabetes mellitus (DM) and essential hypertension has been known for a long time; however, searching for their pathogenetic connections became more profound after they were unified in the term of metabolic syndrome (MS). Each MS component is an independent risk-factor for atherosclerosis. Their complex study in the frames of this new nosology implies the prevention of cardiovascular diseases or starting their treatment at an early stage when these pathogenetic processes are reversible [2].

There are several methods of obesity estimation. Nowadays most widespread is the simple and informative method of the calculation of body mass index (BMI). Alongside the increase of BMI the increase of morbidity and mortality rate is confirmed.

Not only the occurrence of obesity but also fat deposition is of principal significance. MS and its characteristic cardiovascular complications are more common in case of abdominal (visceral) obesity with excess fat deposition in abdominal area in contrast with universal obesity, which is characterized with proportional fat deposition. To detect the visceral obesity, waist circumference (WC) is measured. WC≥80 cm in females and WC≥94 cm in males is considered a risk for cardiovascular disease [1,2].

The redox-system role in atherosclerotic damage of vessels is paid a lot of attention of contemporary scientists. In various components of MS, among of which are obesity and dislipidemia, the dysfunction of fine redox-mechanisms are revealed. The recent works emphasize not only hypercholesterolemia and hyperlipidemia but also oxidative stress condition with lipoperoxides increase and low-density lipoproteins (LDL) oxidative modification. Practically all main stages of atherosclerosis development are under the influence of oxidative LDL: monocyte adhesion to endothelium, monocyte migration through intima and transformation to macrophages, engulfing by macrophages and foam cells formation, smooth muscle cells migration-proliferation, growth factors and cytokines modification, direct endothelium injury, endothelial dysfunction, nitric oxide (NO) synthesis inhibition [3,4,5,6].

Deficiency of endothelial product – NO – intensifies thrombocytes and leukocytes adhesion to the endothelium surface, enhances endothelial permeability, smooth muscle cells migration-proliferation, lipoprotein oxidation, vasoconstriction and hemocoagulation. On the other hand, free-radical NO in excess concentrations inhibits cytotoxic and cytostatic effects, intensifies oxidation of lipoproteins and membrane lipids, and enhances the oxidative stress by participating in the formation of a new very aggressive radical – peroxinitrate [5].

Taking into consideration an important role of NO in cardiovascular function, our aim was to study the influence of weight gain on NO data in patients with MS.

MATERIALS AND METHODS

86 patients (32 males, 54 females) with MS were investigated. The mean age was 61.2±9.6 years. Body mass was estimated by BMI calculation – BMI = body mass (kg)/height (m^2). Ideal BMI is 18,5-24,9 kg/m^2, 25,0-29,9 kg/m^2 is overweight, above 30 kg/m^2 – obesity. The fat deposition was judged by WC. The whole contingent was divided into 4 groups: group III – normal body mass (BMI=18,5-24,9 kg/m^2), group II – overweight (BMI=25,0-29,9 kg/m^2), group III – obesity (BMI=30,0-34,9 kg/m^2) and group IV – obesity (BMI≥35,0 kg/m^2). The control group was represented by 23 practically healthy persons of the same age.

Fasting and postprandial (2 hours after meal) glycemia and systolic and diastolic blood pressure (BP) were investigated.

NO was estimated by electronic-paramagnetic resonance (EPR) method in venous blood. To 1 ml of blood 0.2 ml "spin-trap"-Na diethildithiocarbamate was added. The sample was placed in 0.5 cm diameter polyethylene tubes and frozen in liquid nitrogen at –196°C temperature. EPR-signal was registered on RE1307 radiospectrophotometer.

The obtained data were analyzed statistically by means of Student's criterion using computer program WINKS 4.65 (TexaSoft, USA).

RESULTS

The data of MS patients divided by BMI are presented at the *Tab.1*.

