Reviewer’s report

Title: Plasma levels of alarmin HNPs 1-3 associate with lung dysfunction after cardiac surgery in children

Version: 1 Date: 06 Jun 2017

Reviewer: Amelia Moreira

Reviewer’s report:

Dear authors,

We thank you for your submitted article. Based on the fact that the incidence of post-CPB pulmonary dysfunction ranges from 12 to 50%, and that an earlier detection or severity prediction could help us to personalize the therapeutic strategy for each patient, your research question is quite interesting and clinical relevant. Besides, we often extrapolate data from adult studies and it’s important that we acknowledge the pediatric differences, especially in what concerns the younger patients. That being said we have some comments to your article.

Major comments

1. Outcome

The definition of PaO2/FiO2 is not very clear because we don’t have access to the ventilation parameters (a PEEP level of 5 cmH2O was used for everyone?). As you know, different ventilation adjustments affect P/F ratios. Besides, perhaps the use of the oxygenation index (standardized ventilator parameter) is more indicated in small children.

Moreover, concerning the mechanical ventilation time, there is no explicit reference to the specific extubation criteria (you refer to a standard MV weaning protocol in line 150-151 but we don’t know it - please add it as a supplement). Finally, since you did not show that the basic pathology didn’t influence the HNP level (because you didn’t include it in your multivariate analysis - multiple linear regression model) it was important to show that the duration of MV was equal for all groups, independently of the specific cardiopathy (VSD, ASD, Fallot).

2. Statistical significance

All correlations between HNP and P/F, and HNP and MV time (Figures 2 and 3) are in general very weak, ranging from 0.38 to 0.64. For this reason, your conclusion seems to be too strong. Furthermore, the after-CPB values of HNP 1-3 show important standard-deviations. Therefore it might have been sought to try to work out a cutoff value and/or predict positive value.

3. Cardiogenic pulmonary edema
By protocol, patients with pre or post-surgery cardiogenic pulmonary edema were excluded. What do you mean by "volume overload" (is it chest X-ray assessment by a radiologist?). In addition, it might have been interesting to analyze the HNP level in these patients as well, which should have been stayed low if it’s a selective measure of inflammatory response.

Globally, given this 3 major points (especially the second point) we strongly suggest that you draw your conclusions more cautiously.

Minor comments

Line 153: pulse oximetry saturation (SpO2) at room air?

Line 200: please replace "underwent radical operation for cardiac lesions" by "underwent complete corrective surgery"

Lines 240: were correlated with the severity of lung function decline but not very strongly (please add r values)

Line 266: again, please add r values - positively correlated (r=0.46) with the duration of MV

Line 331-332: please add a sentence mentioning the fact that the correlation is weak, as this is also a limitation to your study

Line 337-338: please reformulate or eliminate this sentence

Line 347: you should rephrase your conclusions more prudently as already stated

Table 1: SpO2 before operation - at room air?

Ultrafiltration volume in ml when you have children weighting 7.9±2.4 Kg makes no sense: you should put it in ml/Kg

Figure 1: since you give numeric data in Table 2 on plasma HNP and cytokine levels Figure 1 does not add any additional information

Figure 2: please correct/ameliorate the label on the x axis which has "after CPB" and "1h after surgery" (it is always after CBP and it’s confusing)

In fact, without more explicit information this figure is extremely difficult to read. Furthermore, it’s difficult to realize that you give the HNP immediately after bypass and 1 h after bypass levels in relation to the 1st day P/F ratio in A and B, and HNP levels immediately after bypass and 1h after bypass in relation to 2nd day P/F ratio in C and D.

By the way it would be pressing to know what was specifically different for the 5 "outlier" patients clouded in upper left half of figure A.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

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