ORIGINAL ARTICLE

Serum paraoxonase enzyme activity and oxidative stress in obese subjects

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KEY WORDS

arylesterase, atherosclerosis, lipid hydroperoxide, obesity, paraoxonase

ABSTRACT

INTRODUCTION Obesity is an important risk factor for atherosclerotic cardiovascular disease. Paraoxonase-1 (PON1) may play a significant role in the prevention of obesity-related accelerated atherosclerosis by hydrolyzing lipid peroxides in oxidized low-density lipoproteins.

OBJECTIVES The aim of this study was to evaluate PON1 and arylesterase enzyme activities and lipid hydroperoxide (LOOH) levels, and to investigate whether there is increased susceptibility to atherogenesis in obese subjects, which might be reflected by increased oxidative stress and decreased PON1 activity. We also aimed to investigate the association between PON1 activity and body mass index (BMI) in this patient group.

PATIENTS AND METHODS The study involved 25 obese subjects and 23 controls. Serum PON1 and arylesterase activity was measured spectrophotometrically. LOOH levels were measured by the FOX-2 assay.

RESULTS Serum basal/salt-stimulated PON1 and arylesterase activities were significantly lower in obese subjects than in controls ($P < 0.001$ for both enzymes), while LOOH levels were significantly higher ($P < 0.001$). BMI was significantly correlated with PON1, arylesterase and LOOH levels ($P < 0.001$, $r = -0.720$; $P < 0.001$, $r = -0.634$; $P < 0.001$, $r = 0.491$; respectively). Serum high-density lipoprotein (HDL) levels were positively correlated with PON1 activity ($r = 0.347$, $P < 0.05$).

CONCLUSIONS Our results indicate that obese subjects have increased oxidative stress and decreased PON1 activity, which might contribute to accelerated atherosclerosis. A decrease in PON1 activity seems positively correlated with BMI and inversely correlated with HDL levels.

INTRODUCTION Oxidative stress has been defined as the disturbance of equilibrium between prooxidant and antioxidant systems in favor of oxidation. The term "oxidative stress" is used to describe a number of chemical reactions involved in the production of free radicals and other reactive molecules that can potentially induce cellular injury.[1] Accordingly, oxidative stress has emerged as one of the principal causes of atherogenic modifications in low-density lipoproteins (LDL) and, consequently, of atherosclerotic disease.[2] High-density lipoproteins (HDL) have a well-established inverse correlation with the incidence of coronary disease.[3] Oxidation of LDL is recognized as an early stage in the development of atherosclerosis, leading to LDL uptake by the macrophage scavenger receptor and hence to formation of foam cells.[3,4]

Several studies have shown that paraoxonase-1 (PON1) protects LDL and HDL against oxidative modification. It can destroy active lipids in mildly oxidized LDL, thereby protecting against the induction of inflammatory responses in arterial wall cells. It has been demonstrated that PON1 deficiency is related to increased susceptibility to LDL oxidation and development of atherosclerosis.[5] Two PON1 polymorphisms have been identified: PON1 Arg/Gln 192 and PON1 Met/Leu 55.[6] Position-192 polymorphism is the major determinant of PON1 activity polymorphisms. However, position-55 polymorphisms also exert a significant but smaller

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Received: January 30, 2011.
Revision accepted: April 21, 2011.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2011; 121 (6): 181-186

effect on PON1 activity.[7] These genetic polymorphisms have been suggested to be independent risk factors for coronary artery diseases.[7]

Obesity is a significant health problem in western countries. It is associated with major risk factors for atherosclerosis including hyperlipidemia, diabetes, hypertension, and metabolic syndrome.[8] Obesity and oxidative stress have been shown to play an essential role in the pathogenesis of atherosclerosis. Moreover, oxidative stress has been reported to be involved in the pathogenesis of various diseases such as hyperlipidemia, diabetes, hypertension, which are also associated with obesity and atherosclerosis.[9]

Several experimental and clinical trials have shown that serum PON1 activity is decreased in obese subjects.[10-12] However, we still have limited knowledge about the association between serum PON1 activity and obesity.[12,13]

The aim of this study was to evaluate PON1 activity and lipid hydroperoxide (LOOH) levels in obese subjects and to investigate whether these subjects are more susceptible to atherogenesis, which might be reflected by increased oxidative stress and decreased PON1 activity. We also aimed to investigate the association between serum PON1 activity and body mass index (BMI) in this patient group.

