Letters to the Editor

Comment on "Relationship between Vitamin D and Nonspecific Low Back Pain May Be Mediated by Inflammatory Markers"

To the Editor:

We have read with great interest the article by Xu et al (1) entitled "Relationship between Vitamin D and Nonspecific Low Back Pain May Be Mediated by Inflammatory Markers" in Pain Physician (2021; 24:E1015-E1023). We applaud the authors for their considerable contribution to the hot topic — is there a role that vitamin D (VitD) plays in nonspecific low back pain (Ns-LBP)? Nevertheless, there are some concerns which should be well addressed, especially when it comes to informing clinical practice of vitamin D supplement for patients with Ns-LBP.

Firstly, the Spearman's statistics might be incorrectly used when examining the correlation between VitD concentrations and inflammatory makers and pain scores (original article's Table 2 and 3). Spearman's rank correlations, are generally used for categorical or continuous variables with non-Gaussian distributions, just like other nonparametric statistical methods (2). However, as was described in Methods and Footnotes (original article's Table 1 and 2), Analysis of Variance was utilized for aforementioned variables, which indicated that these data satisfied the assumption of normal distribution. Then, Pearson's correlation statistics should be used in the same scenario.

Secondly, I would like to draw your attention to several obvious digit typos. The intermediary effect of interleukin-6 (IL-6) on Ns-CLBP was indeed a novel and substantial finding. The authors used multiple regression analyses to quantify the mediating effect and presented a coefficient of 0.314 (P = 0.015) in the original article's Fig. 1 and Table 5. In the Abstract and Result, however, the intermediary effect of IL-6 of 0.045 was reported. There might be errors underlying the inconsistency and the authors had better double check their raw statistical analyses.

Besides, the direction (VitD→IL6→LBP) was preassumed when they conducted the mediating analysis. Another probability should be taken into account that IL-6 has certain effect on VitD, ultimately affecting the LBP risk (IL6→VitD→LBP). The authors firstly presented the triangular relationship between VitD, inflammatory markers and LBP through a series of robust analysis. The association between VitD and inflammatory cytokines has also been reported by previous studies (3, 4). Recently, it was pointed out that IL-6 may suppress VitD signaling pathway in epithelial-mesenchymal transition and stemness (5). It was reasonable to hypothesize a mediating effect in the study. However, considering the complex interplay between biomarkers, the mediating analysis should be performed in both directions.

Lastly, it might be more rigorous to incorporate season-adjusted 25(OH)D values into the regression model. If samples were collected in different seasons, it is important to note that 25(OH)D levels can be affected by seasons since the outdoor activity and sunlight exposure can lead to higher 25(OH)D levels in summer. Certain formula has been put forward, validated and widely used (7-9). Adjusting the 25(OH)D concentrations by the season before ensuing quantitative analyses should make more sense.

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