Author’s response to reviews

Title: Transcutaneous Neuromodulation improved inflammation and sympathovagal ratio in Patients with Primary Biliary Cholangitis and Inadequate Response to Ursodeoxycholic Acid—A Pilot Study

Authors:

Hui Yang (602474759@qq.com)
Hang Yang (15841123892@163.com)
Lixia Wang (wenwensl@yeah.net)
Honggang Shi (1666520879@qq.com)
Bojia Liu (715493908@qq.com)
Xue Lin (1987577265@qq.com)
Qingyong Chang (qychang0409@163.com)
Jiande Chen (jiandedzchen@gmail.com)
Zhijun Duan (cathydoctor@sina.com)

Version: 2 Date: 14 May 2020

Author’s response to reviews:

Dear Editor,
It is a great honor to have the chance of the second time of revision and publication. And thanks for the work and valuable comments from every professor very much.

Review 2 Comments:
Thanks for your kind and careful reviewing and valuable comments which help us a lot.
1. See comments on pdf.
   (1) The random was replaced by allocation.
   (2) Dafuxingyejingsheng science and technology limited company, Beijing, China was added after the gel.
   (3) the “y” was added.
2. However figure 3 and 4 are still difficult to understand. The authors need to explain how to interpret these figures. The colour shows and increase or decrease. But what is changing in the control and pretreatment participants? This needs to be addressed by the authors in the manuscript. It should be explained in the figure legend.
We have tried to explain the heatmap as below.
(1) Figure 3 Modulation of Plasma Bile Acid Metabolism

a is the comparison of plasma BAs in the PBC (pretreatment) to the control group. After statistical analysis, TCDCA, TUDCA, UDCA, GCA, GDCA, GCDCA and TCA were significantly higher in the PBC patients (pretreatment) than the controls, and the color bars responsible for the BAs in PBC group were seen deeper visually. b and c are the comparison of plasma BAs in the PBC group before and after TN and sham-TN with control group, respectively. After TN combined with UDCA, bile acids had no significant change. The color bars were look similar. It indicated no obvious changes in the metabolism of serum bile acids after TN combined with UDCA visually.

(2) Figure 4 Modulation of Fecal Bile Acid Metabolism

a is the comparison of fecal BAs in the PBC (pretreatment) to the control group; b is the comparison of fecal BAs in the PBC group before and after TN and the control group; c is the comparison of fecal BAs in the PBC group before and after sham-TN and the control group. After statistical analysis, there were no significant changes in fecal BAs. The color bars in three heatmap were also look similar. It indicated no obvious changes in the metabolism of fecal bile acids after TN combined with UDCA visually.

3. In response to a question from reviewer 1, the authors have described the method of allocating treatment. The method of allocating patients to TN or sham TN is not random. The patients were alternately assigned to each treatment. Thus the researchers working with the data can tell what treatment was given and this can affect analysis. This allocation method cannot be called random. Please remove the statement that it is random and just leave the description of allocation. In future studies the authors should use a random method to mix up allocation. This should also be added to limitations. It is blind to the patients. However, our doctors knew the order and which treatment patients after the first recruited one would by applied. So, we agree with the reviewer 2. And a limitation was added at the end of the discussion as below.

In addition, on the aspect of allocation method, although it is blind to patients recruited to the trial with time, our physicians responsible for the trial knew the order before recruiting the second case. In the future study, a random method is also needed.