

Peer Review File

Article information: <u>http://dx.doi.org/10.21037/tcr-20-3400</u>

<mark>Reviewer A</mark>

Introduction: it is misspelled with loose information. Please rewrite in order to link the information and make the text clear.

Methods: the objective must be to state that it is the development of a study protocol; put pictures of the placebo needle; place a photo of the acupuncture points used (anatomical location); It was not clear whether the electroacupuncture device will be used in the control group; the information in the Primary results item is loose and not linked; Line 231: describe the acronym ITT in full and put the acronym in parentheses; The methodology should be summarized, leaving the essential information clear and concise.

Discussion: Tell us more about the expected results based on literature. This is the most important part of your study. Write more.

Your study needs to be better explained so that it can be replicated by the reader. Replace figure 2 with an English figure.

Comment 1: it is misspelled with loose information Reply 1: We revised the missing words Changes in the text: Line 68

Comment 2: the objective must be to state that it is the development of a study protocol Reply 2: We have supplemented according to the reviewer's comments. Changes in the text: Line 97-98

Comment 3: put pictures of the placebo needle; place a photo of the acupuncture points used (anatomical location)

Reply 3: Thanks to the reviewers, we have made modified. Changes in the text: We added two figures.

Comment 4: It was not clear whether the electroacupuncture device will be used in the control group

Reply 4: The patients in the control group were still connected to the electroacupuncture device and used the same parameters, but because the needle did not pierce the skin, the patients will not induce De Qi. We have modified the manuscript to make the description clearer.

Changes in the text: Line 222-225

Comment 5: the information in the Primary results item is loose and not linked Reply 5: We modified manuscript and Table to make the description clearer. Changes in the text: Line240-241; Table1-2.0





Comment 6: Line 231: describe the acronym ITT in full and put the acronym in parentheses Reply 6: Thanks to the reviewers, we have made modified. Changes in the text: Line 269

Comment 7: The methodology should be summarized, leaving the essential information clear and concise Reply 7: Thanks to the reviewers, we have made modified. Changes in the text: Line306-309

Comment 8: Discussion: Tell us more about the expected results based on literature. This is the most important part of your study. Write more. Reply 8: Thanks to the reviewers, we have made modified. Changes in the text: Line336-339

Comment 9: Replace figure 2 with an English figure. Reply 9: Thanks to the reviewers, we have made modified. Changes in the text: Fig2

<mark>Reviewer B</mark>

This manuscript is well written and has a carefully designed protocol.

Some suggestions:

1- "SAE" (page 7, line 154) means "serious adverse event"? I suggest specifying the meaning of the acronyms.

2- Recent regards have proposed standards for reporting electronic parameters in electroacupuncture experiments, in order to enable reliable replication. If a more detailed description of the electrical stimulus is not possible, at least for how long the electrical stimulation will be performed and the total duration of the session should be reported.

3- It would be interesting to clarify the reason for choosing the acupuncture points that will be used. If the indication was based on TCM, or on segmental innervation, or on some previously published scientific work or on the potential secretion of some neurotransmitter or hormone that could be useful in the treatment of diarrhea, such as somatostatin, for example.

4- It would also be valuable to support the choice of electrical frequency (reason for choosing 10 Hz) and type of current (reason for choosing continuous stimulus). Regarding the continuous stimulus, consider the potential risk of the axons 'accommodation' effect, which can reduce nervous excitability and the expected effect.

Pertinent readings suggested:

1. Noguchi E. Mechanism of reflex regulation of the gastroduodenal function by acupuncture. Evid Based Complement Alternat Med. 2008 Sep; 5(3):251-6. doi: 10.1093/ecam/nem077. PMID: 18830456; PMCID: PMC2529392



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2. Li H, He T, Xu Q, Li Z, Liu Y, Li F. Acupuncture and regulation of gastrointestinal function. World Journal of Gastroenterology. 2015 Jul; 21(27):8304-8313. doi: 10.3748/wjg.v21.i27.8304

3. Hubacher J, Niemtzow RC, Corradino MD, Dunn JCY, and Ha DH. Standards for Reporting Electroacupuncture Parameters. Medical Acupuncture. 2016 Oct; 249-55. doi: 10.1089/acu.2016.1201

Comment 1: 1- "SAE" (page 7, line 154) means "serious adverse event"? I suggest specifying the meaning of the acronyms.

Reply 1: Thanks to the reviewers, we have made modified. Changes in the text: Line186

Comment 2: 2- Recent regards have proposed standards for reporting electronic parameters in electroacupuncture experiments, in order to enable reliable replication. If a more detailed description of the electrical stimulus is not possible, at least for how long the electrical stimulation will be performed and the total duration of the session should be reported.

Reply 2: Thanks to the reviewers, we have made modified. Changes in the text: Line209-215

Comment 3: 3- It would be interesting to clarify the reason for choosing the acupuncture points that will be used. If the indication was based on TCM, or on segmental innervation, or on some previously published scientific work or on the potential secretion of some neurotransmitter or hormone that could be useful in the treatment of diarrhea, such as somatostatin, for example.

Reply 3: Thanks to the reviewers, we have made modified. Changes in the text: Line202-203

Comment 4: 4- It would also be valuable to support the choice of electrical frequency (reason for choosing 10 Hz) and type of current (reason for choosing continuous stimulus). Regarding the continuous stimulus, consider the potential risk of the axons 'accommodation' effect, which can reduce nervous excitability and the expected effect. Reply4: Thanks to the reviewers. This suggestion is very precise, and it is also the direction which our research team expects to carry out in the next step. As the reviewer said, acupuncture can relieve diarrhea through multiple mechanisms, but there are few studies on acupuncture relieve CID, our research focus on evaluate the effectiveness and safety of acupuncture in alleviating CID, the relationship between needle parameters and efficacy will be the next research object. Changes in the text: None