PATIENTS AND METHODS

The study involved 25 obese subjects and 23 controls. BMI was calculated as weight in kilograms divided by the square of height in meters. The study was conducted according to the Helsinki Declaration as revised in 1989 and approved by the local ethics committee. All subjects were informed about the study protocol and provided their written consent.

All obese subjects and controls underwent standard physical examination, chest X-ray, baseline electrocardiogram, and routine clinical laboratory tests, including liver and kidney function tests. None of the patients had diabetes, hyperlipidemia, hypertension, coronary artery disease, or psychiatric, metabolic, hepatic, or renal disease. None of the subjects used supplemental vitamins or smoked cigarettes.

Control subjects underwent routine physical and laboratory tests to exclude diabetes, hyperlipidemia, hypertension, coronary artery disease, smoking, use of supplemental vitamins, as well as psychiatric, metabolic, hepatic, or renal disease.

Blood sample collection

Blood samples were collected into empty tubes and immediately stored on ice at 4°C. Serum samples were then separated from the cells by centrifugation at 3000 rpm for 10 minutes; lipid parameters and enzyme activity were measured. The remaining serum portions were stored at –80°C and used to analyze LOOH levels.

Measurement of paraoxonase and arylesterase activity

PON1 and arylesterase activity was measured using paraoxon and phenyl acetate substrates. The rate of paraoxon hydrolysis (die-thyl-p-nitrophenylphosphate) was measured by monitoring the increase of absorbance at 412 nm at 37°C. The amount of generated p-nitrophenol was calculated from the molar absorptivity coefficient at pH 8, which was 17 000 M–1 cm–1.[14] PON1 activity was expressed as U/l serum. Phenyl acetate was used as a substrate to measure arylesterase activity. Enzyme activity was calculated from the molar absorptivity coefficient of the produced phenol, 1310 M–1 cm–1. One unit of arylesterase activity was defined as 1 μmol phenol generated/min under the above conditions and expressed as U/l serum.[15]

Phenotype distribution of PON1 activity

The phenotype distribution of PON1 activity was determined by the double-substrate method, which calculates the ratio of salt-stimulated PON1 and arylesterase activities, using paraoxon and phenyl acetate as substrates.[14] The ratio of salt-stimulated PON1 activity to arylesterase activity was used to assign individuals to 1 of 3 possible phenotypes.[14] The genetic polymorphism at codon 192 QR is responsible for the presence of 2 isotypes: A (low activity) and B (high activity). The ratio of the hydrolysis of paraoxon in the presence of I M NaCl (salt-stimulated PON1 activity) to the hydrolysis of phenyl acetate was used to assign individuals to 1 of 3 possible phenotypes: AA (low activity), AB (intermiediate activity), BB (high activity). Individuals were assigned to 1 of 3 possible phenotypes: QQ (homozygous low activity), QR (heterozygous activity), RR (homozygous high activity), which are defined as the ratios of activity with the ranges of 1.56 ±0.32 for QQ (AA), 1.62 ±0.33 for QR (AB), and 1.87 ±0.38 for RR (BB).

Measurement of lipid hydroperoxide levels

Serum LOOH levels were measured with a ferrous ion oxidation-xylenol orange (FOX-2) assay. It involves the oxidation of ferrous ion to ferric ion via the effect of various oxidants. The ferric ion is then measured with xylenol orange. The levels of LOOH are reduced by the application of triphenyl phosphine (TPP), which is a specific reductant for lipids. LOOH levels can be estimated as the difference in values that appear due to the absence or presence of TPP.[16]

Other parameters

The levels of triglycerides (TG), total cholesterol (TC), HDL cholesterol (HDL-C), and glucose were determined using commercially available assay kits (Abbott®) with an autoanalyzer (Aeroset®, Abbott®, Germany). LDL cholesterol (LDL-C) was obtained using the formula: LDL-C = TC – HDL-C – TG/5.

Statistical analysis

Data were presented as mean ± standard deviation for parametric variables. The Student *t* test was used to compare the parameters of obese subjects and healthy controls. The χ^2 test was used to compare PON1 phenotype

TABLE 1 Demographic and clinical data of obese subjects and controls

Parameters	Controls (n = 23)	Obese subjects (n = 25)	*P*
age, y	26 ±3	28 ±2	NS
sex, women/men	10/13	14/11	NS
BMI, kg/m²	21.50 ±1.87	32.21 ±1.34	<0.001
glucose, mmol/l	5.22 ±0.22	5.38 ±0.11	NS
TG, mmol/l	1.52 ±0.24	2.01 ±0.42	<0.01
TC, mmol/l	3.68 ±0.67	4.54 ±0.81	<0.01
HDL-C, mmol/l	1.37 ±0.27	0.89 ±0.15	<0.05
LDL-C, mmol/l	1.61 ±0.55	2.73 ±0.69	<0.01

Values are presented as mean ± standard deviation

Abbreviations: BMI – body mass index, HDL-C – high-density lipoprotein cholesterol, LDL-C – low-density lipoprotein cholesterol, NS – nonsignificant, TC – total cholesterol, TG – triglycerides

TABLE 2 Oxidative and antioxidative parameters in obese subjects and in controls

Parameters	Controls (n = 23)	Obese subjects (n = 25)	*P*
PON1, U/l	62.29 ±13.99	33.53 ±9.86	<0.001
salt-stimulated PON1, U/l	112.04 ±9.44	72.37 ±15.46	<0.001
PON1/HDL-C ratio	1.32 ±0.48	0.92 ±0.34	<0.01
arylesterase, U/l	58.03 ±6.53	45.90 ±4.53	<0.001
LOOH, μmol/l	11.02 ±2.86	14.98 ±3.63	<0.001

Values are presented as mean ± standard deviation

Abbreviations: LOOH – lipid hydroperoxide, PON1 – paraoxonase-1, others – see TABLE 1

TABLE 3 Phenotype distribution in obese subjects and controls

Phenotype distribution	Controls, n	Obese subjects, n	*P*
BB	10	9	>0.05
AB	9	8	>0.05
AA	4	4	>0.05

distribution in patients and controls. The Pearson correlation analysis was used to establish the correlations between BMI and PON1, arylesterase, or LOOH. For examining the impact of independent variables on PON1 activity, linear regression analysis was conducted. The analyses were performed using the SPSS software for Windows Release 11.5 (SPSSInc.). The *P* value of <0.05 was considered statistically significant.

RESULTS Demographic and clinical characteristics of the subjects are shown in TABLE 1. BMI was significantly higher in obese subjects than in controls (P <0.001).

Serum TG, TC, and LDL-C levels were significantly higher in obese subjects than in controls (P <0.01 for both groups), while HDL-C levels were significantly lower (P <0.05; TABLE 1).

Serum basal/salt-stimulated PON1 and arylesterase activities were significantly lower in obese subjects than in controls (P <0.001 for both groups), while LOOH levels were significantly higher (P <0.001; TABLE 2).

LOOH levels were inversely correlated with PON1 and arylesterase in obese subjects (r = 0.527, P <0.001 and r = –0.547, P <0.001, respectively).

There was a significant negative correlation between LDL-C levels and PON1 and arylesterase activity (r = –0.330, P <0.05 and r = –0.373, P <0.01, respectively), as well as between HDL-C and LOOH levels in obese subjects (r = 0.298, P <0.05). In addition, there was a significant positive correlation between HDL–C levels and PON1 and arylesterase activity (r = 0.347, P <0.05 and r = 0.369, P <0.01, respectively), as well as between LDL-C and LOOH levels in obese subjects (r = 0.359, P <0.01).

BMI was significantly correlated with PON1, arylesterase, and LOOH levels in obese subjects (r = –0.720, P <0.001; r = –0.634, P <0.001; r = 0.491, P <0.001; respectively).

A linear regression analysis was performed to identify the factors that exert an independent effect on PON1 activity. Glucose levels, lipid parameters, age, BMI, and LOOH levels were included as independent variables. PON1 activity was correlated with BMI (β = –0.821, P = 0.002), HDL-C (β = 0.257, P = 0.042), and LOOH (β = –0.242, P = 0.038).

