Author's response to reviews

Title: Renin-angiotensin system gene polymorphisms and high blood pressure in Lithuanian children and adolescents

Authors:

Sandrita Simonyte (sandritos@gmail.com)
Renata Kuciene (renatakuciene@yahoo.com)
Jurate Medzioniene (jurate.medzioniene@lsmuni.lt)
Virginija Dulskiene (virginija.dulskiene@lsmuni.lt)
Vaiva Lesauskaite (vaiva.lesauskaite@lsmuni.lt)

Version: 1 Date: 01 Jun 2017

Author’s response to reviews:

Dear Editor and Reviewers’

We kindly appreciate the revision of our manuscript. We have enclosed the original manuscript marked with all the changes made during the revision process (yellow highlight). We hope that the revised manuscript will be acceptable for publication in your journal.

Enclosed please also find our point-by-point response to the comments raised by the reviewers (editors). We would like to take this opportunity to express our sincere thanks to the reviewers and editors who identified areas of our manuscript that needed corrections or modification. We would like also to thank you for allowing us to resubmit a revised copy of the manuscript.

Reviewer reports:

Kirsty Pringle (Reviewer 1):

The study by Simonyte and colleagues examines the distribution of polymorphisms in genes of the renin-angiotensin system and their association with high blood pressure in Lithuanian children and adolescents. The study is well-designed, the results sufficiently presented and the conclusions appropriate. I have only a few suggestions for the authors.

1. Page 4, line 84: please clarify whether you are referring to RAAS concentrations, activity or SNPs

It was corrected. Introduction section, line 80, page 4.
2. Page 4, line 88: please change to "polymorphism in the AGT gene was associated with hypertension in Caucasians.

It was corrected. Introduction section, line 87, page 4.

3. Page 4, line 92: should read "The ACE insertion deletion (ID) polymorphism…"

It was corrected. Introduction section, line 92, page 4.

4. Page 5, line 102 and p10, line 246: "school children" should be two words


5. Page 5, line 104: I suggest this be changed to "might be associated with an increased risk for higher blood pressure and hypertension…"

It was corrected. Introduction section, line 103, page 5.

6. P5, line 110: change to "included a randomly selected sample"

It was corrected. Methods section, line 109, page 5.

7. P5, line 113-114: I suggest this be changed to "there were 7,638 children and adolescents enrolled ages 12 to 15 years…"

It was corrected. Methods section, line 112, page 5.

8. Page 7, line 170: should this be 25 L rather than 25-mL?

It was corrected. Methods section, line 176, page 8.

9. Page 10, lines 228-229 and Table 3: is there also an association with the C allele (in AGTR1) and the D allele in ACE with HBP?

There were no significant associations with the C allele in AGTR1 and the D allele in ACE with HBP. The Chi-square (χ²) value in both the group (HBP and NBP) for the distribution of genotypes of each polymorphism studied was included in the table 2. Line 559, page 24.

10. Page 12, line 275-276: suggest this be changed to "we found significant evidence of an association between the ACE ID genotype in boys…"

It was corrected. Discussion section, line 296, page 12.

Kamna Srivastava (Reviewer 2):
In this manuscript the authors report on distribution of the AGTR1, AGT, and ACE genotypes in the Lithuanian child population and determined whether these genotypes have an impact on HBP in childhood, if any. They further showed that no significant differences in BP between different AGT and AGTR1 genotypes groups were found. However, the evaluated polymorphisms of the AGT and AGTR1 genes did not contribute to the presence of HBP in the present study and may be seen as predisposing factors, while ACE ID genotypes were associated with significantly increased odds for the development of HBP in the Lithuanian child and adolescent population, especially in boys. Although, these gene polymorphisms (AGTR1, AGT and ACE) were widely studied and reported worldwide. It is an important effort by the authors to explore these gene polymorphisms in Lithuanian children and adolescents population. However, it could be more impactful after some minor revisions.

1. page 3, para 4, line 72 reference should be written as (10-11)

References 10 and 11 were changed to 12 and 13. The reference numbers are in square brackets according to submission guidelines of BMC Medical Genetics. Introduction section, line 71, page 3.

2. page 3, para 5, line 74-75 sentence “Epidemiological studies suggest .......variation in blood pressure” should be acknowledged with appropriate references.

It was corrected. Introduction section, line 74, page 3.

3. page 4, para 2, line 92, Authors should define abbreviations upon first appearance in the text e.g. ACE ID (Insertion/Deletion).

It was corrected. Introduction section, line 92, page 4.

4. page 4, para 2, line 97-99, Authors written that “Studies have shown that A/C transversion ....associated with various forms of hypertension” and referred to a single study carried out in essential hypertension (reference 22). Authors please mention the appropriate references for different studies and various forms of hypertension or simply rewrite the sentence.

It was corrected. Introduction section, line 97, page 4.

5. Authors should include the previous studies carried out regarding prevalence and control of hypertension and relationship of childhood to adult blood pressure in Lithuanian population in Introduction section of the manuscript.


It was corrected. Introduction section, line 65 and line 70, page 4.

6. page 6, para 2, line 131-134, “The average of three BP ....in Children and Adolescents” should be referenced as [23].

It was corrected. Methods section, line 140, page 6.

7. Authors should describe the justification for calculation of sample size and the limitations of the study. Association of genes with the disease should have the justification of the statistical power of the study, which should be mentioned in study design under methodology section of the manuscript.

It was corrected. Methods section, line 119-122, page 5.

8. The inclusion and exclusion criteria for the selection/recruitment of study subjects should be discussed in the detail under the sub-heading study design, Methodology section of the manuscript.

It was corrected. Methods section, line 115-118, page 5.

9. Authors have stated that participants were randomly selected for the present study from Kaunas city and Kaunas district, located in Kaunas County, Lithuania. But It was not mentioned anywhere in the manuscript about the ethnicity of the study subjects, such as for how many generations they had been living in that particular region.

It was corrected. Discussion section, line 117-118, page 13.

10. The Chi-square (χ2) value in both the group (HBP and NBP) for the distribution of genotypes of each polymorphism studied should be included in the table 2 or results section.

The Chi-square (χ2) value in both the group (HBP and NBP) for the distribution of genotypes of each polymorphism studied was included in the table 2. Line 559, page 24.

11. In discussion section, Authors should discuss the expression of these RAAS genes and their association with the genotypes in case of high blood pressure and the mechanism associated with pathogenesis of disease.

It was corrected. Discussion section, line 274-288, page 12.

12. There are many grammatical errors throughout the manuscript. Authors should check the entire manuscript for grammatical and spelling errors. It would be better, if authors consult some technical writing expert.
The present manuscript was proof-read by a native English speaker, and we hope that our revised version has better English than the previous version.