Group	*n*	*Age, years*	*BMI, kg/m²*	*WC, cm*	*Glycemia, mg/dl*		*BP, mm.Hg.*		*NO, mm/mg*
					Fasting	Postpr.	Systolic	Diastolic	
I	15	58.4±11.2	22.7±2.0	91.5±8.0	182.4±58.3	272.1±92.5	141.5±23.8	79.6±11.8	14.1±2.7
II	24	56.8±11.2	28.3±1.4	101.2±8.7	166.7±59.9	215.3±85.3	138.1±22.7	84.2±9.3	11.3±4.2
III	29	59.0±8.5	32.2±1.4	110.8±6.7	196.3±64.9	237.5±71.2	163.4±21.7	87.7±10.3	11.7±2.8
IV	18	63.0±8.2	37.7±1.4	119.3±11.7	173.3±51.8	226.5±51.1	163.1±19.4	88.8±9.2	9.5±2.4
C	23	55.6±6.2	22.1±1.9	90.2±6.2	93.5±6.5	122.8±15.3	118.0±8.8	75.5±5.2	15.8±0.8
				$p_{1-2}<0.001$ $p_{1-3}<0.001$ $p_{1-4}<0.001$ $p_{2-3}<0.001$ $p_{2-4}<0.001$ $p_{3-4}=0.01$ $p_{1-C}=NS$ $p_{2-C}<0.001$ $p_{3-C}<0.001$ $p_{4-C}<0.001$		$p_{1-3}=0.049$ $p_{1-4}=0.045$ $p_{2-3}=0.017$ $p_{2-4}=0.019$ $p_{1-C}<0.001$ $p_{2-C}<0.001$ $p_{3-C}<0.001$ $p_{4-C}<0.001$	$p_{1-3}=0.023$ $p_{1-4}=0.017$ $p_{1-C}=NS$ $p_{2-C}<0.001$ $p_{3-C}<0.001$ $p_{4-C}<0.001$	$p_{1-3}=0.009$ $p_{1-4}<0.001$ $p_{3-4}=0.008$ $p_{1-C}=0.032$ $p_{2-C}<0.001$ $p_{3-C}<0.001$ $p_{4-C}<0.001$

Tab.1 *NO and MS component parameters data in groups formed by BMI.*

In the presented groups NO lowering was statistically significant between I and III ($p_{1-3}=0.009$) and also between I and IV ($p_{1-4}<0.001$), that reflects endothelial function deterioration in both groups of obese patients (BMI 30.0-34.9 kg/m² and BMI≥35 kg/m²) in comparison with the group of normal body mass patients. It's remarkable that NO decrease was statistically significant between the two (III and IV) groups of obese patients ($p_{3-4}=0.008$). It indicates the activation of atherogenic processes parallel with progression of obesity. In all four groups NO EPR-signal was significantly decreased in comparison with the control group ($p_{1-C}=0.032$; $p_{2-C}<0.001$; $p_{3-C}<0.001$; $p_{4-C}<0.001$). In the whole contingent BMI correlated inversely with NO data ($r=-0.462$, $p<0.001$).

Despite of WC difference in males and females in relation of cardiovascular risk, in the whole contingent WC correlated inversely to NO ($r=-0.301$, $p=0.049$). Age, fasting and postprandial glycemia data were not significantly different between the groups.

While investigating BP, alongside BMI rise systolic BP increase has been revealed, which became statistically significant between groups I and III ($p_{1-3}=0.049$), and I and IV ($p_{1-4}=0.045$), also II and III ($p_{2-3}=0.017$), and II and IV ($p_{2-4}=0.019$). In all four groups systolic BP exceeded the control parameter with high statistical significance ($p<0.001$). Nevertheless, in the whole contingent systolic BP data did not correlated significantly with NO ($r=-0.241$, NS). Analyzing diastolic BP between groups I and III ($p_{1-3}=0.023$), and I and IV ($p_{1-4}=0.017$) the significant difference has been revealed. In comparison with the control group diastolic BP was significantly higher in the overweight and obese patients ($p<0.001$).

