WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Atherogenic Risk Factors in Coronary Heart Surgery Patients : The Role of Paraoxonase 1 Interaction and Genotyping.

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Introduction

Coronary heart disease (CHD) caused by atherosclerosis of the coronary arteries is the leading cause of death in developed countries. For many years, extensive research has been conducted to identify CHD risk factors. Age, gender, hypertension, diabetes, obesity, elevated total cholesterol and LDL cholesterol (LDL-C), low concentration of HDL cholesterol (HDL-C), smoking, and a history of premature cardiovascular disease are all considered independent risk factors for CHD. It is reported based on large population studies. A low concentration of cholesterol transported by the HDL fraction is one of the most important risk factors for CHD, whereas a high serum HDL concentration protects against it. In recent years, a lot of research has been done on how HDL protects arteries from damage caused by free radicals and stops atherosclerotic plaques from forming. Increased oxidative stress is thought to be a factor in the development of atherosclerosis. Specific enzymes associated with HDL particles, such as paraoxonase (PON), glutathione peroxidase (GPX), and platelet activating factor acetyl hydrolase (PAF-AH), play an important role in antioxidant capacity. PON1 is one of three enzymes (PON1, PON2, and PON3) encoded by a chromosomal family of genes. Although in vitro studies show that this enzyme hydrolyzes peroxidized phospholipids, the precise mechanisms of PON antioxidant function are unknown. According to some studies, decreased PON1 activity increases the risk of developing atherosclerosis and may be considered an additional strong risk factor for CHD. Other studies have found that lower PON1 paraoxonase and arylesterase activities are related to the severity of coronary artery lesions in patients with coronary artery disease. High PON1 activity reduces the recurrence of CHD symptoms and improves the prognosis following coronary artery bypass grafting (CABG). PON1 activity has been found to be influenced by genetic polymorphism, and studies have been conducted to determine which polymorphic form of PON1 can predict CHD. It has been reported that Q alloenzyme from the coding region has a greater ability to hydrolyze peroxided lipids and protect LDL particles from peroxidation processes than R alloenzyme. Several studies were conducted to determine whether people with the isoenzyme PON1 192R are more susceptible to coronary artery disease than people with the PON1 192Q form. Some experiments confirmed the assumed relationship, while others yielded opposite results. Some researchers reported a link between the presence of allele 55L and atherosclerosis, while others denied this link. In a more recent meta-analysis of the link between PON2 311 C/S polymorphism and CHD, the authors found a link between evaluated polymorphism and CHD in Caucasians but not in Asians or Hispanics. Wheeler et al. published the results of a meta-analysis on the potential associations between PON1 gene polymorphisms in positions 108, 55, and 192 and the risk of CHD. There was only a weak link found between the presence of PON1 allele 192R PON1 and CHD. There are no correlations between the investigated polymorphisms (PON1 55L/M, 192Q/R, PON2 311C/S, PON3 99A/A) and the occurrence of documented acute cardiovascular incidents in the prospective Northwick Park Heart Study II. Individuals with the genotypes PON1 55LM or 55MM and PON2 311CC, on the other hand, were found to be 3.5-fold more susceptible to cardiovascular incidents than those with any other haplotype combination. In a large case-control study assessing the possible influence of PON1 status on CHD But the authors found that CHD patients had much less PON1 activity and concentration than healthy people, and this was true no matter what their genotype was. Many environmental factors influence paraoxonase activity, and decreased enzyme concentration and activity were observed independently of genotype in disorders that accelerate the development of atherosclerosis, such as diabetes, hypercholesterolemia, or renal failure. So, it was suggested that both genotype and enzyme serum activity should be looked at together as possible signs of CHD. The goal of this study was to find out how PON1 genetic polymorphism, enzyme activity, and other known risk factors for CHD, like high blood pressure, high total cholesterol and LDL, low HDL concentration, smoking, a family history of early CHD, and age, relate to each other in people who have already been diagnosed with atherosclerosis.

Methodology

The study population consisted of 100 unrelated patients from various hospitals in Indore (50 men and 50 women) aged 40–60 years. Following a coronary angiogram that revealed >50% narrowing of at least one of the major coronary arteries, all patients were admitted to the Cardiosurgery Departments of selected hospitals in Indore for coronary artery by-pass grafting. Age, gender, hypertension, diabetes, overweight/obesity, abnormal lipid profile, smoking, and family history of premature cardiovascular disorders, as well as previous infarction or statin treatment, were all considered. Hypercholesterolemia and hypertriglyceridemia are defined as total cholesterol and triglyceride levels greater than 200 mg/dL and 150 mg/dL, respectively. BMI was calculated as weight in kilogrammes divided by height in metres squared, with obesity defined as BMI greater than 30 kg/m2 and overweight defined as BMI greater than 25 kg/m2. Diabetes was defined as a fasting glucose level greater than 126 mg/dL and/or treatment with hypoglycemic drugs; hypertension as a diastolic blood pressure greater than 140/90 mmHg and/or hypertension treatment. Smoking was defined as smoking at least one cigarette on a daily

basis. A positive family history was defined as the presence of cardiovascular disease in at least one first-degree relative under the age of 60. Purposive sampling was used in the cross-sectional study design. Blood samples for analysis of lipid profile, PON1 activity, and polymorphism were collected via venipuncture in heparin or EDTA coated tubes prior to surgery.

