Lack of association of CYP11B2-344C/T polymorphism with essential hypertension: a meta-analysis

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Abstract: Objective: A meta-analysis was carried out to evaluate the correlation between CYP11B2-344C/T polymorphism and essential hypertension susceptibility. Methods: By retrieving relevant databases and collecting domestic and international literatures about the correlation between CYP11B2-344C/T polymorphism and essential hypertension, the quality of literature were evaluated according to NEWCASTLE-OTTAWA case-control study quality rating scale (NOS). RevMan 5.0 was used to select the best genetic model, analysis the heterogeneity, calculate combined OR and the 95% CI. Results: 8532 subjects were included in this study. Compared with the control group, the OR (95% CI) values of dominant model, recessive model, and additive model were 1.01 (95% CI: 0.81~1.25), 1.03 (95% CI: 0.83~1.19) and 1.10 (95% CI: 0.93-1.29). Conclusion: There is no evidence to confirm that CYP11B2 (-344C/T) polymorphism is associated with susceptibility of essential hypertension.

Keywords: CYP11B2, polymorphism, essential hypertension, meta-analysis

Introduction

Essential hypertension is a complicated disorders resulting from interaction between genetics and environmental factors [1-3]. There were two ways of analyzing the correlation between gene polymorphism and essential hypertension. One was calculating the odds ratio (odds ratio, OR) of gene in case and control groups. The other was calculating genotypes of standardized mean difference (standardized mean difference, SMD) between systolic and diastolic blood pressure [4]. CYP11B2 was the hot topic for susceptibility gene of essential hypertension and previous studies suggested that there was no correlation between gene polymorphism and susceptibility of essential hypertension in Chinese Han people [5-10]. However, the sample size and the results were inconsistent among the previous studies.

In recent years, there were many published papers to further explore the correlation between CYP11B2 gene polymorphism and hypertension [11-15]. In this study, these studies were collected at home and abroad, and evaluated the effect of CYP11B2-344C/T polymorphism on essential hypertension susceptibility by meta-analysis methods.
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Exclusion criteria

(1) Review articles. (2) The reports repeated the same population. (3) The frequency distribution of gene loci cannot be obtained. (4) Diagnostic criteria were different from other studies. (5) Genotype distribution in the control group did not meet the Hardy-Weinberg (HW) equilibrium.

Classification of case-control studies

The included studies were scored according to NEWCASTLE-OTTAWA case-control study quality rating scale (NOS). The included literatures which scored less than 6 points were classified as Class B literatures.

Quality control of process

Documents were retrieved by two independent researchers, and trade-offs were determined according to the standard; in case of disagreement, another researcher participated to review and make a decision. In first screening, titles and abstracts were read, and literature may meeting the standards were reserved; in secondary screening, full texts of the documents were accurately retained, strictly in accordance with the standard to select qualified literature; for suspicious literature, search and supplementary information before deciding whether to exclude.

Data extraction

The following information of literature were extracted: title, the first author's name, year of publication, study type, study sample source and population, age, gender, sample size, frequency distribution of gene loci and the mean and standard deviation of genotype corresponding blood pressure.

Statistical analysis

Chi-square test was used to test HW equilibrium of genotypes in each study group, and P <0.05 was deemed as HW disequilibrium. RevMan 5.0 software was used for heterogeneity test; if there was heterogeneity, a random-effects model was used for data consolidation, otherwise a fixed-effects model was used to merge OR values and 95% confidence intervals (95% CI). RevMan 5.0 software was used to draw the forest plot and funnel plot.

Publication bias and sensitivity analysis

We omitted one study at a time to perform sensitivity analysis. RevMan software was used to

Table 1. The characteristics of included studies

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<th>Authors</th>
<th>Publication Year</th>
<th>Country</th>
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CYP11B2 polymorphism and EH

The basic situation of included literature

A total of 18 documents [5-22] were included. Literature on the correlation between CYP11B2 polymorphism and essential hypertension susceptibility contained 4739 cases and 3793 controls (Table 1).

Results

The basic situation of included literature

A total of 18 documents [5-22] were included. Literature on the correlation between CYP11B2 polymorphism and essential hypertension susceptibility contained 4739 cases and 3793 controls (Table 1).

Meta-analysis

The distribution of genotype frequencies in control population selected for the study was in line with HW equilibrium; after heterogeneity test, data were merged to determine the best genetic model including dominant model, recessive model, and additive model. Meta-
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Analysis showed that -344C/T polymorphism was not associated with essential hypertension susceptibility (Figures 1-3).

Publication bias and sensitivity analysis

Quality evaluation of 18 literatures based on NOS standard showed that 11 literatures were classified as A and 7 articles were classified as Class B. First of all, the Class B documents were removed and meta-analysis was performed again. The results showed that the effect of the loci on essential hypertension susceptibility had no genetic effects, which was consistent with the previous results. We also omitted one study at a time and did not found significant changes for the OR value, indicating that the meta-analysis results were reliable. Begg’s test was used to test publication bias; the results showed that its quantitative Kendall correlation coefficient was not statistically significant ($Z = 1.04, P = 0.123$). The funnel plot also suggested no publication bias (Figure 4).

Discussion

Aldosterone synthase plays an important role in renin-angiotensin-aldosterone system which regulates blood pressure, with the activity of 1β- hydroxylase, 18-hydroxylase and 18-oxidase. It is the cytochrome P450 oxidase in mitochondrial; its coding gene CYP11B2 is located on chromosome 8 (8q22). CYP11B2 is the hot spot for essential hypertension susceptibility genes. In this study, 18 studies on the correlation between CYP11B2-344C/T polymorphism and essential hypertension were collected, including a total of 8532 cases; the effect of the variability on primary hypertension
susceptibility was studied by meta-analysis. The results show that, CYP11B2 (-344C/T) polymorphism was not associated with hypertension, although aldosterone is an important intermediate link between blood pressure and CYP11B2 (-344C/T) gene. The binding rate of -344C with SF-1 is four times higher than that of -344T, which can promote the synthesis and secretion of aldosterone. In addition to regulating blood pressure by water and salt metabolism, aldosterone also can affect blood pressure levels through the regulation of insulin receptor expression and glucose transporter. Li et al. [23] found that CYP11B2 (-344T/C) C allele can increase aldosterone levels, reduce B cell function and decrease the sensitivity of insulin, may affecting the level of blood pressure. Population-based polymorphism studies of this gene are still controversial; Davies et al. [24] consider that urinary aldosterone level is the intermediate factor between phenotype and genotype; individuals carrying the T allele have high urinary aldosterone content. On the contrary, Pojoga et al. [25] reported that plasma aldosterone levels of hypertension patients with CC genotype were significantly higher than that of patients with TC genotype, which was higher than that of the TT genotype. Meta-analysis of Sookoian et al. [26] showed that the gene polymorphism had no association with systolic and diastolic blood pressure. This study shows that the effect of the loci on susceptibility of essential hypertension has no genetic effects, which is inconsistent with the meta-analysis findings of Cheng and Xu [27]; the former conclusion is that C allele is correlated with the susceptibility of essential hypertension in Chinese population. This study has not yet found the correlation between the gene polymorphism and the susceptibility of essential hypertension. However, in the present study, we did not investigate other factors which will be included in the exploration of essential hypertension susceptibility, such as the linkage disequilibrium between -344C/T and CYP11B1, they can work together to promote the synthesis of aldosterone, thus increase the risk of essential hypertension susceptibility. Therefore, further studies related to the interaction between genetics and environmental factors should be conducted.

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Disclosure of conflict of interest

None.

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References

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