Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Pharmacological Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Pharmacological Research

journal homepage: www.elsevier.com/locate/yphrs

The true effect of traditional Chinese medicine on the clinical outcome of hospitalized patients with COVID-19?

Dear Editor,

We read with great the retrospective study by Tseng et al., which investigated the effect of traditional Chinese medicine (TCM) - NRICM101 and NRICM102 on the clinical outcome of hospitalized patients with COVID-19 [1]. Using propensity score-matched methods, they found that NRICM101 and NRICM102 were significantly associated with a lower risk of intubation/ICU admission or death among patients with mild-to-severe COVID-19. However, we have serious concern about confounding effect of anti-COVID-19 treatment.

In this study, patients can receive TCM and other anti-COVID-19 medications, including remdesivir, corticosteroid and interleukin-6 blockades. In the comparison between NRICM101 plus usual care (study group) and usual care (control group), we found the use of remdesivir and corticosteroid was more frequent in the study group than the control group (remdesivir: 5.3% vs 1.3%; corticosteroid: 23.2% vs 16.6%). Based on the current guideline and evidence, these two agents would provide clinical benefit for indicated patients with COVID-19 [2–4]. Thus, we wonder whether the clinical benefit was brought by NRICM101 only or NRICM101 plus remdesivir or corticosteroid. To clarify this issue, a sensitivity test to compare the clinical effect of NRICM101 only plus usual care and usual care is needed. Similarly, IL-6 blockade was more frequently used in the study group (NRICM102 plus usual care) than the control group (usual care)(20.3% vs 8.1%), so the confounding effect of IL-6 blockade on the outcome requires a sensitivity test to clarify.

Additionally, the patients in the comparison between NRICM102 plus usual care and usual care had mild-to-moderate COVID-19 (WHO Clinical Progression Scale score ≤ 4) and about half of them had their severity score < 4, which did not need hospitalization. However, all patients in this study were hospitalized. We wonder whether the main cause of hospitalization may be other than COVID-19. Similarly, all patients in the comparison between NRICM102 plus usual care and usual care had severe COVID-19 (WHO Clinical Progression Scale score > 4), in which remdesivir and corticosteroid should be given according to the present guideline [2]. However, only $< 20\%$ and $< 70\%$ of patients received remdesivir and corticosteroid, respectively (table 2). Thus, we wonder whether the findings of the present study [1] can be generalized in the real world.

Finally, this study subjects were infected with alpha variant; however, omicron variant has become the predominant variant since 2022. Additionally, the tolerability of NRICM101 and NRICM102 were not evaluated in this study. Before further study demonstrates the effect and safety of TCM against omicron variant, the use of NRICM101 and NRICM102 should be cautiously.

Data Availability

No data was used for the research described in the article.

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https://doi.org/10.1016/j.phrs.2022.106437

Received 27 August 2022; Accepted 6 September 2022

Available online 8 September 2022