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Letter to the Editor

# Antibodies against *Chlamydia pneumoniae* in stable angina and interleukin-6 levels

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Inflammation is a key mechanism in atherogenesis and the rapid progression of coronary artery disease. Tissue lesion occasions the release of chemical mediators, cytokines, accompanied by an increase in the blood concentrations of acute phase reactants, such as fibrinogen, C-reactive protein, serum amyloid A protein, sialic acid and ceruloplasmin and a reduction of those of albumin. It has been observed that these proteins are higher in patients with ischemic heart disease and, furthermore, who have a higher tendency to present adverse cardiovascular incidents [1]. On the other hand, the inflammation appears to be directly linked to the 'vulnerability' or 'instability' of the atheromatous plaques that predispose to disruption and acute coronary incidents. The inflammatory mechanism, therefore, can represent the final common connection channel of chronic infection between atherogenesis and the clinical manifestations of coronary artery disease [2].

Infection by *C. pneumoniae* can induce a chronic immune activation mediated by cytokines, which directly contribute to the chronic damage of the endothelial cell or stimulate the synthesis of acute phase reactants (fibrinogen, C-reactive protein). Chronic infection may also increase the expression of procoagulants derived from the monocytes, such as tissular factor and, therefore, increase the risk of localized thrombosis or embolization [3]. The object of our study was to evaluate whether or not the positivity of antibodies against *C. pneumoniae* modified interleukin-6 levels in a group of patients with stable angina

IL-6 was determined in a group of patients (36 males and 15 females) with stable angina. The inclusion criteria of stable angina was defined according to the Spanish Society of Cardiology. For the control group, 27 blood samples were taken from healthy donors and people who submitted to analytic controls. Interleukin-6 was determined by ELISA technique (enzyme-linked immunoabsorbent assay) in blood samples (Human ELISA IL-6 Endogen Inc., Woburn, MA, USA), with a coefficient of variation (CV) of 2–5%. Anti-*Chlamydia pneumoniae* IgG were determined by the micro-immunofluorescence (micro-IF) test. The patients were stratified in two groups according to antibody titer: group 1 in which no anti-*C. pneumoniae* antibodies (seronegative) were detected and group 2 with a titer above 1/64 (seropositive).

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The statistical analysis was made by a Pentium II computer using the SPSS 9.0 statistics program using a Fisher's test, chi-square test, the Mann–Whitney *U*-test.The study conformed to the norms of the Hospital Ethics Committee and in accordance with the Helsinki Declaration.

No statistically significant association was found in the group with stable angina between the IL-6 values and the presence (IL-6: $0.45 \pm 0.37$ pg/ml, $n=30$) or absence (IL-6: $0.37 \pm 0.52$ pg/ml, $n=21$) of antibodies against *C. pneumoniae*. A statistically significant association of $P=0.001$, calculated by the Mann–Whitney test, did exist between IL-6 levels of the cases represented by a group of patients with stable ischaemic heart disease and those of the control group of persons without ischaemic heart disease pathology. In this group the levels was undetectable and 0.042 pg/ml in the first group.

There are some studies that support the relation between *C. pneumoniae* and IL-6. Kaukoranta et al. [4] demonstrated in vitro that *C. pneumoniae* inoculated into mononuclear cells of peripheral human blood grew in the cells and induced the secretion of cytokines, IL-6 among them. The cytokine response was concentration-dependent, although it is not known if the intracellular growth of the *C. pneumoniae* plays a role in the induction of cytokines. Along the same line, Heineman et al. [5] demonstrated that *C. pneumoniae* grows in the monocytic cells and that it is a strong inductor among other cytokines of IL-6.

In our study no statistically significant association was observed between seropositivity for *C. pneumoniae* and the IL-6 level but there was difference between the group of patients with stable angina and the control group. Our results support the hypothesis that in the pathogenesis of ischaemic heart disease, an inflammatory mechanism may intervene, the IL-6 constituting a systemic marker of inflammation that facilitates passage of an arteriosclerotic lesion to a vulnerable plaque. This data differs from the results obtained by other researchers, the majority of whom detected an increase in IL-6 in situations of instability or stress, unstable angina and acute myocardial infarction. Vergassola et al. [6] likewise observed very high levels of IL-6 in 100% of the 17 patients studied with acute myocardial infarction, as opposed to detectable levels of said cytokine in the control group. They also detected a good correlation between the IL-6 levels and the IgA antibody against *C. pneumoniae*. We did not find these correlation, although we did not determine IgA antibodies. Studies of a larger population are necessary in order to evaluate the possible role of *Chlamydia pneumoniae* in the induction of IL-6.

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