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The adoption of repeated measurement of variance analysis and Shapiro–Wilk test

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I read with interest the article by Ni *et al*. [1], who conducted a randomized, open-label, parallel-controlled, multicenter clinical trial on the use of Shuanghuanglian (SHL), a traditional Chinese patent medicine, in treating cases of COVID-19, from which they drew a very important conclusion — combining SHL with standard care could enhance antiviral effects and improve clinical outcomes in patients with COVID-19. I agree with most of the conclusions in this article and appreciate that the conclusion and the results are beneficial to the future trial design. However, after careful reading, I would like to put forward the inadequacies of the article.

First, as the authors described in the "Materials and methods" section, "We also collected other laboratory measurements, including blood routine (leukocytes, lymphocytes, eosinophils, platelets, etc.), liver function (alanine aminotransferase (ALT) …… and coagulation function on day 0, day 7, and day 14 until discharged or other endpoint event had occurred." In addition to taking the intervention factor (whether or not to imply SHL and its dose) into account on study outcomes, we also need to consider the influence of time factors on the experiment. It is considered that repeated measurement of variance analysis should be used in the random control trial when repeated measurements of the same observation indicator are required at different times [2]. However, the authors did not represent the statistical method in detail in the "Materials and methods" section, which easily leads to misapprehensions.

According to the "Statistical analysis" part reported by the authors, they conducted a normality test via Kolmogorov–Smirnov (KS) test, which is suitable for the assumption that the parameters of the distribution are completely known. However, it is difficult to specify the parameters initially or completely without knowing the distribution of specific data. The parameters need to be estimated based on the sample data. The conclusion may be misleading when using the original KS statistics in this situation, and results in the probability of Type I error often smaller than the probability given in the KS test standard table [3]. Among the four tests considered, i.e., Shapiro–Wilk (SW) test, Kolmogorov–Smirnov (KS) test, Lilliefors (LF) test, and Anderson–Darling (AD) test, the SW test is the most powerful test for all types of distribution and sample size, while the KS test is the weakest [4]. Besides, SPSS software stipulates that when the sample size is $3 \leqslant n \leqslant 5000$, the result shall be subject to SW test, while the sample size is $n > 5000$, KS test should be utilized for normality distribution analysis [5,6]. A more precise analysis of the normality test could have been done by adopting SW test rather than KS test in this paper.

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Compliance with ethics guidelines

Jie Wei declares no conflicts of interest. This manuscript is a correspondence and does not involve a research protocol requiring approval by the relevant institutional review board or ethics committee.

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