Results

We looked at the relationships between PON1 paraoxonase and arylesterase activities and classic CHD risk factors like gender, age, hypertension, diabetes mellitus, obesity or overweight, cigarette smoking, CHD medical history, previous infarct, and statin treatment. Furthermore, associations between PON1 gene polymorphism, PON1 activity, and serum lipid profile parameters such as total cholesterol concentration, LDL cholesterol concentration, HDL cholesterol concentration, triglyceride concentration, and total cholesterol/HDL cholesterol ratio (cardiac index) were investigated. The correlations between serum PON 1 activity and CHD risk factors in the patient group, i.e., diabetes mellitus and PON1 paraoxonase activity, were found to have a significant negative correlation ($R = 0.247$, $p = 0.030$). The median paraoxonase activity in diabetic patients was 110.88 (17.31-226.15) U/mL, which was significantly lower ($p = 0.026$) than its value in non-diabetic patients, which was 179.39 (28.12-388.09) U/mL. The TT genotype was more common in diabetic patients than in non-diabetic patients among patients with CHD, but the difference was not statistically significant ($p = 0.339$).

Conclusions

Study concluded that even though their lipid profiles are the same, diabetic patients with CHD have less paraoxonase activity than patients who are not diabetic. Serum PON1 activity is linked to diabetes and a family history of cardiovascular disease (CHD) in patients with overt CHD. This may be an additional factor that can be used to measure cardiovascular risk in this group of patients.

Reference

1) Murray CJ, Lopez AD..Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study.. Lancet, 349 (1997), pp. 1498-504 http://dx.doi.org/10.1016/S0140-6736(96)07492-2 | Medline
2) Tomás M, Latorre G, Sentí M, Marrugat J.. Función antioxidante de las lipoproteínas de alta densidad: un nuevo paradigma en la arteriosclerosis..
3) Rev Esp Cardiol, 57 (2004), pp. 557-69
4) Wilson PW, d'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB.Prediction of coronary heart disease using risk factor categories.. Circulation, 97 (1998), pp. 1837-47
5) Harel M, Aharoni A, Gaidukov L, Brum Harel M, Aharoni A, Gaidukov L, et al. Structure and evolution of the serum paraoxonase family of detoxifying and anti-atherosclerotic enzymes.Nat Struct Mol Biol, 11 (2004), pp. 412-9
6) Mackness MI, Arrol S, Abbott C, Durrington PN.Protection of low-density lipoprotein against oxidative modification by high-density lipoprotein associated paraoxonase.Atherosclerosis, 104 (1993), pp. 129-35
7) Rosenblat M, Gaidukov L, Khersonsky O, Vaya J, Oren R, Tawfik DS, et al.The catalytic histidine dyad of high density lipoprotein-associated serum paraoxonase-1 (PON1) is essential for PON1-mediated inhibition of low density lipoprotein oxidation and stimulation of macrophage cholesterol efflux.. Biol Chem, 281 (2006), pp. 7657-65
8) Ng CJ, Wadleigh DJ, Gangopadhyay A, Hama S, Grijalva VR, Navab M, et al..Paraoxonase-2 is a ubiquitously expressed protein with antioxidant properties and is capable of preventing cell-mediated oxidative modification of low density lipoprotein.J Biol Chem, 276 (2001), pp. 44444-9
9) Mochizuki H, Scherer SW, Xi T, Nickle DC, Majer M, Huizenga JJ, et al.. Human PON2 gene at 7q213: cloning, multiple mRNA forms, and missense polymorphisms in the coding sequence. Gene, 213 (1998), pp. 149-57
10) 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, 52 (1993), pp. 598-608
11) Wheeler JG, Keavney BD, Watkins H, Collins R, Danesh J..Four paraoxonase gene polymorphisms in 11212 cases of coronary heart disease and 12786 controls: meta-analysis of 43 studies.Lancet, 363 (2004), pp. 689-95
12) Mackness B, Davies GK, Turkie W, Lee E, Roberts DH, Hill E, et al.Paraoxonase status in coronary heart disease:are activity and concentration more important than genotype? Arterioscler Thromb Vasc Biol, 21 (2001), pp. 1451-7
13) Aubó C, Sentí M, Marrugat J, Tomas M, Vila J, Sala J, et al.Risk of myocardial infarction associated with Gln/Arg 192 polymorphism in the human paraoxonase gene and diabetes mellitus. The REGICOR Investigators.Eur Heart J, 21 (2000), pp. 33-8
14) Hasselwander O, Savage DA, McMaster D, Loughrey CM, McNamee PT, Middleton D, et al.Paraoxonase polymorphisms are not associated with cardiovascular risk in renal transplant recipients..Kidney Int, 56 (1999), pp. 289-98
15) Zuliani G, Cherubini A, Volpato S, Palmieri E, Mecocci P, de Rango P, et al..
16) Genetic factors associated with the absence of atherosclerosis in octogenarians.J Gerontol A Biol Sci Med Sci, 57 (2002), pp. M611-5.