Author’s response to reviews

Title: Systemic reaction to and interference with urine protein measurements after intravenous fluorescein injection

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Author’s response to reviews:

BOPH-D-19-00200 Response to editor and reviewer

Editor Comments:

Dear dr. Tian,

In this letter we will answer the comments you made. We feel that the paper considerably improved.

1. The manuscript is fairly well written, but could benefit from a native English speaker providing some minor suggestions for syntax, grammar and flow.

AU: The manuscript is edited by the American Journal Experts. All changes to the manuscript are indicated in the text by using track changes. If it is possible we will attach the American Journal Experts certificate.
2. Upon resubmission, please make sure that your manuscript contains the following seven sections under the heading 'Declarations' at the end of the main text:

   AU: We made sure the manuscript contains all seven sections under the heading Declaration.

3. Please include a point-by-point response to the comments, describing any additional experiments that were carried out. Please also ensure that all changes to the manuscript are indicated in the text by highlighting or using track changes.

   AU: We included this point-by-point response to the comments. All changes to the manuscript are indicated in the text by using track changes.

Michael A. Klufas (Reviewer 1):

Dear Dr. Klufas,

We thank you for carefully reading our manuscript. In this letter we will answer the comments you made. We feel that the paper considerably improved.

1. Title - would change to "Systemic reaction and interference with urine protein measurement after intravenous fluorescein injection"

   AU: We changed the title to "Systemic reaction to and interference with urine protein measurements after intravenous fluorescein injection" (line 1)

2. Abstract - case presentation - should be "peripapillary" rather than "parapapillary"

   AU: We changed parapapillary to peripapillary. (line 65)

3. Anaphylaxis is a known complication of fluorescein injection but I agree should have appropriate supportive measures including oxygen and EpiPen available in case of anaphylaxis to prevent morbidity/mortality from this test

   AU: We agree that appropriate supportive measure including oxygen and EpiPen should be available in case of anaphylaxis. We added this statement. (line 74-76)
4. Key words: would include 'urinalysis'
AU: We added urinalysis as a key word. (line 90)

Background
5. Line 4 - can consider 'vasculature' rather than 'vessels'
AU: We changed vessels to vasculature. (line 96)

6. Line 5 - can remove 'subretinal'
AU: We removed subretinal. (line 97)

7. Line 8-9 - should include the incidence of the different side effects, i.e. nausea and vomiting are much more common than anaphylaxis
AU: We included the incidences of the side effects. (line 100, 101, 103-105)

Case description
8. Line 16 should be 'peripapillary neovascularization'
AU: We changed parapapillary neovascularisation to peripapillary neovascularization (line 111)

9. I would include if there was evidence of retinal hemorrhage or exudation on SD-OCT for this case - if either of those were present then the FA was likely not necessary but not unreasonable to perform.
AU: we added a clarification: Ophthalmic examination showed a suspected lesion and bleeding near the optic disc, and the SD-OCT of the macula showed a macula pucker. (line 112-113)

10. Likewise authors should state the dose/volume of fluorescein dye that was injected in this case
AU: We described the dose and volume of fluorescein dye that was injected in this case. (line 119)

11. Should also state that epinephrine was or was not administered given anaphyaxis that seemed to improve with oxygen and intravenous fluids
AU: We added the statement that epinephrine was not administered. (line 134-135)

Discussion

12. Lines 8-13, I would include the preferred treatment for anaphylaxis after fluorescein injection - in this case, intravenous fluids and oxygen were sufficient, but many times subcutaneous or intramuscular epinephrine is needed. In the USA, EpiPen is mandatory in clinics where fluorescein angiography is performed
AU: We added a short description of the treatment of an anaphylactic reaction. (line 159-166)

13. Final concluding paragraphs, authors should state that patients should be properly consented to understand the risks of fluorescein angiography, the clinical need for this test and the potential treatments are available in the clinic in the cases of adverse reactions.
AU: We fully agree with your comment. We adjusted these considerations. (line 216-218)