Role of Vitamin D on the modulation of atherogenesis: an *in vitro* model of monocyte-derived macrophages

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Introduction: Lipid accumulation in monocyte-derived macrophages leads to the development of foam cells and the following formation of atherosclerotic plaque, an essential factor of atherosclerosis. Calcitriol (1,25-(OH)2D3) is the active metabolite of vitamin D which is produced in most of our tissues and cells. Among the several functions exerted by the vitamin D, it seems to have a protective role against atherosclerosis through the modulation of immune system. However, the mechanisms of action underlying this effect are still not completely elucidated.

Objective: The aim of this study is to evaluate the capacity of calcitriol to modulate the lipid accumulation in an *in vitro* model of monocyte-derived macrophages.

Methods: Monocytes (THP-1 cells) were differentiated to macrophages and treated with a fatty acids solution (500 µM of oleic/palmitic acid in a ratio 2:1) and calcitriol at different concentrations (0.1, 1, 10, 50 and 100 nM). The lipid accumulation has been evaluated through the utilization of a lipophilic dye (Nile Red) capable to stain intracellular lipid droplets. The protein levels of the markers related to the lipid metabolism has been assessed by using ELISA kits. The results obtained have been analysed through the analysis of variance (ANOVA).

Results: The findings showed the capacity of 1,25-$(OH)_2D_3$ to reduce lipid accumulation at the concentrations of 50 e 100 nM ($p<0.01$), while no effect has been observed at lower concentrations (0.1, 1, 10 nM). The calcitriol tested at 50 nM determined an increase in ABCA1, CPT1A and PPAR-γ, while a reduction in CD36 and C/EBP-beta protein levels ($p<0.01$).

Conclusion: Physiological concentration of the active metabolite of vitamin D seems to exert a positive role on the modulation of lipid accumulation in monocyte-derived macrophages. Its effect could be mediated by the modulation of different proteins involved in the lipid metabolism at the level of atherosclerotic plaque, suggesting a potential protective role of 1,25-$(OH)2D_3$ on atherosclerosis.

Keywords: Vitamin D; Monocyte-derived macrophages; Lipids; Atherogenesis.