Author's response to reviews

Title: The effects of ibuprofen on the physiology and survival on the rabbit endotoxic shock

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PDF covering letter
Answers to the Reviewer’s report:

To: Prof Gordon Bernard;

1- What new information were these investigators seeking?

There are many studies use of ibuprofen on septic/endotoxic shock model. However, there are some contrary results especially on survival time. In our department, we gave ibuprofen to a few septic patients with antibiotics and we had observed a little improvement survival under the base of Bernard studies. We wanted to make a controlled study with an animal model. The first two sentences were added at introduction part of the manuscript.

2 - How does this work contribute to the literature (other than confirming the results of others)?

It is hard to answer actually.

Minor points:

1- Table 1 - a mean respiratory rate of 473 is reported. This surely must be an error.

Minor points: Table 1 has an error: a respiratory rate had written 473; it was corrected as “73.3±3.5”

2- English grammar and syntax errors should be corrected.

Grammar and syntax error was tried to correct.

To: Prof Jean-Louis Vincent;

1- Abstract: Abstract: Why do the authors refer to the undesirable effects of endotoxic shock on respiratory rate and heart rate? Is it not a normal response to develop tachypnea, tachycardia and fever when endotoxin is administered?

We corrected the sentence “The undesirable effects of endotoxic shock on respiratory rate, heart rate, and arterial pressure (MAP) were alleviated by ibuprofen administration” as “Ibuprofen improved respiratory rate, heart rate, and arterial pressure (MAP)” We made a grammar error previously. Of course, endotoxin administration develops tachypnea, tachycardia and fever.

2. End of abstract and elsewhere in the text: Patients may not develop endotoxic shock but septic shock in a broader sense.

We wrote, “Patients might be developed septic shock instead of endotoxic shock”

3- Introduction: The introduction should be extended in view of this literature review and raise important questions which were not addressed in the previous studies.
The introduction was extended in view of literature that signed by Prof Vincent.

4- Results: The entire results section is difficult to read. It seems that ibuprofen administration had hardly any effect on respiratory rate and heart rate (but this is of minor importance).

I had tried to correct grammar and syntax error and I sent to http://www.abdn.ac.uk/mps. I am still waiting for an answer from Biomedes.

5- Discussion, third paragraph: Reference to the work by Bernard et al is confusing here: Bernard did clinical studies with ibuprofen.

I had written “Bernard et al” mistakenly instead of “Balk et al.” It was corrected as Balk et al.

6- Discussion: Once again, the restoration of vascular tone resulting in a greater arterial pressure may be beneficial but the effects on heart rate and respiratory rate are more questionable.

The sentence “Ibuprofen has little effect on respiratory and heart rate” was added.

7- Discussion: Again, the authors should largely refer to the clinical study performed by Bernard et al: Is it still necessary to perform these animal experiments when the effects in humans have been well described?

Prof Vincent actually is right in this subject. Bernard et al. are well described the effects of ibuprofen. However, there are some contrary results especially on survival time.

8- Discussion: Many studies have shown that endotoxin administration can result in an acute decrease in the white blood cell count. Can the authors propose an explanation to explain the lack of effect of ibuprofen on white blood cell count and platelet count?

This sentence was added “Ibuprofen has little effect on platelet and WBC count, but not statistically significant.”

9- The effects of ibuprofen on arterial pressure are worth a figure.

Any change was made.

10- Figure 1: Why does the respiratory rate go down to zero only in-group 2?

At every group respiratory rate go down zero at the end. However, at figure the study time was limited 600 minutes. Only one rabbit was lived at min 300th and 360th in-group 2. It affected this line at group 2. If we extend time to min 660th that showed at figure 1, it could be seen respiratory rate go down zero at all groups.