Author's response to reviews

Title: Intraprostatic injection of botulinum toxin type-A relieves bladder outlet obstruction and induces prostate apoptosis

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Author's response to reviews: see over
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Manuscript #: MS: 1772383999881211 -

Manuscript Title: Intraprostatic injection of botulinum toxin type-A relieves bladder outlet obstruction and induces prostate apoptosis

Dear Editor Team:

Thank you for the positive review and please find enclosed our revised review article entitled “Intraprostatic injection of botulinum toxin type-A relieves bladder outlet obstruction and induces prostate apoptosis” (MS: 1772383999881211). We appreciate the helpful comments of the reviewers, we have made all the recommended changes. The following are our responses (point to point) to the comments of reviewers.

Reviewer: HC Kuo
Q1: In dog model, the authors used 100 units for prostate injection; the dose was much greater than used in human model.

A1: We appreciate the reviewer’s comments and discussed this issue as “in the canine model, we used BTX-A 100 U for prostate injection, which dose might be about 2 times of the dose used in human (100 U for 15 kg in canine/200 U for 60 kg in human). However, the component of human prostate is different from the canine prostate. Species differences might have different responses to BTX-A treatment [23], therefore, the selected dose of BTX-A 100 U for the canine model cannot be completely interpreted to the human dose.” In the revised manuscript page 10, line 18, to page 11, line 4.

Q2: Did the authors estimate the prostate volume before BTX injection?

A2: As reviewer pointed out, we have addressed this issue as “the average prostate volume was not significantly changed after saline or BTX-A injection (from 11.8±0.9 cc to 12.5±1.1cc and 11.0±0.5cc to 10.1±0.4cc, respectively).” in the revised manuscript page 8, line 4 to 6.

Reviewer: Giuseppe Brisinda
Q1: The title is not appropriate. The authors have been documented that intraprostatic
injection of Botulinum toxin type A induces prostate apoptosis only in dogs.

A1: It is hard to get enough prostate tissue from human for analysis. Therefore, we used the canine model to see the immunohistological change after BTX-A injection. The title is accurate and the other two reviewers did not object.

Q2: The bibliography could be more complete;

A2: As reviewer pointed out, we have added 3 references (reference 13, 14, and 23) in the revised manuscript to make references more complete.

Q3: The follow up is not long enough.

A3: We will continue follow up of these patients for further report.

Q4: The authors indicate that the patients have been treated with antibiotics and with sedation. They should indicate the drugs and the doses used.

A4: We appreciate the reviewer’s comments and discussed this issue as “all patients received perioperative antibiotics with cefazolin 1 g (i.v.) and intravenous sedation with propofol 50 mg in the lithotomy position.” in the revised manuscript page 6, line 10 to 11.

Q5: The toxin has been diluted with a volume of 4 ml of saline. This volume is double than that commonly used. The reason for this choice should be explained.

A5: We used the volume according to our previous study (Ref 13). We address this issue as “as previous study described, each lobe of the prostate received 100 U of BTX-A (Botox®, Allergan) dissolved in 4 ml of normal saline in the revised manuscript page 6, line 12 to 13.

Q6: The QOL index is reported without mentioning an appropriate reference.

A6: As reviewer pointed out, we have added a reference (Ref 19). We have addressed the meaning of QOL scale as “quality of life indices (QOL, 0-6, indicating increasing severity of symptoms and low quality of life)” in the revised manuscript page 7, line 3 to 4.

Reviewer: Clare Fowler

Q1: I suspect references to published work in this area is incomplete.
A1: As reviewer pointed out, we have added 3 references (reference 13, 14, and 23) in the revised manuscript to make references more complete.

Q2: In my view it should be stated that the criteria in Taiwan are for the use of human subjects and animals in research studies of unlicensed treatments.

A2: We should get the approval of institutional review board for human and animal study. We have addressed this issue as “the animal study was conducted at veterinary hospital, National Pingtung University, with the approval of the institutional review board.” in the revised manuscript page 5, line 3 to 4 and “the study was approved by the institutional review board of Chang Gung Memorial Hospital Kaohsiung and informed consent was obtained.” in the revised manuscript page 6, line 3 to 5.

Thank you once again for the positive review and helpful comments. We hope the revised manuscript is now acceptable for publication in the BMC Urology.

Sincerely,

Michael Chancellor, MD
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