Author's response to reviews

Title: Body mass index contributes to sympathovagal imbalance in prehypertensives

Authors:

GOPAL KRUSHNA PAL (drgkpal@gmail.com)
ADITHAN CHANDRASEKARAN (adithan50@gmail.com)
ANANTHANARAYANAN PALGHAT HARIHARAN (phananthanarayanan@gmail.com)
TARUN KUMAR DUTTA (tkduttajipmer@yahoo.co.uk)
PRAVATI PAL (drppal@rediffmail.com)
NIVEDITA NANDA (ananda31@rediffmail.com)
LALITHA VENUGOPAL (lalitha.jipmer2010@gmail.com)

Version: 3 Date: 9 May 2012

Author's response to reviews: see over
From: Dr. G. K. Pal, MD
Professor and Head,
Department of Physiology,
JIPMER, Puducherry - 605 006, India.
E-mail: drgkpal@gmail.com
Fax: 0-91-413 – 2272067, Kind Attn.: G. K. Pal, Prof. of Physiology.
Phone: 0-91- 93442 91160

Date: 9th May, 2012

To: The Editor-in-Chief,
BMC Cardiovascular Disorder.

Subject: Submission of revised manuscript.

Reference: Manuscript ID No. MS: 1550140124673602
Title: Body mass index contributes to sympathovagal imbalance in prehypertensives

Sir,

Kindly find attached herewith our revised manuscript titled “Body mass index contributes to sympathovagal imbalance in prehypertensives” for your kind consideration for publication at the earliest in your esteemed journal ‘BMC Cardiovascular Disorder’. While revising the manuscript, we have carefully made appropriate changes as per suggestions of reviewers and recommendation of the editors. All the major changes in revised manuscript are highlighted in blue color. We have improved the language of the manuscript with the help of a Professor of English.

Point-by-point response to reviewer’s queries are enclosed herewith as per editorial advise.

Thanking you, yours sincerely,

Dr. G. K. Pal
For Reviewer 1:

(All major changes in the manuscript are highlighted by blue color)

**Major Compulsory Revisions**

1. In the previous Ref. No. 29 [Effect of gender on sympathovagal imbalance in prehypertensives. *Clin Experiment Hypertens* 2012, 34(1):31–7.], the objective of the study was to assess the sex difference in sympathovagal imbalance (SVI) in prehypertensives. The groupings of subjects (males and females) were done as per the gender of the subjects. In this previous study, the association of BMI and WHR with SVI was assessed by simple Pearson correlation. However, the independent contribution of BMI to SVI was not assessed. In the present study, subject groupings (normal BMI and higher BMI) are done as per the level of BMI of the subjects and contribution of BMI as an independent variable to SVI is assessed by multiple linear regression analysis. Moreover, in the present study, SVI in prehypertensives with normal BMI has been compared with the prehypertensives with higher BMI, which was not done in previous study. Also, the sample size of prehypertensive group in the present study (n=63) is more than that of the previous study (n=57). Conclusion of the present work represents further progress in the field.

For the **Associate Editor’s enquiry**, our other publication (Sympathovagal imbalance in prehypertensive offspring of two parents versus one parent hypertensive. *Int J Hypertens* 2011; 2011:263170) is a different work in which we have studied SVI in children born to hypertensive parents.

2. Inspite of the modest sample size, we found a huge difference in LF-HF ratio between normotensive and prehypertensive groups. In our all previous reports (G. K. Pal et al, Ind J Physiol Pharmacol, 2009; G. K. Pal et al, Clin Experiment Hypertens 2009; G. K. Pal et al, International J Hypertens 202010; G. K. Pal et al, Clin Experiment Hypertens 2012) we found a similar values for LF-HF ratio in
normotensive and hypertensive subjects with modest sample size. It is true that such a big difference was not observed in previous studies (ARIC, Framingham). This difference in observation could be due to the racial difference in basal LF-HF ratio, as there is report of ethnic variation in HRV indices [Ref. No. 35. Zhibin Li, et al. A longitudinal study in youth of heart rate variability at rest and in response to stress. Int J Psychophysiol. 2009; 73(3): 212–217]. Now, this has been addressed in discussion as instructed by our esteemed reviewer. Please refer 3rd to 6th lines of the first paragraph, page 12.

3. Recruitment modality has been more explained now. Age criterion for subject selection has been included. In our country, JIPMER is a premier medical institute and institute of national excellence. Recruitment of staff in JIPMER is performed by nationwide advertisement and general selection. Hence, the staffs of JIPMER represent the people from all over the country representing different region and strata of the society. Therefore, inclusion of staff of JIPMER in the study apparently represents the general population and therefore the bias is minimal.

4. As the level of physical fitness is a major determinant of vagal tone, subjects regularly performing physical exercises were excluded from the study. This has been mentioned in the exclusion criteria of subjects. Also, obese or overweight subjects with physical fitness were included in the study group. The inclusion and exclusion criteria are almost rewritten. Please refer first paragraphs of page 5 and 6.

