Reviewer's report

Title: Altered cardiac rhythm in infants with bronchiolitis and respiratory syncytial virus infection

Version: 1 Date: 11 September 2010

Reviewer: Massimiliano Fabbiani

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In this study, Esposito et al. evaluate the occurrence of heart rhythm alterations in infants with bronchiolitis. The main findings are the observation of a higher frequency of sinoatrial block, an higher mean and maximum heart rate, and an higher low-frequency power and low/high-frequency power ratio in RSV-infected children. Interestingly, the occurrence of sinoatrial block seemed to be correlated to RSV viral load. Moreover, the described alterations showed a complete resolution after disease recovery.

The study is well designed, methodology appears appropriate, results are interesting and the manuscript is well written. The main limitation is the low number of subjects enrolled and this is correctly recognized in the discussion section.

Some issue needs to be addressed before acceptance.

MINOR ESSENTIAL REVISION

1. Statistical analysis should be better described. In particular it should be specified if authors used tests for paired samples when they compared continuous variables at the 2 different time points in the same patient group (baseline versus 28 days in RSV infected infants; baseline versus 28 days in RSV negative infants), as appropriate.

2. Table 1.

The authors state that no significant between-group difference was observed. However, a column showing the exact p value for each variable comparison should be added. Also a statistical trend can be of some value when comparing groups with a low number of patients.

The last two rows are confusing. Is the comparison related to the proportion of patients in the 2 groups with at least a respiratory infection or an antibiotic course in the last 3 months? Or between the mean (SD) number of respiratory infections or antibiotic courses in each patient group? Please clarify.

3. Table 2.

As suggested above, a column showing the exact p value for each variable comparison should be added.

A row showing mean (SD) temperature in the 2 groups should be added.
Are there some patients treated with oral bronchodilators? If so, this should be specified and the proportion in the 2 groups should be compared. This is important since it could explain the observed differences in heart rate.

4. Table 3.
In the table, for the comparison of mean heart rate in RSV-positive children the symbol “ is repeated 2 times, please verify.
In the notes, symbols are described in a confusing manner. The symbol ° is used for 2 different comparison, the symbol ^ showed in the table is not shown in the notes.

5. Table 4.
It is interesting that all the 3 cases of severe bronchiolitis showed a sinoatrial block. The very low number of subjects with severe infection could have limited the statistical power to detect between group differences according to disease severity. This limitation should be more clearly recognized in the discussion.
Moreover, since some reports in the literature have shown a correlation between viral load and disease severity, in a sensitivity analysis it should be verified if the association of sinoatrial block with high RSV viral load remain significant even after excluding patients with severe disease (and probably an high viral load). If the association persist, this should be reported in the results and should be discussed. This further analysis can be important to support the hypothesis that the virus itself can play a role in the pathogenesis of cardiac findings, independently from disease severity.
If some patients received oral bronchodilatators, it should be verified whether their proportion differed between patients affected or not by sinoatrial block.

6. Line 254-257. This hypothesis appears to be purely speculative. The cited reference (number 30) refers to intrauterine death and there is no demonstration of RSV infection nor in the mother neither in the fetus. I suggest that this part is removed.

7. Line 267. This conclusion appears to be too strong. I suggest to substitute the term “plays” with “could play”.

DISCRETIONARY REVISIONS
1. Line 103. Typographical error: “Oxiyetry” instead of “oximetry”.
2. Section methods, echocardiografic studies. Was pulmonary pressure estimated or signs of pulmonary hypertension evaluated? If so, this should be reported in the methods section.
3. Line 384. Reference number 28 is duplicated (number 8) and should be removed.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests