Author's response to reviews

Title: A protocol of histone modification-based mechanistic study of acupuncture in patients with stable angina pectoris

Authors:

Ning Wang (39725409@qq.com)
Sheng-Feng Lu (crazywind@vip.qq.com)
Hui Chen (1078137043@qq.com)
Jian-Fei Wang (353980182@qq.com)
Shu-Ping Fu (53894289@qq.com)
Chen-jun Hu (hucjhyl@126.com)
Yi Yang (657172145@qq.com)
Fan-rong Liang (0001170@cdutcm.edu.cn)
Bing-Mei Zhu (zhubm64@hotmail.com)

Version: 4 Date: 7 April 2015

Author's response to reviews: see over
Dear Tom:

Thank you so much for giving us one more chance to correct our mistake. Based on your last email, we are now re-uploading our manuscript numbered as 8544528181364039 to BMC Complementary and Alternative Medicine website. The following is the full explanation we have sent to you last time by email.

After reviewing your previous comments, we believe that we have made a mistake in our manuscript, which has led you misunderstand our true intentions. We erred in copying our answer from the cover letter and pasting directly into the updated manuscript, without correcting the word “pilot” to “prospective”. Our study is a full trial but not a “pilot study” because of the following reasons:

1. Our animal experiments have proved that acupuncture can regulate the expression of genes (17-Fu SP, He SY, Xu B, Hu CJ, Lu SF, Shen WX, Huang Y, Hong H, Li Q, Wang N et al: Acupuncture promotes angiogenesis after myocardial ischemia through H3K9 acetylation regulation at VEGF gene. PLoS One 2014, 9(4):e94604.; 18-Huang Y, Lu SF, Hu CJ, Fu SP, Shen WX, Liu WX, Li Q, Wang N, He SY, Liang FR et al: Electro-acupuncture at Neiguan pretreatment alters genome-wide gene expressions and protects rat myocardium against ischemia-reperfusion. Molecules 2014, 19(10):16158-16178). Thus, there was no need to design a pilot study to test the theory again. The aim of our protocol is to investigate the gene expression profiling and to determine whether histone modifications are involved in gene regulation following electro-acupuncture treatment in humans. This is a completely novel approach in the field of human stable angina pectoris.

2. We do not need to set up a “pilot study” for the clinical efficacy of acupuncture on stable angina pectoris, since our group has already published a protocol on the clinical effects of acupuncture in Trials (Dehua Li et al. Acupuncture for chronic, stable angina pectoris and an investigation of the characteristics of acupoint specificity: study protocol for a multicenter randomized controlled trial. Trials 2014, 15:50.); Fanrong Liang is a corresponding author in both protocols. Now this study is focusing on epigenetic study, as which we have mentioned in our answer to reviewer Dr.Cun-Zhi Liu’s third question.

3. We sincerely apologize for the mistake we have made on our use of the term “pilot study” and “pilot experiment”. Our intention was to use “pilot experiment” solely to answer reviewer Dr. Cun-Zhi Liu’s seventh question.

4. In order to better explain how we calculated the sample size in this study, we provided a formula that we used for the calculation. Sample size is calculated based on the primary clinical measure of effect-frequency of angina attacks, according to the formula:

\[ n = \frac{2(u_2 + u_2)^2 \sigma^2}{\delta^2} \]

Where \( n \) is the sample size of trial group/control group, \( \alpha \) is the significance level,1-\( \beta \) is the power of a test, and \( \delta \) is the mean difference between trial group and control group.
In this study, $\alpha=0.05$, $\beta=0.10$, and $\delta$ is estimated at 4.5 between Neiguan group and control group based on the primary clinical data. Therefore, $n=20$ is in each group, justifying that the sample size in these groups was reasonable.

We are sorry for the trouble that this error may have caused. We hope that our protocol will be published in BMC Complementary and Alternative Medicine soon. If you have further questions, please feel free to let me know. Thank you very much for your time and your assistance in this matter!

Sincerely

Bing-Mei Zhu

Uploaded list:
1. Final version of MS
2. Reviews' reports for our revised manuscript and the answers (downloaded from our account)