

## **Responses to Reviewer #1**

### **Q1. What is ED95 in pharmacology?**

Response: Thank you for your valuable suggestions. We are very sorry for this misunderstanding. We have revised ED95 as the minimal effective dose of intranasal SUF when combined with intranasal DEX for moderate sedation of EUS in at least 95% of patients (ED95) in our manuscript revised manuscript (page 2, line 11-13).

### **Q2: Do you have a reference for this dose of intra nasal dexmedetomidine (1 µg/kg)?**

Response: Thanks for your thoughtful review. The reference for 1 µg/kg DEX has been showed in the discussion section. (page 9, line 2-8, Reference 15 and 19).

### **Q3. Do you have a reference for the time interval of 25 minute?**

Response: Thanks for your careful review. The reference for 25 minute interval has been showed in the discussion section. (page 9, line 23-26, Reference 1).

### **Q4. Mention the volume of each medication, especially in different doses of fentanyl.**

Response: Thanks for your careful review. The total volume of SUF and DEX in our study is less than 1 mL. Dexmedetomidine is undiluted parenteral solution, 100 µg/ml and there is no patient exceeding 100 kg, therefore the average volume of dexmedetomidine is no more than 1 mL. Sufentanil is undiluted parenteral solution, 50 µg/ml and there is no patient exceeding 100 kg, therefore the average volume of SUF is no more than 0.6 mL. Moreover, there was a 25 minute interval between administration of intranasal DEX and SUF. Therefore, there is adequate period for nasal membrane to absorb DEX before SUF administered.

**Q5. Do you have a reference for the time interval of forty-five minute?**

Response: Thanks for your careful review. The reference for forty-five minutes has been showed in discussion part (page 9, line 23-25, Reference 15).

**Q6. In table 5, where are other SUF doses??**

Response: Thanks for your careful review. Due to the high rate of successful sedation with the 0.3 µg/kg SUF dose, the CRM never recommended higher doses. Thus, the 0.4 and 0.5 µg/kg SUF doses were never tested (page 7, line 24-27).

**Q7. The first four paragraphs of the discussion section are not needed.**

Response: Thank you for your valuable suggestions. We have deleted these paragraphs accordingly.

**Q8. The average volume of dexmedetomidine in the present study??**

Response: Thanks for your careful review. The average volume of dexmedetomidine in our study is less than 1 mL. Dexmedetomidine is undiluted parenteral solution, 100 µg/ml and there is no patient exceeding 100 kg, therefore the average volume of dexmedetomidine is no more than 1 mL.

## **Responses to Reviewer #2**

**Q1: In the Aims of ABSTRACT, the abbreviation of endoscopic ultrasonography (EUS) must be defined upon first appearance in the Abstract.**

Response: Thanks for your careful review. We have revised in our manuscript in the ABSTRACT section (page 2, line 13).

**Q2. In the Results of ABSTRACT section, the 95% credibility interval was wrong, it should be presented as 95% confidence interval.**

Response: Thanks for your careful review. We have revised in our manuscript in the ABSTRACT section (page 2, line 26).

**Q3. In the 2.1. Study population of METHODS section, heart rate (HR) < 50 bpm is abbreviated name, it needs to be presented as complete spelling.**

Response: Thanks for your careful review. We have revised in our manuscript In METHODS section (page 4, line 28-29).

**Q4. In the 2.2. Performance of sedation of METHODS section, the noninvasive blood pressure can be presented as BP.**

Response: Response: Thanks for your careful review. We have revised in our manuscript In METHODS section (page 4, line 29-30).

**Q5. In the 2.6. Statistical analysis of METHODS section, mean (sd) are abbreviated name, it needs to be presented as complete spelling.**

Response: Thanks for your valuable suggestions. We have revised as mean (standard deviation, SD) (page 7, line 10).

**Q6. In In the 2.6. Statistical analysis of METHODS section, appropriate statistical analysis should be performed. Statistical tables and figures should be checked and followed statistical norms.**

Response: Thank you for your valuable suggestions. The statistical analysis has been checked by Dr. Na Zeng from the Department of Methodology Platform, Institute of Clinical Medicine, Beijing Friendship Hospital. All the Statistical tables and figures are checked and followed statistical norms.

### **Responses to Reviewer #3**

**Q: The authors determined the ED95 of intranasal sufentanyl along with intranasal DEX for EUS under sedation. This study and sedation preparation took 45 minutes (25 minutes for DEX and then 20 min for**

**sufentanyl action) before the EUS can be started. The average EUS time was less than 30 minutes. This can limit the role of combining the intranasal DEX and SUF for a procedure of short duration especially in a high volume centre because it can waste the endoscopy suit time and increase the procedure cost unless the preparation is done in a separate induction room (with full monitoring) and save the endoscopy suit time. This should be mention in limitation.**

Response: Thank you for your thoughtful advice. It was added in the DISCUSSION section according to your suggestions in our revised manuscript (page 11 line 10-15).

We tried our best to improve the manuscript and made some changes in the manuscript. We appreciate your work sincerely and hope that our revisions will be qualified for the journal.

We look forward to hearing from you soon and would be glad to respond to any further questions and comments.

Best Regards,

Xing Tao

Department of Anesthesiology, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China