Reviewer's report

Title: Relationship of 24-hour ambulatory blood pressure and heart rate with markers of hepatic function in cirrhotic patients

Version: 1 Date: 14 April 2010

Reviewer: Matthias J. Bahr

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The authors describe the use of 24-h ambulatory blood pressure and heart rate monitoring in patients with liver cirrhosis. The rationale behind this study are the circulatory disturbances seen in patients with advanced liver disease, namely peripheral vasodilation followed by a decrease in blood pressure and an increased heart rate. Usually, these effects will be compensated for by more heart activity leading to a higher cardiac output. However, in recent years, it has become clear that cardiac function may be affected by chronic liver disease, a syndrome called cirrhotic cardiomyopathy. Especially those patients who cannot compensate the increased needs for cardiac output are at risk to develop complications such as the hepato-renal syndrome. Therefore, the identification of patients with major circulatory disturbances might improve patient care by preventing secondary complications.

Major Compulsory Revisions

What teaches us the paper by Tzamouranis et al? There is always two ways in how clinical studies may advance current knowledge: First, it may deepen our understanding for clinical pathophysiology. Second, it may improve clinical care.

In the introduction, the authors focus on the improvement of clinical patient care by their study. In detail, they want to answer the question whether 24-hour blood pressure recording provides more relevant information than single office BP measurements.

However, in his respect there are some shortcomings in the study:

- First, the most endangered patients, namely those who are at highest risk for deterioration of their situation were excluded from the study (serum creatinine >133 µmol/l, serum sodium <130 mmol/l). In addition, also patients with hepatic encephalopathy were excluded. The reason to do this remains unclear. It is also unclear whether any stage of HE was excluded (even subclinical?). There were Child C patients in the study group. No sign of HE in these patients?

Looking at the results, one gets the impression that nonexistent correlations between liver function and circulatory parameters may be, at least in part, due to the protocol restrictions of the study group. Another reason for the worse results in 24-hour monitoring appears to be the differences in daytime activity in ambulatory patients.
- Second, the patients were taken off cardio-vascular medication for at least 7 days prior to the measurement of circulatory parameters. In clinical practice we would not want to establish a test that leaves our patients for such long periods without protection from b-blockers, especially as rebound effects of b-blocker withdrawal are well known. Therefore, the study conditions do not reflect clinical practice. We cannot conclude from the data delivered by the study that patients taking cardio-vascular drugs should be controlled by office-based BP measurement.

- Third, to show correlations between circulatory parameters and tests / scores of liver function does not establish these tests as useful means in the monitoring of patients with liver cirrhosis. In fact, it is the part of information that is outside of the correlations which is additional. A new test is especially worthy if it provides additional data. Therefore, a correlation to other endpoints should be sought: survival, development of complications, deterioration of liver function. The recruitment of patients stopped in 2006. As the number of patients is not very high, it appears possible to acquire the above mentioned data, which would strengthen the current study enormously.

In conclusion, the clinical usefulness of the presented data is limited, but could be easily improved.

Regarding the advancement of clinical pathophysiology understanding the study provides some interesting data. Using this viewpoint, the study conditions without the use of cardio-vascular active drugs allow a clearer picture.

- The most interesting point for me was that the highest correlations between circulatory and liver function parameters were found for albumin. This points to the role of plasma oncotic pressure for the development of circulatory disturbances in cirrhosis which obviously needs to be mentioned at the side with peripheral vasodilation.

- The biggest shortcoming of the current study with regard to the understanding of pathophysiology is the small set of circulatory parameters. Especially with regard to the ongoing discussion on the role of cirrhotic cardiomyopathy it would have been interesting to have echocardiographic data or at least ECG or 24-hour ECG. For practical reasons, these data will probably not be available. However, it should be possible to provide a set of age and sex-matches healthy controls for the BP and heart rate data.

Originality of the data: There are a few data published on 24-hour BP monitoring in cirrhosis. The authors cite 2 papers originating from one center published in 1995 and 1997. The differences to the current study are clearly labeled in the discussion. There is definitively a need to collect more of these basic data for the completion of our pathophysiologic picture of circulatory changes in cirrhosis. Therefore, I am very much in favor of publishing the current manuscript after a thorough revision.
Minor comments
- Methods, subjects, exclusion criteria: As heart failure might develop secondary to cirrhosis, how was heart failure defined? What about other significant heart diseases, e.g. CHD?
- Methods, BP measurements: Have left-right arm differences been excluded?
- Methods, statistics: What kind of correlation coefficient was calculated?
- Table 2: Headings, change “Group BC” in “Group B”. Table: formatting errors.
- Table 5: Table can be omitted. Results can be presented as non-significant in the text. The low number of significant results in this table will disappear if corrections for multiple testing are used.
- Additional figure: Correlations between serum albumin and BP / HR should be presented as scatter plots.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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