

EFFECTS OF FLUVASTATIN THERAPY ON THE PATTERN OF PROTEIN EXPRESSION IN MONOCYTES OF PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Antiphospholipid syndrome (APS) is an acquired autoimmune disorder of unknown pathogenesis that is defined by the association of arterial or venous thrombosis and/or pregnancy morbidity in the presence of antiphospholipid antibodies: anticardiolipin antibodies and lupus anticoagulant. Recently, new genes and proteins differentially expressed in blood monocytes from APS patients with thrombosis, such as annexin II, RhoA proteins or protein disulfide isomerase (which are also related to the effect of specific autoantibodies on that disease), have been found.

In addition to their anti-inflammatory and immunomodulatory properties, statins have been shown antithrombotic effects, although the molecular mechanisms involved are not fully understood yet.

In this study, by using proteomic techniques, we analyzed changes in protein expression of monocytes of APS patients after statins therapy.

Ten patients with APS and previous history of thrombosis received Fluvastatin (40 mg/day) for one month. Then, proteomics, Western blot and RT-PCR analysis were accomplished.

The therapy with Fluvastatin reversed the changes produced in the expression levels of proteins altered in APS patients with thrombosis vs healthy donors, such as annexin II, Rho A proteins or PDI. These levels then slowly returned to basal levels, although remained significantly altered three months after the end of the treatment. Only RhoA protein levels remained lowered. Although these finding merits further research, it might be speculated that after removal of statins, plasma mevalonate levels remained reduced after statins treatment, thus maintaining Fluvastatin effects on APS patient monocytes. Moreover, statins may have affected other soluble plasma markers of monocyte perturbation in APS patients (e.g. soluble TF, D-dimer, LDL-ox.), thus explaining the slow return to baseline levels of the other altered proteins.

Our study has identified changes in the protein expression patterns of monocytes from APS after statins treatment. These findings might provide new targets for rational pathogenesis-based therapies of this autoimmune disorder.

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