DISCUSSION

On the basis of the investigation of the endothelial function main marker - NO - in patients with MS, according to weight gain the following results were obtained. In all four groups (and among them normal body mass patients) NO EPR-signal was lower in comparison with healthy individuals that can be explained with MS occurrence itself, one of its components - diabetes mellitus decompensation and hyperglycemia influence on redox-system and also the age factor of the contingent (the mean age - 61.2±9.6 years) [7,8]. Alongside the weight gain NO EPR-signal was decreasing further. It became statistically significant for obese patients in comparison with normal body mass and overweight patients. It's remarkable that NO decrease was statistically significant between the obese patients groups (III and IV).

In the whole contingent BMI inversely correlated with NO. Such kind of correlation has been detected between NO EPR-signals and WC.

Along the weight gain another MS component - arterial hypertension - data were deteriorated, which was expressed by significant increase of systolic and diastolic BP between groups.

As we have mentioned above, NO decrease parallel with weight gain indicates redox-system imbalance, intensification of oxidative stress and pro-inflammation processes. They lead to various types of damage, including particularly aggressive - cardiovascular system

injury. In oxidative stress condition endothelium is not able to adequately secrete NO and other vasoactive substances. It causes the vasoconstriction, increase of coagulation, the hyperproduction of free radicals, the activation of growth factors, cytokines and transcriptional factors, the intensification of atherogenic processes. Endothelial dysfunction enhances oxidative stress, which in its turn inhibits antiatherogenic activity of endothelium. According to our results established vicious cycle is expressed more severely along with weight gain.

CONCLUSIONS

It could be concluded that body mass influences on blood nitric oxide values in patients with MS. BMI and WC significantly correlates inversely with blood NO levels. Alongside the BMI increase systolic and diastolic BP data are deteriorated. Therefore, in MS patients redox-system imbalance is revealed.

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Влияние массы тела на показатели оксида азота в крови у пациентов с метаболическим синдромом

Нино Элошвили, Манана Коплатадзе, Давид Вирсаладзе, Эльдар Имедидзе

Кафедра эндокринологии Тбилисского государственного медицинского университета, Грузия

Р Е З Ю М Е

В развитии кардиоваскулярных заболеваний большая роль уделяется дисбалансу редокс-системы, что связано с данными свободного радикала – оксида азота (NO). Изучено влияние массы тела на показатели NO у пациентов с метаболическим синдромом (МС). Обследовано 86 пациентов с МС. Определялись: индекс массы тела (ИМТ), окружность талии, данные гликемии и артериального давления (АД). Концентрация NO в крови изучалась методом электронно-парамагнитного резонанса (ЭПР) по интенсивности NO ЭПР-сигнала. Пациенты подразделены на 4 группы: I группа – нормальная масса тела (ИМТ=18,5-24,9 кг/м^2), II группа – избыточный вес (ИМТ=25,0-29,9 кг/м^2), III группа – ожирение (ИМТ=30,0-34,9 кг/м^2) и IV группа – ожирение (ИМТ $\geq$ 35,0 кг/м^2). Снижение NO оказалось достоверным в обеих группах тучных пациентов III и IV по сравнению с нормой – I группой (p_{1-3}=0.009 и p_{1-4}<0.001, соответственно). NO ЭПР-сигнал достоверно отличается в III и IV группах (11.7$\pm$2.8 и 9.5$\pm$2.4 мм\мг, соответственно; p=0.008). Во всех четырех группах показатель NO оказался достаточно ниже контроля параметра. У всех обследованных между показателями ИМТ и NO выявилась обратнокоррелятивная зависимость (r=-0.462, p<0.001). Подобная зависимость имела место и между окружностью талии и NO (r=-0.301, p=0.049). С повышением ИМТ выявилось достоверное увеличение данных окружности талии и систолического и диастолического АД. Эти данные достоверно превышали аналогичные параметры контрольной группы.

КЛЮЧЕВЫЕ СЛОВА: *метаболический синдром, оксид азота, беременность, масса тела*