Author's response to reviews

Title: Relative adrenal insufficiency and hemodynamic status in cardiopulmonary bypass surgery patients. A prospective cohort study.

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Author's response to reviews: see over
Reviewer Luis Ramos

*In page number 4: ...or 12 to 15 mmHg of pulmonary artery occlusion pressure; 15 and mmHg must be separated.

*In page number 11: Author's contributions, ...processing blood simples; "simples", must be corrected for samples.

These questions have been corrected in the reviewed manuscript.

Reviewer Patricia López

Authors:

*Components attached to diferents departments not specify their qualifications or workplace.

We added our qualifications.

Background:

*The objectives of the work is not see the risk factors but if etomidate is a risk factor.

The main objective was to determine the risk factors for relative adrenal insufficiency (RAI) in cardiopulmonary bypass patients. But when we observed the high association of etomidate with RAI (OR 6.55), we decided to perform a propensity score analysis in order to avoid selection bias.

Method:

- Being a prospective cohort study, but did not specify when the term finish.

We report our study following the STROBE recommendations. The first line after Study design and patients, describe the period of study (“A prospective cohort study was performed from January to July 2007…”).

- Drugs and Immulite Synacthene should bear the R trademark.

We apologize our mismatch. We have added this suggestion.
- In the sedolajación perioperative management and analgesia with midazolam, fentanyl and cisatracurium were administered as a continuous infusion rather than bolus, which surprises me because it is usually given an initial bolus.

Effectively, anesthetic induction was achieved by a single bolus of the above mentioned drugs following by a continuous perfusion.

- Duration of norepinephrine therapy is not refer.

Certainly we forgot to report appropriately norepinephrine time therapy. In table 3 we reported time as dose (last cell row), previously we reported “Norepinephrine (mcg/kg/min) hrs”, now we have taken “(mcg/kg/min)” off.

- Define renal failure when creatinine levels are> or equal to 1.5 mg / dl. Based on what parameters to be decided from this number?.

Our laboratory reference levels for serum creatinine are from 0.5 to 1 mg/dL. Therefore we assumed that a percentage increase in serum creatinine $\geq 50\%$ (1.5-fold from baseline), that means equal or greater than 1.5 mg/dL, accomplished with diagnostic criteria from the Acute Kidney Injury Network for kidney injury.

- Complication of surgery are painfully missing.

We described a non significant differences of length of stay and mortality between groups (Table 1). Now we have added percentage of re-exploration caused by bleeding.

- Given that many patients make it advisable to ascertain Vasoparalysis fluid balance.

We don’t understand this sentence.

-Tables:

The scale of Parsonnet reference needed.

This suggestion has been added in the reviewed manuscript.
-Discussion:

- It is assumed that hypotension is secondary to adrenal failure as etomidate produces only give us diagnosis central venous pressure, mean arterial pressure and systemic vascular resistance index. It is well known that there are other causes of shock in patients undergoing cardiopulmonary bypass Vasoplegia, hemorrhage or cardiogenic shock. It should also measure parameters such as systolic volume, lactic acid as an indicator of tissue hypoperfusion or mixed venous saturation.

Relative Adrenal Insufficiency may explain, at least in part, postoperative vasoplegia. Glucocorticoids promote the maintenance of cardiac contractility and vascular tone and decrease the production of nitric oxide, a major vasorelaxant and modulator of vascular permeability. Therefore, factors affecting the release and action of cortisol may modify the hemodynamic response to stress. In our study we did not observed differences in postoperative bleeding (hemorrhage) between groups (now it has been added in table 1). Cardiogenic shock would show high vascular resistances instead of lower resistances. Also we did not observe significant differences between groups (No RAI vs RAI) in systolic volume index (36.1±5.6 vs 35.1±4.7; P=0.74), lactic acid (2.4±0.9 vs 2.3±0.8; P=0.32) and mixed venous saturation (70±10 vs 69±9; P=0.89) at 4h.

- Did the authors consider substituting adrenal function with hydrocortisone?.

After this study was carried out etomidate has not been used routinely. Nevertheless, when administration of this drug is done, now it is standard practice to communicate this to the ICU team so that we can manage accordingly.