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LETTER TO THE EDITOR

Colchicine resistance and low vitamin D in familial Mediterranean fever

We read with interest the study by Özer et al.[1] evaluating the association between colchicine resistance and vitamin D levels in familial Mediterranean fever (FMF). Patients with ≥ 3 attacks within the last 6 months period, while using 2 mg/day colchicine were defined as colchicine-resistant in this study. They compared the vitamin D levels of colchicine-resistant and nonresistant FMF patients. They found significantly lower vitamin D levels in colchicine-resistant group. Besides, the mean colchicine dose was significantly higher in colchicine-resistant patients than the nonresistant ones. Regarding that deficiency of vitamin D may cause increased inflammatory response; the authors speculated that vitamin D deficiency might be a factor in etiopathogenesis of colchicine resistance. We wish to make minor criticism about the interpretation of the results.

It is not clear whether low vitamin D levels observed in patients with FMF are a triggering factor or a consequence of the disease. Recently, we reported another study about the lower vitamin D levels in pediatric FMF patients than their healthy peers.[2] We found a negative correlation between cumulative colchicine dose and serum vitamin D level in multivariate logistic regression analysis. Karatay et al.[3] reported low vitamin D levels in patients with Behcet's disease and also demonstrated a strong relationship between colchicine use and low serum vitamin D levels as in our study. Similarly, Özer et al.[1] reported a significantly higher mean colchicine dose in resistant patients, in whom lower vitamin D levels were observed. To date, the exact mechanism of colchicine is unknown. Regarding the inverse correlation of colchicine dose and vitamin D level in our previous study, we suggested that further studies were needed to explain the role of colchicine on vitamin D metabolism. We speculated that the negative correlation of vitamin D and colchicine dose might be related to gastrointestinal malabsorption and gastrointestinal adverse effects related to colchicine. Indeed, in some patients, colchicine may cause gastrointestinal side effects, such as diarrhea.[4] Previous studies showed that colchicine might induce reversible vitamin B12 malabsorption by altering the function of ileal mucosa, but not by intestinal hypermotility.[5] However, to date, no study has investigated whether colchicine causes intestinal malabsorption of vitamin D.

The authors speculated that deficiency of vitamin D might cause increased inflammatory response, thus higher inflammatory activity in colchicine-resistant patients. However, they did not include any acute phase reactants; such as C-reactive protein (CRP), erythrocyte sedimentation rate or serum amyloid A in their study. Although we could not show a significant correlation between CRP and vitamin D levels in our previous study, Erten et al.[6] found a significant negative correlation between low serum vitamin D levels and acute-phase reactants. They suggested that decreased vitamin D levels in patients with FMF could be another indirect sign, but not the reason, of ongoing inflammation. Besides, the study by Yılmaz et al.[7] and Anık et al.[2] showed that vitamin D deficiency in FMF was not associated with disease severity score.

In conclusion, low vitamin D status might be a consequence of the disease or its treatment, rather than being the reason of colchine resistance. We suggest that multiple regression analysis, rather than univariate analysis, would better identify the predictors of colchicine resistance. The results of study by Özer et al. once more considered that the role of colchicine on vitamin D metabolism needs to be elicited.

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