Author’s response to reviews

Title: The Effects Of Desflurane And Sevoflurane On Nesfatin1 Levels In Laparoscopic Cholecystectomy

Authors:
Ayça Tuba Dumanlı Özcan (draycaozcan@gmail.com)
Cemile Altın Balcı (drcemilebalci@gmail.com)
Serpil Erdoğan (drserpilerdogan@gmail.com)
Merve Ergin (drmerceergin@gmail.com)
Ali Çiftçi (draliciftci@gmail.com)
Halil Kara (drhalilikara@gmail.com)
Şemsi Aksoy (drmaksoy@gmail.com)
Abdulkadir But (akadirbut@gmail.com)

Version: 2 Date: 07 Oct 2017

Reviewer reports:

Martin Schlaepfer (Reviewer 1):

Major comments:

General comments:

Introduction: The authors give some background about nesfatin-1: they explain, that it was discovered in 2006 and explain some of its pleiotropic effects. I would appreciate to learn the reason, why they study nesfatin-1 in the context of laparoscopic cholecystectomy, what might be the impact for patients when they have altered nesfatin-levels (after laparoscopic cholecystectomy) and why they think, the protein levels might be influenced by the type of surgery investigated and by the type of anesthetic (sevoflurane and desflurane).

Although stress response in abdominal surgery was investigated in the past and inhalation anesthetics were found to reduce the stress response, nesfatin has never been measured as a neuroendocrine marker. Hence the authors wanted to explore a possible correlation between the nesfatin levels and the surgery stress response. The authors were in a good place to conduct this
study as laparoscopic cholecystectomy is an abdominal surgery that is frequently performed in their clinic.

Methods: As stated above: the whole manuscript has to be adapted (abstract, results and discussion): you cannot talk about higher nesfatin-levels, when your statistical test proved otherwise. You may include in the discussion, that there might have been a significant difference in case your study had had more power.

It is corrected

Discussion: Like in the introduction section, the authors provide many of nesfatin's (discussed) effects, but they don't put these effects into the context of their study. This is urgently recommended.

It is corrected.

Specific comments:

p4l40: you cannot talk about higher levels when the difference is not significant! It is corrected.

p9l58 and ff: Your statistical test does not allow this sentence, it should instead say: "Post-operative nesfatin levels in both groups were not significantly increased compared to preoperative levels". It is corrected.

p10, figure 1: Please provide a figure legend explaining, what the figure shows us (box plots, what percentiles, what are the error bars etc.). We explained it.

p10l42: postoperative levels were not "higher" according to your statistical test. You may discuss, that there might be a trend in case your study had more power. It is corrected.

Minor comments:

p4l11: background not background. It is corrected.

p4L26: "Patients were divided into two groups randomly" change to: "Patients were randomized into two groups" It is corrected.

p6l16: The sentence about the randomization is rather difficult to understand. You might facilitate the sentence by writing: "Prior to anesthesia induction, patients were randomly assigned to two groups using a sealed envelope system." It is corrected.

p6l23: "monitored" not "monitorized" It is corrected.

P6l23: "a 20 gauge catheter" instead of "granule" It is corrected.
p6l45: if patients have been assigned to the group prior to anesthesia induction you have to adapt this sentence. E.g. "For anesthesia maintenance, the patients received 6% desflurane or 2% sevoflurane in 40% O2 and 60% air, according their randomization." It is corrected.

p6l60: The infusion rate was reduced in case of hypotension? Please clarify. It is corrected.

p7l0: I take, you injected "metoclopramide" - please correct.

It is corrected.

p7l1: intubation not entubation. It is corrected.

p10l45-53: please provide references for these statements. we provided with references.

p10l55-62: please provide references. we revised references.

Gaetano Scaramuzzo (Reviewer 2):

The manuscript "The effects of Desflurane and Sevoflurane on Nesfatin-1 levels in Laparoscopic Cholecystectomy" explores the effect of two hypnotic agents on plasmatic level of Nesfatin-1 in patients undergoing laparoscopic cholecystectomy.

The authors evaluated the plasmatic level of nesfatin-1 before and after surgery in 40 patients and found no statistically significant difference (before - after surgery) in both anesthetic drug groups and no difference between the two drug groups.

