Genetic Polymorphisms CYP2J2*7 and CYP2C8*3 and Effects on the Level of Risk for Coronary Artery Disease

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Abstract

In the present study we analyzed the impact of a genetic variant in CYP2C8 on coronary artery disease (CAD) in Bulgarian population. We conducted a case-control study to determine whether the common genetic variation rs890293 (CYP2J2*7) in CYP2J2 gene was associated with the risk of CAD.

Introduction

Cytochrome P450 2C8 is a polymorphic enzyme responsible for the biosynthesis of vasoactive substances from arachidonic acid. Cytochrome P450 (CYP) 2J2 is expressed in the vascular endothelium and it metabolizes arachidonic acid to biologically active epoxyeicosatrienoic acids (EETs) [1,2].

Methods

We analyzed 99 patients with CAD and 377 controls for a potential correlation of the CYP2J2 polymorphism G-50T. 96 of these 99 patients were tested for the presence of polymorphisms CYP2C8. To evaluate the genotypes of the sample real time PCR with predesigned TaqMan SNP Genotyping Assays (Applied Biosystem) for rs890293 was used. The deviation of allele polymorphism CYP2J2*7 and CYP2C8*3 on the balance of Hardy-Weinberg and the frequency of the T allele with χ² test was studied.

Results

The main dichotomous and nondichotomous and clinical characteristics of the study group are shown in the Table 1 and 2.

The frequency of genotypes of the T allele CYP2J2*7 and CYP2C8*3 is shown on the Tables 3 and 4. In the group of people with MI, the percentage of this T allele in CYP2C8*3 is slightly greater than in the control group.

An analysis of the connection between gender and the likelihood of CAD among polymorphisms in the CYP2J2*7 and CYP2C8*3 is made. The results are shown in Table 5 and Table 6.

The obtained p-value is p=0.3656 which shows that the hypothesis of no association have to be rejected. The chances for people with T-allele polymorphism in the CYP2C8*3, CAD occur on average 1.7 times higher than those who did not carry this allele. CI of OR (1.0334÷2.8746) with 95% probability. CI indicated that it could be argued with a 95% probability that the presence of T allele in CYP2C8*3 increases the risk of CAD.

Table 1: Dichotomous clinical characteristics of the group.

| Characteristic | Number | Percentage |
|---------------|--------|------------|
| BMI [kg/m²]   | 27.98  | 5.13       |
| Triglyceride levels [mmol/l] | 2.13 | 0.77 |
| Cholesterol levels [mmol/l] | 5.90 | 0.98 |
| HDL [mmol/l]  | 1.42   | 0.62       |

Table 2: Nondichotomous clinical characteristics of the group.

| Alleles | Group with coronary artery disease - 99 | Control group - 377 | Total – 476 |
|---------|----------------------------------------|---------------------|-------------|
| TT      | Number Percentage                      | Number Percentage   | Number Percentage |
|         | 2                                     | 2.02                | 2.03         | 4           | 0.84       |
| TG      | 12                                    | 12.12               | 39           | 11.57       | 51          | 10.71      |
| TT or TG| 14                                    | 14.14               | 41           | 12.10       | 55          | 11.55      |
| GG      | 85                                    | 85.86               | 336          | 87.90       | 421         | 88.45      |
| Frequency | 0.0808                                   | 0.057               | 5.7          | 0.062       | 6.2         |
| p-value  | 0.0067                                   | 0.4586              | 0.0888       |             |             |

Table 3: The frequency of genotypes of the T allele in CYP2J2*7.

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The obtained p-value and OR are \( p=0.9489 \) and \( OR=0.9717 \) with CI=0.8612÷2.5369. The obtained values shows that it is unlikely sex to influence on CAD chances among T allele CYP2J2*7 carriers.

The obtained statistical parameters are \( p=0.1091 \) and \( OR=1.4917 \) with CI=0.9130÷2.4374. The obtained values shows that it is unlikely sex to influence on CAD chances among T allele CYP2J2*7 carriers.

The obtained statistical parameters are \( p=0.3194 \) and \( OR=1.2017 \) with CI=0.9301÷1.5799. The obtained values shows that it is unlikely sex to influence on CAD chances among T allele CYP2C8*3 carriers.

The obtained statistical parameters are \( p=0.0441 \) and consequently there is statistical significant association between smoking and CAD among T allele CYP2J2*7 carriers.

The obtained p-value and OR are \( p=0.8005 \) and \( OR=1.1719 \) with CI=0.3423÷4.011. The analysis shows that sex doesn’t influence on CAD chances among T allele CYP2J2*7 carriers.

The analysis of results shows that polymorphism CYP2C8*3 is more important for the occurrence of CAD compared with CYP2J2*7 in the study. Demonstrates a statistically significant association between the presence of the T allele and smoking respectively CYP2J2*7 and CYP2C8*3 carriers.

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