The PON1 phenotype distribution was calculated in both groups. The resulting ratio was used to identify subject phenotypes: homozygous AA (PON1192QQ), heterozygous AB (PON1192QR), and homozygous BB (PON1192RR). PON1 phenotype distribution of the subjects was not significantly different between these 3 groups (P >0.05). There was no significant difference in PON1192Q and R polymorphism distribution between obese subjects and controls (P >0.05; TABLE 3).

DISCUSSION We observed that PON1 and arylesterase activity was significantly lower and LOOH levels significantly higher in obese subjects than in controls.

Several studies have suggested that there is an association between increased oxidative stress and BMI in obese subjects.[17,18] We observed a positive correlation between LOOH levels and BMI. Our finding was consistent with the previous reports.[17,18] A number of studies have also suggested that there is a negative correlation between PON1 activity and BMI in this patient group.[12,13] However, Rector et al.[19] described lower serum PON1 activity in patients with reduced body weight. In the present study, we demonstrated a negative correlation between BMI and PON1 or arylesterase activity in obese patients.

PON1 is an antioxidant enzyme that inhibits oxidative modification of LDL and contributes to most of the antioxidative activity that has been attributed to HDL. PON1 can destroy active lipids in mildly oxidized LDL.[20] Most serum PON1 is bound to the surface of HDL. Sorenson et al.[21] demonstrated that PON1 is a lipid-dependent enzyme; in fact, the conformation of PON1 within the hydrophobic environment of HDL is crucial

for its activity. Phospholipids, especially those with long fatty acid chains, stabilize PON1 enzyme and are required to bind PON1 to lipoprotein surface.[21]

Several studies have shown modifications of lipid and lipoprotein metabolism in obese subjects. Hypercholesterolemia, high TG and LDL-C levels, and low HDL-C levels are frequently observed in this patient group.[22,23] Modifications of lipoprotein levels and composition are possibly related to the higher risk of cardiovascular disease associated with obesity.[24] Furthermore, several studies have suggested increased oxidative stress in obese subjects, with a higher susceptibility to lipid peroxidation of LDL isolated from obese subjects compared with healthy subjects.[9,25] It has been suggested that an increase in oxidative damage could be due to a decrease in antioxidant activity. In fact, low levels of β-carotene and α-tocopherol have been observed in serum and in LDL obtained from obese subjects.[25]

Atherosclerosis, the major cause of morbidity and death in western countries, involves complicated interactions between arterial cells, blood cells, and plasma lipoproteins.[26] Oxidative stress, that is, imbalance between the amount of reactive oxygen species (ROS) and antioxidant defence mechanisms, plays an important role in atherogenesis.[27] Oxidative modification of LDL is the key stage during early atherogenesis, which contributes to cholesterol and oxysterol accumulation in the arterial wall and to lesion development.[28] Oxidized lipids are observed in atherosclerotic lesions and have been shown to be related to the progression of atherosclerosis.[29] During the development of atherosclerosis, PON1 accumulates in the arterial wall.[30] In addition, PON1 hydrolyzes lipid peroxides in atherosclerotic lesions,[31] where they promote progression of atherogenesis.[31] ROS and lipid peroxidation products decrease PON1 production in the liver[32] and inactivate HDL-bound enzyme.[20] On the other hand, reduced PON1 activity may cause increase in plasma lipid peroxidation products. Furthermore, PON1 activity is reduced in atherosclerotic vascular diseases (e.g., acute myocardial infarction) or conditions, in which atherosclerosis is common (e.g., diabetes, familial hypercholesterolemia).[33,34]

Although reduced serum PON1 activity is well documented in obese subjects, the cause of this alteration remains unclear. However, there are two important points to note. First, since PON1 is associated with HDL-C, reduced PON1 activity could be associated with decreased HDL-C levels.[35] Second, it is well known that serum PON1 activity is generally considered to vary in response to the consumption of PON1 for the prevention of oxidation.[20] Our findings of decreased HDL-C levels and increased serum LOOH levels in obese subjects, which reflect oxidative stress, were consistent with other reports. In our study, serum HDL-C levels were positively correlated with PON1 activity, so decreased serum HDL-C levels do not seem to be responsible for reduced PON1 activity, at least in our subjects. In contrast, PON1 activity was inversely correlated with LOOH levels; thus, it can be suggested that decreased PON1 activity may be, in part, due to consumption of PON1 for the prevention of oxidation.