Although the paper contains original and interesting scientific data, some major revisions are needed.

(Since page numbers are missing, the comments refers to the page number from the first page of the manuscript)

1. Methods

o Page4, Line 50: "patients in the second group received 2% of sevoflurane"; please specify also the O₂ and the air fractions delivered.

It is corrected.

o Please clarify the ventilation during surgery (e.g. provide some information about the PEEP level used during surgery).

It is explained in the method.
10 mg of ephedrine when MAP was <50, and the infusion dose was lowered. Can the authors explain which drug infusion was reduced? Was the sevoflurane/desflurane dosage lowered in case of haemodynamic instability?

It is explained in the method.

The authors calculated a sample size of 42 patients but they state in the methods to have enrolled in the study 40 patients. In Table 1, the total number of patients enrolled is 42. Please revise this point.

It is corrected.

2. Results

There is no reference in the manuscript about how the authors defined "Other comorbid diseases".

It is explained which diseases were they.

"There were no significant differences in pre-intubation, post-intubation, intraop15, intraop30, and post-extubation SAP (p=0.498), DAP (p=0.399), MAP (p=0.279), and heart rate (p=0.501) between the groups". Please provide a better explanation of the data acquisition timing in the materials and methods section. Moreover, can the authors explain why they acquired SpO₂ and EtCO₂ data but no information are provided in the results section?

We made new table for this data.

Table 2: please add units of measurement to the table.

It is corrected.

The authors found no difference in nesfatin-1 increase between the diabetic and non-diabetic population. Algul S. et al.[1] recently found differences in plasmatic levels of Nesfatin-1 between diabetic and non diabetic patients. Can the author provide data about the baseline level in the two groups?

There was no statistically significant difference between pre- and post-op nesfatin levels in diabetic patients (n = 7) and non-diabetic patients (n = 35) (p = 0.303 and p = 0.370). nesfatin levels in postoperative compare to prep have increased in statistically similar manner in diabetic patients and nondiabetic patients (p=0.974).

3. Discussion

"Nesfatin is considered an important determinant of postoperative ileus and discharge". Can the authors add a reference to this point? Is there any clinical evidence of this?
Did the author evaluate the relation between the postoperative level of Nesfatin-1 and the duration of postoperative ileum?

It is added.

o Page 10, Line 33: "stress limited to 30 min increased nesfatin-1 secretion". Please check the reference (Nesfatin-1 production or secretion?).

It is corrected.

o Page 11, Line 16: "The results of studies analyzing stress response to surgery have revealed elevated postoperative nesfatin-1 levels, and reduced bowel motility". Please provide a valid reference for this statement. Did the authors find any correlation between the duration of surgery and the postoperative levels of Nesfatin-1?

More over no correlation has been observed between nesfatin levels and operation time. as seen in table 4 which lists correlation coefficients:r (blue print) and p (red print). The file is attached now.

o Page 11, Line 19-38: the authors state that nesfatin-1 levels increase after surgery, but in the results section there is still no significant variation of its levels before and after surgery. Please review the sentence in accordance to your findings.

It is corrected.

4. Conclusion

o Page 11, Line 36-38: the authors state that nesfatin-1 levels increase after surgery but in the results section there is still no significant variation of its levels before and after surgery. Please review the sentence and the conclusion in accordance to your findings.

It is corrected.

MINOR COMMENTS

- English grammar revision is needed for some parts of the manuscript (e.g. "entubation", page 2; "backgraund", page 2 and 3; "desfluran" and "sevofluran", figure 1) It is corrected.

- Page 2: "mean systolic and diastolic arterial pressures": did the author evaluate the average systolic pressure or the mean and the systolic pressure (comma needed)? It is corrected.

- Page 3: at the end of the abstract the sentence "peripheral nefatin-levels" can be confusing. "Plasmatic levels of nesfatin-1" can be an option of revision. It is corrected.
- Supplemental material is partially not in English language. Please provide an English translation for a further examination. It is corrected.

- In the "Ethics approval and consent to participate" section the authors refer to the study as a "retrospective" study. The study can be considered, actually, an interventional (prospective) study.

It is corrected.