Reviewer's report

Title: Patterns of heart rate variability and cardiac autonomic modulations in controlled and uncontrolled asthmatic patients

Version: 2
Date: 10 June 2015

Reviewer: Gavin P Pinniger

Reviewer's report:

This study addresses an interesting topic of heart rate variability in asthma patients. Previous studies have identified an apparent paradoxical relationship of high parasympathetic activity with low HRV. This study attempted to further examine this phenomenon by distinguishing between controlled asthmatic (CA) and uncontrolled asthmatic (UA) patients based on ACT scores. Interestingly, CA patients appeared to have higher HRV than UA and healthy control patients which suggests the need to account for disease severity when evaluating HRV and autonomic regulation in asthma patients. I have some concerns regarding the experimental procedures and interpretation of the results as indicated below.

Major Compulsory Revisions

1. P2. L19. The statement that “low HRV literally means decreases protective power of vagal reflexes on the heart or increased the harmful effects of cardiac sympathetic stimulation” is at best a very poorly worded description of the clinical relevance of HRV and at worst an extremely simplistic interpretation that indicates a lack of understanding of the complex association between autonomic regulation and cardiovascular health.

2. P6. L1. Subjects in the control and asthmatics groups were matched for age, gender, weight and height, however there were twice as many asthmatic subjects as control subjects. How could the asthmatic subjects be matched if there was no corresponding control subject?

3. P6. L9. Information on anti-asthma treatments were recorded, but not reported in the manuscript. To assist in the interpretation of the results it would be helpful to know what anti-asthma treatments the patients were on, did treatments differ for the UA and CA groups, and how these treatments might impact on HRV measures.

4. P6. L17. Description of the recording procedures for HRV requires more detail. What was the duration of the recordings, were subject seated or supine, was respiratory frequency monitored during HRV recordings? Considering that HRV is strongly modulated by respiration, and subjects had respiratory disorders, a measure of respiratory rate should be included in the analyses.

5. P6. L23. How were the LF and HF spectral densities normalised to provide LF Norm, and HF Norm parameters?
6. P10. L14. Adjustment for MHR and AAT does not account for different results from this study with previous studies showing reduced HRV in asthma patients. Even with the non-adjusted data in Table 3, there are no differences in HRV measures between HS and UA groups.

7. The author examined LF and HF indices of HRV as a measure of sympathetic and parasympathetic autonomic regulation. While it is widely accepted that the HF component is a reflection of parasympathetic/vagal regulation, the validity of the LF component as a measure of sympathetic tone is a more contentious issue (eg Martellie et al Am J Physiol Heart Circ Physiol. 2014 Oct 1;307(7):H1005-12; Goldstein et al Exp Physiol. 2011 Dec;96(12):1255-61). The author should acknowledge the limitation of the LF measures as a reflection of sympathetic tone when discussing the balance in autonomic regulation of HR.

8. P7. L21. The description of results presented in Table 2 is confusing. Each of the parameters are significantly different between groups, but no post-hoc analysis are presented, and how are these data “well matched with asthma control”? 

Minor Essential Revisions.

9. P2. L8. AACHR is defined in the abstract but does not appear anywhere else in the manuscript. Presumably this has been replaced by MHR?

Introduction

10. P7. L16. MABP is not defined in the manuscript and does not appear in Table 1.

11. P7. L20. Data presented in Table 1 are grouped by AS and HS, however, considering the data are analysed according to CA, UA, and HS groups, it would be helpful to report the data in Table 1 for the same groups, especially for MHR which is used for the general linear model.

12. P8. L1. The units for the frequency components should be ms²/Hz, as indicated in the table. And the units for HF norm, nu, should be defined.

13. P8. L9. Data are presented in Figures 1 & 2. However, these figures have no vertical axis labels, no figure legends and appear to repeat data already presented in the table and in the text.

14. Table 3. I don’t understand how you can have a negative ratio for LnLF/HF!

15. General minor comments.

There are multiple spelling and grammatical errors repeated throughout the manuscript:

Eg. derive instead of drive; changes in heart rates instead of heart rate; the use of the term “proved” repeatedly throughout the manuscript is not appropriate in the scientific context; myofilaments not myofilamrnts.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests