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RESPONSE TO LETTER

The Efficacy of Chaihu-Guizhi-Ganjiang Decoction on Chronic Non-Atrophic Gastritis with Gallbladder Heat and Spleen Cold Syndrome and Its Metabolomic Analysis: An Observational Controlled Before-After Clinical Trial [Response to Letter]

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Dear editor

We all appreciate Zhu's insightful comments.[1] First, regarding the associations between smoking, drinking, dietary habits, and disease duration with disease outcomes and progression, which Zhu previously raised, these factors were not included in this study.[2] Due to the application of traditional Chinese medicine, patients with chronic non-atrophic gastritis seldom smoke or drink alcohol. During the consultation period, the doctor's prescription will obviously ask patients to abstain from these behaviors as well as maintain healthy eating habits. Thanks to the professors, we will collect those important data to guarantee the correctness of the result.

It is true that we may not have sufficiently considered these factors, or their impact may have been underestimated, in the case of patients with milder symptoms who may experience spontaneous relief from stomach upset after momentarily altering bad habits, avoiding stressful situations, or reducing stress. It is a good suggestion to re-analyze the original data after patients modify their behaviors and lower their stress levels, with particular attention to those with milder symptoms. This will be completed in our further research.

We carried out a brief 28-day trial in order to account for patient acceptance and other confounding variables that arise from long-term investigations. We do agree, though, that a 28-day treatment may not be enough to fully evaluate the impact of the intervention. Furthermore, because of patient treatment requirements and ethical review, we did not establish a placebo control group. In order to evaluate the treatment effect's durability and ascertain whether the treatment plan has to be modified, we therefore want to carry out a long-term follow-up study. Additionally, a placebo control group will be planned to be incorporated into the subsequent research. This will assist us in differentiating between potential psychological comfort and actual therapy results. Certainly, we will make sure that every aspect of the study's design and implementation, including the use of placebos, complies with ethical guidelines.

Furthermore, it is challenging to account for the number of steps and the means of transportation taken by the patient before they arrive at the blood collection location from their home on the day of the collection due to their lack of exercise prior to blood collection. Exercise does, however, have an impact on BCAA levels, and in a follow-up controlled

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trial, we will ascertain how variations in plasma BCAA levels relate to both exercise and the stomach environment. This will entail monitoring individuals' activity routines and collecting plasma samples at various intervals (for example, before and after meals). It is confirmed that all patients maintained a resting state for at least half an hour before the blood drawing. The relationship analysis between inflammatory variables and GNAG syndrome is of importance. Therefore, those factors, including COX-2, TNF-α, and IL-10 levels will be enrolled in the further research.

Also, there are not enough data about CGGD's safety. Actually, the patients have received one-month follow-up, in which they did not report any side effects, such as fever, sweating, or mild diarrhea.

It was so sorry that the numbers of the enrolled patients were limited owing to the COVID-19 in 2020. We all agree that more thorough biological insights will be obtained by including multi-omics data (such as transcriptomics and proteomics) in the investigation. To better understand the mechanism of action, we will employ mass spectrometry and high-throughput sequencing technology to examine how CGGD affects patient metabolite levels, protein expression, and gene expression.

Disclosure

The authors report no conflicts of interest in this communication.

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