

Format for ANSWERING REVIEWERS



September 17, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: manuscript NO 4784.doc).

Title: Effect of low-dose amitriptyline on globus pharyngeus and its side-effects

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4784

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated, the paper has been extensive editing with respect to the English language.

2 Revision has been made according to the suggestions of the reviewer

(1) Old figure 2 has been divided into figure 2-5, so more clearly explain the variation of the side effects.

(2) In table 3, those abbreviations have been clarified used in the figure.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Dear Editor:

I greatly appreciate the editorial comments by NO. 00028580 peer review referring to our recent manuscript (NO.4784) in Express Submission and Peer-review System. (Title: Effect of low-dose amitriptyline on globus pharyngeus and its side-effects). In view of the originality in the clinical field at home and abroad, we hope to publish the article more quickly.

I would like to respond a few questions concerned by peer review.

Answers are as follows:

Question2: Patients presented to gastroenterology units in the Guangzhou First People's Hospital, Guangzhou Nansha Central Hospital were recruited according to the Rome III criteria for Functional Esophageal Disorders consecutively between September 2011 and January 2013.

Question 3: Enrolled patients have not received empiric PPI therapy before the 2-months exclusionary

period. (A few patients had received PPI therapy a short time, but not standardized).

Question 4: Trained doctors assessed baseline of anxiety or depression of patients by standard anxiety and depression scale (HAMA-14, HAMD-17).

Question 5: In fact, this study (article NO.4784) is a part of our registered clinical trial "Epidemiology survey and the effects of low-dose Amitriptyline on Intractable Functional Dyspepsia: A prospective, randomized, controlled study" (Clinical trial registration number: ChiCTR-TRC-12001968), so we want to use the Clinical trial registration number (ChiCTR-TRC-12001968) in this article.

Question 7: Although the primary end-points were set after one month treatment, uncomfortable symptoms of most patients had disappeared within four weeks. With the improvement of symptoms, GETS scores and SF-36 scores also continued to improve.

I also greatly appreciate the editorial comments by NO._02456835 peer review referring to our recent manuscript in Express Submission and Peer-review System. I would like to respond a few questions concerns by peer review.

Answers are as follows:

Question1: Although clinical evidence is insufficient, PPI usually be used to empirical treatment in globus pharyngeus. In the process of our research, the effects of low-dose Amitriptyline on functional gastrointestinal disorders, we found that low-dose amitriptyline has a positive effect on globus pharyngeus. Therefore, we design the randomized controlled trial to compare the efficacy and side effects of low-dose amitriptyline (AMT) with proton pump inhibitor (PPI) treatment in patients with globus pharyngeus.

Question2: Based on Rome III criteria about newly diagnosed functional esophageal disorders, we chose the patients who absence of obvious evidence of acid reflux. These patients who have obvious heartburn, acid reflux symptoms and evidence of GERD under endoscopic were excluded. We did not have a 24-hour esophageal PH monitoring and PPI diagnostic treatment to rule out possible hidden acid reflux.

Question3: Only a patients younger than 18 years old (17 years old male patient), use of conventional treatment that PPI therapy. As for the efficacy and tolerability of low-dose amitriptyline on pediatric patients will be our research direction in the future.

Question4: In recent years, a lot of literature reported low-dose amitriptyline treatment in patients with functional gastrointestinal disorders. Our research group also found that low-dose amitriptyline has a

positive effect on intractable functional gastrointestinal disorders and functional abdominal pain.

Sincerely yours,

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