High body weight in obese subjects is caused by increased content of fat in body composition. Adipose tissue has a known endocrine activity, namely, that of adipokines. They are associated with PON1 activity[13,36] and atherosclerosis. On the other hand, it is known that PON1 stability and optimal activity is dependent on ApoAI lipoprotein and phospholipids.[37] Pedrosa et al.[37] demonstrated a decrease in HDL-C and ApoAI lipoprotein in obese children.

Serum PON1 activity greatly varies among individuals and populations due to the PON1 codon 192 genetic polymorphism.[38] Jarvik et al.[38] suggested that the PON1 phenotype is a better predictor of vascular and carotid artery disease. Additionally, PON1 activity may be affected by lifestyle factors, such as diet and smoking, which are accepted as controllable risk factors for atherosclerosis.[39] In our study, there was no significant difference in PON1192Q and R polymorphism distribution between obese subjects and controls.

In conclusion, our results indicate that increased oxidative stress and decreased PON1 activity in obese subjects could contribute to accelerated atherosclerosis. This decrease in PON1 activity seems to be associated with BMI and, in part, with lower HDL levels in obese subjects.

REFERENCES

1 Halliwell B. Antioxidants in human health and disease. Annu Rev Nutr. 1996; 16: 33-50.

2 Steinberg D. Low density lipoprotein oxidation and its pathobiological significance. J Biol Chem. 1997; 272: 20963-20966.

3 Laplaud PM, Dantoine T, Chapman MJ. Paraoxonase as a risk marker for cardiovascular disease: facts and hypotheses. Clin Chem Lab Med. 1998; 37: 431-441.

4 Ng CJ, Shih DM, Hama SY, et al. The paraoxonase gene family and atherosclerosis. Free Radical Biol Med 2005; 38: 153-163.

5 Canales A, Sanchez-Muniz FJ. [Paraoxanase, something more than an enzyme?]. Med Clin (Barc). 2003; 121: 537-548. Spanish.

6 Adkins S, Gan KN, Mody M, La Du BN. Molecular basis for the polymorphic forms of human serum paraoxonase: arylesterase: glutamine or arginine at position 191, for the respective A or B allozymes. Am J Hum Genet. 1993; 52: 598-608.

7 Mackness B, Mackness MI, Arrol S, et al. Effect of the molecular polymorphisms of human paraoxonase (PON1) on the rate of hydrolysis of paraoxon. Br J Pharmacol. 1997; 122: 265-268.

8 Grundy SM. Obesity, metabolic syndrome and coronary atherosclerosis. Circulation. 2002; 105: 2696-2698.

9 Halliwell B, Gutteridge JMC, Cross CE. Free radicals, antioxidants, and human disease: where are we now? J Lab Clin Med. 1992; 119: 598-620.

10 Bełtowski J, Wójcicka G, Jamroz A. Leptin decreases plasma paraoxonase 1 (PON1) activity and induces oxidative stress: the possible novel mechanism for proatherogenic effect of chronic hyperleptinemia. Atherosclerosis. 2003; 170: 21-29.

11 Bełtowski J, Jamróz-Wisniewska A, Borkowska E, Wójcicka G. Differential effect of antioxidant treatment on plasma and tissue paraoxonase activity in hyperleptinemic rats. Pharmacol Res. 2005; 51: 523-532.

12 Ferretti G, Bacchetti T, Moroni C, et al. Paraoxonase activity in high-density lipoproteins: a comparison between healthy and obese females. J Clin Endocrinol Metab. 2005; 90: 1728-1733.

13 Bajnok L, Seres I, Varga Z, et al. Relationship of endogenous hyperleptinemia to serum paraoxonase 1, cholesteryl ester transfer protein, and lecithin cholesterol acyltransferase in obese individuals. Metabolism. 2007; 56: 1542-1549.

14 Eckerson HW, Wyte MC, La Du BN. The human serum paraoxonase/arylesterase polymorphism. Am J Hum Genet. 1983; 35: 1126-1138.

