Journal of Hypertension: Open Access

Atanasova, J Hypertens 2013, 2:2
DOI: 10.4172/2167-1095.1000118

Research Article Open Access

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 samples 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 χ^2 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 is slightly greater than in the control group - 14.14% respectively versus 12.10% of patients with T-allele (Table 3). The frequency of presence of the T-allele was also greater in the group with infarction (8.08%) than in control group (5.7%). The obtained p-values for the statistical significance of the hypothesis that the distribution of the T-allele in CYP2J2*7 corresponds to the balance of the Hardy-Weinberg are greater than 0.05 and, therefore, for all groups of this hypothesis cannot be rejected.

The resulting p-values for both polymorphism (for CYP2C8*3, p = 0.7901 and p = 0.0670 CYP2J2*7) indicates that the distribution of T allele CYP2C8*3 with high probability close to balance Hardy Weinberg, than in the CYP2J2*7 (Table 3 and 4).

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 show that the hypothesis of no association can not be rejected. The odds ratio (OR) for polymorphism in the CYP2J2*7 is 1, 35 with CI=0, 7034÷2, 5900. The results show that there is not evidence for association between the T-allele and CAD.

The obtained p-value is p=0.0356 which show 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.

An analysis of the connection between gender and the likelihood of

Characteristic	Number	Percentage
Men	60	60.61
Women	39	39.39
Smokers	44	44.44
Hereditary	40	40.40
Hypertension	92	92.93
Type 1 diabetes	2	2.02
Type 2 diabetes	25	25.25

Table 1: Dichotomous clinical characteristics of the group.

Characteristic	Average	Average deviation
BMI [kg/m^2]	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	
	Number	Percentage	Number	Percentage	Number	Percentage
TT	2	2.02	2	0.53	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	8.08	0.057	5.7	0.062	6.2
p-value	0.0670		0.4586		0.0868	

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

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Received May 14, 2013; **Accepted** June 17, 2013; **Published** June 20, 2013

Citation: Atanasova GN (2013) Genetic Polymorphisms CYP2J2*7 and CYP2C8*3 and Effects on the Level of Risk for Coronary Artery Disease. J Hypertens 2: 118. doi:10.4172/2167-1095.1000118

Alleles	Group with coronary artery disease - 99		Control group - 377		Total – 459	
	Number	Percentage	Number	Percentage	Number	Percentage
TT	2	2.08	3	0.83	5	0.84
TG	26	27.08	67	18.46	93	10.71
TT or TG	28	29.16	70	19.29	98	11.55
GG	68	70.84	293	80.71	361	88.45
Frequency	0.1562	15.62	0.1006	10.06	0.1122	11.22
p-value	0.7901		0.6974		0.7153	

Table 4: The frequency of genotypes of CYP2C8 * 3.

CAD / T- allele	Yes	No	Total
Yes	14	41	**55**
No	85	336	**421**
Total	**99**	**377**	**476**

Table 5: Association of the T-allele CYP2J2*7 with CAD.

CAD / T- allele	Yes	No	Total
Yes	28	70	**98**
No	68	293	**361**
Total	**96**	**363**	**459**

Table 6: Association of the T-allele CYP2C8*3 with CAD.

CAD / Sex	Yes	No	Total
Men	6	16	**22**
Women	8	25	**33**
Total	**14**	**41**	**55**

Table 7: Association between gender and CAD among carriers of the T allele in the CYP2J2*7.

CAD / Sex	Yes	No	Total
Men	15	38	**53**
Women	13	32	**45**
Total	**28**	**70**	**98**

Table 8: Association between gender and CAD among carriers of the T allele in CYP2C8*3.

CAD / Sex	Yes	No	Total
Men	54	181	**235**
Women	31	155	**186**
Total	**85**	**336**	**421**

Table 9: Association between gender and CAD among participants without T-allele in the CYP2J2*7.

CAD / Sex	Yes	No	Total
Men	42	153	**195**
Women	26	140	**166**
Total	**68**	**293**	**361**

Table 10: Association between gender and CAD among participants without T-allele in CYP2C8*3.

CAD among the carriers of the T allele polymorphisms in the CYP2J2*7 and CYP2C8*3 is made. The results are shown in Table 7 and 8.

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.

Smoker / T- allele	Yes	No	Total
Yes	5	9	**14**
No	39	46	**85**
Total	**44**	**55**	**99**

Table 11: Association between the T allele in the CYP2J2*7 and smoking in the group with CAD.

Smoker / T- allele	Yes	No	Total
Yes	17	11	**28**
No	26	42	**68**
Total	**43**	**53**	**96**

Table 12: Association between the T - allele in CYP2C8*3 and smoking group with CAD.

The obtained p-value and OR are p=0.9489 and OR=0.9717 with CI=0.4034÷2.3404. The analysis shows that sex doesn't influence on CAD chances among T allele CYP2C8*3 carriers.

Analyzed is the relationship between gender and the likelihood of CAD among participants without T-allele polymorphisms in the CYP2J2*7 and CYP2C8*3. The results are shown in Table 9 and 10.

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=0.1547 and OR=1.4781 with CI=0.8612÷2.5369. The obtained values shows that it is unlikely sex to influence on CAD chances among T allele CYP2C8*3 carriers.

Table 11 and 12 shows the results of the association between the presence of the T allele and smoking respectively CYP2J2*7 and CYP2C8*3.

The obtained statistical parameters are p=0.4780 and OR=0.6553 with CI=0.2027÷2.1187. The obtained values shows that there isn't association between smoking and CAD among T allele CYP2J2*7 carriers.

The obtained p-value is p=0.0441 and consequently there is statistical significant association between smoking and CAD among T allele CYP2C8*3 carriers. The odds ratio is 2.4965 with CI 1.0125÷6.1555. The results indicate that the chances for CAD are 2.5 times greater to smokers.

Conclusions

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 in CYP2C8*3 and smoking group with CHD (OR = 2.4965, CI = 1.01256.1555). Odds smokers, carriers of the T allele to realize CHD were 2.5 times higher compared to non-smokers.

Acknowledgement

This work was support by Grant number № D-1/2011 – MU Pleven.

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