Hypertension Research (2013) 36, 465–466

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CORRESPONDENCE

Response to Xuan

Hypertension Research (2013) **36,** 465–466; doi:10.1038/hr.2012.212; published online 7 March 2013

We are grateful to the author who shared his comments and suggestions[1] regarding several issues of our meta-analysis[2] to the editor. After carefully reviewing the authors' comments and checking the raw data and our original article, we are pleased to reply to and/or clarify his questions point by point.

First, because a departure from the Hardy–Weinberg equilibrium (HWE) in controls may indicate the existence of migration, selection and mutation in population terms, which may imply poor study quality, we excluded studies that are not in HWE from our meta-analysis. The author mentioned that there were three articles that did not deviate significantly from the HWE.[3–5] After recalculation, we found that these three articles are in HWE ($P=0.066$, $P=0.129$, $P=0.078$). Thus, as the author said, these three articles should have been included.

Second, the author mentioned that there were 15 additional articles that should have been included in our meta-analysis.[3–17] After re-searching for articles relative to the association between C677T polymorphism and pre-eclampsia (PE), we found only four of the articles mentioned by the author.[3–6] Therefore, these four studies should have been included in our meta-analysis.[3–6] Another four of the studies had incomplete data and should not have been included because only data for allele T and TT genotype were provided.[7–10] Furthermore, another seven articles were not included because they did not refer to the association between the MTHFR C677T polymorphism and PE.[11–17] Otherwise, we found one other study that should also have been included in our meta-analysis.[18] And so, these five studies should have been included.[3–6,18]

Third, the author stated that their previous study indicated that the −677T frequencies of the *MTHFR* gene were different between East Asian (China, Japan and Korea) and South Asian (India) populations.[19] We read the meta-analysis that analyzed the relationship between the *MTHFR C677T* gene and myocardial infarction, which is different from our meta-analysis. And also we analyzed the heterogeneity in the Discussion section in our meta-analysis.

Taking these into account, we have now performed a new analysis by adding the five studies.[3–6,18] The pooled results showed that the MTHFR C677T polymorphism was significantly associated with PE ($P=0.01$, odds ratio (OR) = 1.26, 95% confidence interval (CI) = 1.04–1.52, $P_{heterogeneity}=0.03$, for the dominant genetic model; $P=0.02$, OR = 1.26, 95% CI = 1.04–1.52, $P_{heterogeneity}=0.001$, for the recessive genetic model; $P=0.004$, OR = 1.34, 95% CI = 1.10–1.64, $P_{heterogeneity}=0.007$, for the additive genetic model). The results of the subgroup analysis showed that MTHFR 677T had the effect of increasing the PE risk for the recessive genetic model ($P<0.0001$, OR = 2.15, 95% CI = 1.66–2.80, $P_{heterogeneity}=0.16$), the additive comparison ($P<0.0001$, OR = 2.56, 95% CI = 1.88–3.47, $P_{heterogeneity}=0.24$) and allele contrasts ($P<0.0001$, OR = 1.52, 95% CI = 1.31–1.77, $P_{heterogeneity}=0.13$) in the Asian population, whereas there was no evidence of an association between MTHFR C677T polymorphisms and PE observed in Caucasians.

The conclusion from this new analysis agrees with that of our previous study.[2] In summary, the constructive comments provided help to our study to reach more persuasive conclusions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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