15 Haagen L, Brock A. A new automated method for phenotyping arylesterase (E.C.3.1.1.2.) based upon inhibition of enzymatic hydrolysis of 4-nitrophenyl acetate by phenyl acetate. Eur J Clin Chem Clim Biochem. 1992; 30: 391-395.

16 Nourooz-Zadeh J. Ferrous ion oxidation in presence of xylenol orange for detection of lipid hydroperoxides in plasma. Methods Enzymol. 1999; 300: 58-62.

17 Keaney JF Jr, Larson MG, Vasan RS, et al.; Framingham Study. Obesity and systemic oxidative stress: clinical correlates of oxidative stress in the Framingham Study. Arterioscler Thromb Vasc Biol. 2003; 23: 434-439.

18 Davì G, Guagnano MT, Ciabattoni G, et al. Platelet activation in obese women: Role of inflammation and oxidant stress. JAMA. 2002; 288: 2008-2014.

19 Rector RS, Warner SO, Liu Y, et al. Exercise and diet induced weight loss improves measures of oxidative stress and insulin sensitivity in adults with characteristics of the metabolic syndrome. Am J Physiol Endocrinol Metab. 2007; 293: E500-506.

20 Aviram M, Rosenblat M, Billecke S, et al. Human serum paraoxonase (PON 1) is inactivated by oxidized low density lipoprotein and preserved by antioxidants. Free Radic Biol Med. 1999; 26: 892-904.

21 Sorenson RC, Bisgaier CL, Aviram M, et al. Human serum Paraoxonase/Arylesterase's retained hydrophobic N-terminal leader sequence associates with HDLs by binding phospholipids: apolipoprotein A-I stabilizes activity. Arterioscler Thromb Vasc Biol. 1999; 19: 2214-2225.

22 Nieves DJ, Cnop M, Retzlaff B, et al. The atherogenic lipoprotein profile associated with obesity and insulin resistance is largely attributable to intra-abdominal fat. Diabetes. 2003; 52: 172-179.

23 Després JP, Moorjani S, Lupien PJ, et al. Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. Arteriosclerosis. 1990; 10: 497-511.

24 Sowers JR. Obesity and cardiovascular disease. Clin Chem. 1998; 44: 1821-1825.

25 Kuno T, Hozumi M, Morinobu T, et al. Antioxidant vitamin levels in plasma and low density lipoprotein of obese girls. Free Radic Res. 1998; 28: 81-86.

26 Ross R. Atherosclerosis an inflammatory disease. N Engl J Med. 1999; 340: 115-126.

27 Harrison D, Griendling KK, Landmesser U, et al. Role of oxidative stress in atherosclerosis. Am J Cardiol. 2003; 91: 7A-11A.

28 Witztum JL, Steinberg D. Role of oxidized low density lipoprotein in atherogenesis. J Clin Invest. 1991; 88: 1785-1792.

29 Ylä-Herttuala S, Palinski W, Rosenfeld ME. Evidence for the presence of oxidatively modified low density lipoprotein in atherosclerotic lesions of rabbit and man. J Clin Invest. 1989; 84: 1086-1095.

30 Mackness B, Hunt R, Durrington PN, Mackness MI. Increased immunolocalization of paraoxonase, clusterin and apolipoproteins A-I in the progression of atherosclerosis. Arterioscler Thromb Vasc Biol. 1997; 17: 1233-1238.

31 Aviram M, Hardak E, Vaya J, et al. Human serum paraoxonase (PON1) Q and R selectively decrease lipid peroxides in human coronary and carotid atherosclerotic lesions. PON1 esterase and peroxidaselike activities. Circulation. 2000; 101: 2510-2517.

32 Van Lenten BJ, Wagner AC, Navab M, Fogelman AM. Oxidized phospholipids induce changes in hepatic paraoxonase and ApoJ but not monocyte chemoattractant protein-1 via interleukin-6. J Biol Chem. 2001; 276: 1923-1929.

33 Mackness B, Mackness MI, Arrol S, et al. Serum paraoxonase (PON1) 55 and 192 polymorphism and paraoxonase activity and concentration in non-insulin dependent diabetes mellitus. Atherosclerosis. 1998; 139: 341-349.

