Vitamin D replacement in pre-menopausal women ameliorates cholesterol-related serum lipoprotein functions, adipokines profile and vascular markers of subclinical atherosclerosis

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Background. Low vitamin D (vitD) status has been linked to increased cardiovascular (CV) risk, but the effects of vitD supplementation on CV disease and its determinants, such as lipid metabolism, are not entirely clarified. We hypothesized that vitD may modulate cholesterol-related lipoprotein functions more than their serum concentration. Among such functions are the HDL cholesterol efflux capacity (CEC), inversely correlated to CV risk, and the pro-atherogenic serum cholesterol loading capacity (CLC), respectively reducing and promoting macrophage cholesterol accumulation. We evaluated the impact of vitD status normalization on CEC, CLC, adipokine profile and subclinical atherosclerosis in premenopausal women.

Methods. Healthy premenopausal women with vitD deficit (n=31) were scheduled for vitD replacement. HDL CEC was measured by a radioisotopic assay and serum CLC by cholesterol fluorimetric quantification in macrophages. Serum adipokines were measured by ELISA. Subclinical atherosclerosis was evaluated by flow-mediated dilation (FMD), pulse wave velocity (PWV) and augmentation index (AI), measured with standard techniques.

Results. VitD replacement restored normal levels of serum 25(OH) vitD (from 9.88 ± 4.13 to 24.57 ± 5.35 μg/L). Total CEC from macrophages significantly improved (+ 19.5%; $p<0.01$) after vitD replacement, due to a specific increase in the ABCA1-mediated CEC (+ 70.8%; $p<0.0001$). No change was observed in cholesterol aqueous diffusion nor in ABCG1-mediated CEC. Serum CLC was significantly reduced (-13.3%; $p = 0.0026$) after replacement. After vitD replacement adiponectin and resistin plasma levels were increased (+50.6%; $p<0.0001$) and decreased (-24.3%; $p<0.0001$) respectively. CEC, CLC and adipokine modifications were paralleled by a significant improvement of FMD (+3.1%; $p<0.0001$), PWV (-4.1%: $p<0.0001$) and AI (-10.6%; $p = 0.0015$).

Conclusions. VitD replacement ameliorates lipoprotein functions involved in macrophage cholesterol homeostasis together with adipokine profile and subclinical atherosclerosis vascular parameters. These new data support a beneficial effect of vitD supplementation in CVD prevention.