5. As per advice of the esteemed reviewer, rate pressure product (RPP) is excluded from the multivariate analysis. Age has been included in the multivariate model (Please refer Table 5). Other covariates such as smoking, alcohol intake and physical fitness are not included in the model as these factors were among the exclusion criteria for selecting the subjects.

6. Statistical analysis has now been reviewed and thoroughly checked as per the advice of the Lecturer in Biostatistics of our institute. There were some errors in the previous analysis. All mistakes have been corrected in Table 3 and other tables.
7. Previous literature of autonomic balance in overweight and obesity is now adequately cited and discussed. Please refer the highlighted portion of last paragraph of page 14 and first and second paragraphs of page 15. For this, nine new references (Ref. No. 39 to 47) are added to the list of references.

**Minor Essential Revisions**

1. The tests performed were two-tailed (please see, it is now mentioned in statistical analysis section). The mention of ‘four’ groups was a typographical error; correction has also been made as ‘three’ groups.
2. As per suggestion, the data of SDNN has been included in the study. Please refer Table 2.
3. The non-normalized data are listed in the footnote of Table 2. As per suggestion, data of absolute LF and HF powers have been incorporated (Please refer Table 2) and discussed.
4. Corrections have been made to all language errors and typographical errors throughout the manuscript.
5. Inclusion and exclusion criteria are modified as per suggestion. This section is almost rewritten. Please refer page no. 5 and 6.
6. Reports of three studies on HRV in hypertension (Schroeder et al, 2003, Liao et al, 1996 and Singh et al 1998) are now included and discussed in ‘Discussion’ section. Please see last paragraph of page 12 and first paragraph of page 13). For this purpose, three more references are added (Please refer Ref. No. 32 to 34).
7. Informed consent of the subject has been included in ‘inclusion criteria’ section. Please refer last sentence of first paragraph of page 5.

**Discretionary Revision**

As per suggestion of our esteemed reviewer, the data of % change of absolute LF and HF powers are presented in the figure format (Figure 1).
For Reviewer 2:

1. Correction has been made to the word ‘heart rate variability’ in key word section.
2. As per the suggestion of the esteemed reviewer, the number of references cited in ‘Background’ section has been reduced. Earlier, there were thirty-three references in ‘Background’ section; that are now reduced to 24 references after deletion of nine references.
3. As per the suggestion of the esteemed reviewer, aims and objective of the study is now rewritten in the last paragraph of ‘Background’ section, incorporating independent contribution of BMI etc. Please see the last sentence of last paragraph of page 4.
4. The scientific basis of selection of ‘inclusion criteria’ for groups 1, 2 and 3 has been justified by providing references to it (now they appear as references 25 and 26). Please see the middle paragraph of page 5. Now the ‘Inclusion and Exclusion criteria’ are almost rewritten as depicted in page 5 and first paragraph of page 6.
5. Exercises cited here are regular practice of physical activities such as morning walk, cycling, swimming etc. that are known improve vagal tone and decrease BP; whereas yoga is the methodical practice of yogic techniques that usually does not include intense physical activities. Practice of yoga includes asanas, meditation, pranayama etc. that are also recently reported to decrease BP. Thus, yoga is different from physical exercise. This explanation has been included in text in the last sentence of discussion and appropriate references are cited.
6. The query is that if BMI correlates with LF-HF ratio in group 2 (Prehypertensives with normal BMI) and in group 3 (Prehypertensives with higher BMI) as depicted in Table 3, then how can BMI be a major predictor of SVI in prehypertensives? There was an error in correlation of LF-HF ratio with BMI in all the groups, as pointed out by our esteemed first reviewer. After correction of this mistake, no significance was obtained between LF-HF ratio and BMI in any of the groups. Therefore, Pearson correlation was done to asses the association of BMI with LF-HF ratio in all prehypertensives subjects taken together, in which a high level of significance
(p=0.000) was observed (please refer Table 4) indicating the sufficient link of BMI to SVI in prehypertensive subjects. Also, BMI has independent contribution to SVI imbalance in prehypertensives (Please refer Table 5). Thus, BMI emerges as a major predictor of SVI in prehypertensives. This point, which was not well explained in ‘Discussion’ earlier, has now been described properly as per the advice of our esteemed reviewer.

7. In statistics part of Table 1 and 2, ‘p’ values as depicted in last column of the tables are different for different parameters. This is because ‘p’ values primarily depend on the magnitude of difference of values between the groups. For example, for the parameter ‘age’, as the difference between the groups was not much, the ‘p’ value was not significant (p=0.6521). Whereas, for the parameter like ‘RPP’ the values between the groups were much different, hence the ‘p’ value for RPP was highly significant (p<0.0001). Similarly, for the parameter ‘LFnu’ in Table 2, as the difference between the groups was moderate, the ‘p’ value for LFnu was moderately significant (p=0.0004), whereas for the parameter ‘HFnu’ the difference between the groups was comparatively more, hence the ‘p’ value for HFnu was considerably significant (p<0.0001). We believe our esteemed reviewer will agree with us.