34 Ayub A, Mackness MI, Arrol S, et al. Serum paraoxonase after myocardial infarction. Arterioscler Thromb Vasc Biol. 1999; 19: 330-335.

35 Dirican M, Akca R, Sarandol E, Dilek K. Serum paraoxonase activity in uremic predialysis and haemodialysis patients. J Nephrol. 2004; 17: 813-818.

36 Seres I, Bajnok L, Harangi M, et al. Alteration of PON1 Activity in Adult and Childhood Obesity and Its Relation to Adipokine Levels. Adv Exp Med Biol. 2010; 660: 129-142.

37 Pedrosa C, Oliveira BM, Albuquerque I, Simões-Pereira C, et al. Metabolic syndrome, adipokines and ghrelin in overweight and obese schoolchildren: results of a 1-year lifestyle intervention programme. Eur J Pediatr. 2011; 170: 483-492.

38 Jarvik GP, Rozek LS, Brophy VH, et al. Paraoxonase (PON1) phenotype is a better predictor of vascular disease than is PON1(192) or PON1(55) genotype. Arterioscler Thromb Vasc Biol. 2000; 20: 2441-2447.

39 Mackness B, Davies GK, Turkie W, et al. Paraoxonase status in coronary heart disease: are activity and concentration more important than genotype? Arterioscler Thromb Vasc Biol. 2001; 21: 1451-1457.

ARTYKUŁ ORYGINALNY

Aktywność paraoksonazy w surowicy a stres oksydacyjny u osób otyłych

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SŁOWA KLUCZOWE

arylesteraza, miażdżyca, nadtlenki lipidów, otyłość, paraoksonaza

STRESZCZENIE

WPROWADZENIE Otyłość stanowi ważny czynnik ryzyka rozwoju chorób układu sercowo-naczyniowego na podłożu miażdżycowym. Paraoksonaza-1 (PON1) może odgrywać ważną rolę w zapobieganiu rozwojowi przyśpieszonej miażdżycy u osób otyłych poprzez hydrolizę nadtlenków lipidowych w utlenionych lipoproteinach o małej gęstości.

CELE Celem badania była ocena aktywności enzymów PON1 i arylesterazy oraz pomiar poziomu nadtlenków lipidowych u osób otyłych, a także ustalenie, czy u osób otyłych występuje wzmożona podatność na rozwój miażdżycy, co mogłoby wynikać ze zwiększonego stresu oksydacyjnego i zmniejszonej aktywności PON1. Badano również związek między wskaźnikiem masy ciała (*body mass index* – BMI) a aktywnością PON1 w tej grupie chorych.

PACJENCI I METODY Badaniem objęto 25 osób otyłych oraz 23 osoby stanowiące grupę kontrolną. Aktywność PON1 i arylesterazy w surowicy zmierzono spektrofotometrycznie. Poziom nadtlenków lipidowych oznaczono za pomocą metody FOX-2.

WYNIKI Podstawowa oraz stymulowana aktywność PON1 i arylesterazy w surowicy była znamiennie mniejsza u osób otyłych w porównaniu z grupą kontrolną (P <0,001 dla obu enzymów), podczas gdy poziom nadtlenków lipidowych był znacząco wyższy (P <0,001). Zaobserwowano znamienną korelację pomiędzy BMI a poziomami PON1, arylesterazy i nadtlenków lipidowych (odpowiednio P <0,001, r = –0,720; P <0,001, r = –0,634; P <0,001, r = 0,491). Stwierdzono również korelację pomiędzy poziomami lipoprotein o dużej gęstości (*high-density lipoprotein* – HDL) a aktywnością PON1 w surowicy (r = 0.347, P <0.05).

WNIOSKI Nasze wyniki sugerują, że u osób otyłych występuje zwiększony stres oksydacyjny i zmniejszona aktywność PON1, co może się przyczynić do przyśpieszonego rozwoju miażdżycy. Zmniejszenie aktywności PON1 wydaje się korelować wprost proporcjonalnie z BMI, a odwrotnie proporcjonalnie z poziomami HDL.

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Praca wpłynęła: 30.01.2011.
Przyjęta do druku: 21.04.2011.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2011; 121 (6): 181-186
Tłumaczyła lek. Anna Kalińska