Dr. Rios Fernández, *et al*, reply

To the Editor:

Gambichler and colleagues[1] have concluded that prevalence of vitamin D deficiency is high in patients with systemic sclerosis (SSc) and is probably not dependent on the patient's geographic origin. In the past decade there has been renewed interest in vitamin D, with a proliferation of published studies on the effects of vitamin D in varying clinical conditions. Classically, vitamin D has been linked to mineral metabolism and its deficiency with bone disease, but interest in the nonskeletal effects has been increasing since the discovery of vitamin D receptors and the 1α-hydroxylase enzyme in multiple tissues. Vitamin D is known to promote cellular differentiation, inhibit cellular proliferation, and reduce the growth of certain tumors. Vitamin D is required for the expression of cathelicidin by macrophages, and involved in bacterial killing and reduction of the risk of infections, and has effects in proinflammatory cytokines, regulatory T cells, and immune responses[2]. In this respect vitamin D deficiency has been associated with conditions such as cancer and allergic, autoimmune, and cardiovascular diseases[3]. The bulk of current data is based on observational, epidemiological studies, which are useful for generating hypotheses but not for revealing causality.

Vitamin D deficiency has been found to be very common in patients with SSc[4,5,6], independent of their geographic locations. In the general population, vitamin D deficiency has been related to reduced sun exposition, inadequate vitamin D intake, and overweight. In patients with SSc there are many other factors, such as inactivity, malabsorption, renal insufficiency, skin thickness, and drug use. However, the prevalence of vitamin D insufficiency in patients with SSc probably would not be different from that of the general population. Our group found a similar prevalence in postmenopausal women, premenopausal asthmatic women, and patients with diabetes and Crohn's disease[7]. The question of interest is the relationship of vitamin D insufficiency with clinical manifestations and the course of the disease. The principal problem is that the published studies are cross-sectional, which does not allow conclusions about a cause-effect relationship. Otherwise, the possible relations found in different studies are inconclusive (systolic pulmonary artery pressure, skin thickness), in part because of the small sample sizes or because findings could be incidental. The only way to answer these questions will be with more large, prospective studies.

Most experts recommend levels of 25OH vitamin D > 30 ng/ml in order to lower the risk of infections and cardiovascular disease. We do not know if patients with SSc experience additional benefits, but these patients have greater risk of cardiovascular disease[8], which justifies maintenance of high levels of 25OHD. In order to keep optimal levels of vitamin D, baseline measurement of vitamin D should be performed periodically, keeping in mind that levels are higher in summer months and lower in winter. The recommended supplements are insufficient, as we have shown. In our experience oral calcifediol supplement 10,640 IU every 2–4 weeks achieves optimal levels in most patients.

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