Effects of vitamin D3 on human lung fibroblasts derived from patients with idiopathic pulmonary fibrosis

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Résumé

Idiopathic pulmonary fibrosis (IPF) is a progressive and fatal interstitial lung disease. Currently, no treatment can stop the progression of IPF. Vitamin D3 (VD) reduces experimental lung fibrosis in murine models and prevents in vitro the activation of murine lung fibroblasts. Moreover, depletion of VD may be associated with a reduced survival of patients with IPF. In this context, we determined in the present study if VD can prevent the pro-fibrotic functions of human lung fibroblasts (HLFs) isolated from patients with IPF. IPF and control HLFs were derived from surgical lung biopsies collected from patients with IPF or with primary lung cancer, respectively. VD (10-100 nM) barely prevented the TGF-β1-induced differentiation in HLFs. At 100 nM, VD slightly reduced the expression of the pro-fibrotic marker α-smooth muscle actin and had no effect on fibronectin and collagen-1 expression. In contrast, 100 nM VD strongly inhibited the aerobic glycolytic metabolism induced by TGF-β1 in IPF HLFs. VD (3-100 nM) also potently reduced the basal and PDGF-dependent proliferation of control and IPF HLFs. Using gene silencing technology, we demonstrated that such effects were mediated by the vitamin D receptor. In addition, 100 nM VD altered the cell cycle by increasing the percentage of IPF HLFs arrested in the G0/G1 phase and by downregulating the expression of various cell cycle regulatory proteins. In conclusion, our study shows that low VD concentrations reduced in vitro pro-fibrotic functions of HLFs. These results suggest that it might be interesting to assess potential clinical benefits of vitamin D supplementation in patients with IPF, especially in slowing lung function decline.

Mots-Clés: lung fibrosis, nutrition, metabolism

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