

Peer Review File

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Reviewer A

It is an interesting clinical trial to investigate the efficacy and safety of Sanfeng Tongqiao Diwan in the therapy of UACS. It is a randomized, double-blind, placebo-controlled clinical trial, so the results are quite reliable. The authors found Sanfeng Tongqiao Diwan improved the symptoms and the quality of life of patients with UACS and showed acceptable safety. There are some points need to be clarified.

Comment 1: Since it is a clinical trial, the authors should list the inclusion criteria, exclusion criteria and elimination criteria.

Reply 1: Thank you for the comment. We supplemented and improved the content of inclusion criteria, exclusion criteria and elimination criteria in the Method section.

Changes in the text: Page 5 line 21-33 (Inclusion criteria); Page 5 line 34, page 6 line 1-9 (Exclusion criteria); Page 6 line 10-12 (Elimination criteria).

Comment 2: For diagnosis of UACS, CVA, EB need to be excluded. Although they excluded those COPD and other common causes of chronic cough, they did not mention how to exclude in the research.

Reply 2: Thank you for the comment. We have added more details about the criteria for diagnosis of UACS, including (IV) normal spirometry without airway hyper-responsiveness, (V) normal eosinophil percentage in induced sputum. These criteria ensured that CVA, EB was excluded.

Changes in the text: Page 5 line 31-33.

Comment 3: Since it is a clinical trial, did the authors perform registration on website of Chinese clinical trial registry?

Reply 3: Yes, this clinical trial has been registered with the Chinese Clinical Trial Registry (No. ChiCTR-2300069302).

Shown in the text: Page 3 line 9-10.

Reviewer B

1.First, the abstract is inadequate and needs revisions. The background did not explain why Sanfeng Tongqiao Diwan is effective and safe and what the knowledge gap is in relation to its efficacy and safety. The methods need to describe the inclusion criteria, randomization method, and follow up methods. The results need to describe the clinical characteristics of the two groups, the effectiveness rate of the placebo group, measurement values of all outcomes of the

two groups, and accurate P values. The conclusion needs comments for the clinical implications of the findings.

Responses

We have modified our text as advised of the background (see Page 2, line 49-54), of the methods (see Page 2, line 55-66), of the results (see Page 2, line 67-83), and of the conclusion (see Page 3, line 84-88).

2.Second, the introduction of the main text need to describe the development of Sanfeng Tongqiao Diwan, its pharmacological mechanisms, and explain why it is potentially safe and effective for UACS, as well the knowledge gap for its efficacy and safety data. The authors need to have comments on its strengths relative to western medicines.

Responses

In Western medicine, anti-inflammatory and anti-allergy drugs are the basic therapeutic approaches for UACS, while the clinical symptoms still recurrently occur and there are certain side effects in long-term use. Sanfeng Tongqiao Diwan contains *Scutellaria baicalensis* (Huang qin), *Schizonepeta tenuifolia* (Jing jie), *Asarum sieboldii* (Xi xin), and *Notopterygium incisum* (Qiang huo). Thanks to their effects of clearing heat and dispelling wind, dispelling cold and opening orifices, some research indicates that it can alleviate acute, recurrent, and chronic rhinitis in adults and no drug-related adverse responses was observed (see Page 4, line 112-117). We did a systematic review of PubMed and Wanfang Database up to Sep, 2022, with search terms related to UACS, traditional Chinese medicine (TCM), clinical trial and Sanfeng Tongqiao Diwan, but no published study can be search. Therefore, the use of TCM to treat UACS has a broad prospect.

3.Third, in the methodology of the main text, the authors must explain why placebo in the control group is acceptable in the ethics approval since this may be harmful for the health of patients in the control group. The authors should use effective western medicines in the control group. Please describe the sample size estimation and details of the follow up of the patients. In statistics, please describe the handling of missing data and the statistical analyses in both the PP and ITT subsets. The authors need to describe the test of normality of continuous variables and the statistical comparisons of such variables between the two groups. Since there were only two groups, ANOVA is incorrect. Please ensure $P < 0.05$ is two-sided.

Responses

We add the sentences “ the placebo group...are added” (see Page 4, line 133-136), “which is... successful blinding” (see Page 4, line 138-141) in the section of methodology.

In the section of statistical analysis, we add the sample size estimation, the definition of FAS, PP and SS data set, and imputation strategy of missing values (see Page 7-8, line 230-240).

We have modified our text as advised of the details of the follow up of the patients (see Page 5/Line 149-165) and Figure 1 (see Page 14, line 434).

We also have modified our text as advised of the statistical analyses (see Page 8, line 241-251).

Reviewer C

1. **CONSORT Checklist** needs to be re-checked and updated, please make the following revisions both to your manuscript and CONSORT checklist accordingly:

Item 17b, this item is only for binary outcome. Outcomes that are not binary are not required to be reported in this item. Please check.

17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended

P8/L258;P17/L457-458

Results/2, Table2

Reply 2: Thank you for raising this question. We have modified the CONSORT checklist accordingly.

2. Abstract should be within 200-350 words. Please shorten your Abstract.

Reply 2: Thank you for the comment. The abstract has been modified to around 340 words.

Change in the text: Page 2 line 62, line 70-71; Page 3 line 76-77.

3. Please provide **editable** version of Figure 1 in Word/PPT format since it's a flow diagram.

Reply 3: Figure 1 in Word format has been included in the attached file.