

## Cholesterol and chloroquine

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To the Editors of the Brazilian Journal of Rheumatology

The effect of antirheumatic drugs, including antimalarials, on the metabolism of lipoproteins is currently object of interest of researchers. The study by Rossoni et al.,<sup>1</sup> published in the July-August 2011 issue of the Brazilian Journal of Rheumatology, has addressed this topic and evaluated the effect of chloroquine on the total cholesterol and HDL-cholesterol levels of patients with systemic lupus erythematosus (SLE). After adjusting for the use of statin and corticosteroids through multivariate analysis, those authors have reported that those serum levels are similar in patients using and not using antimalarials.

The complete evaluation of the lipid profile, regardless of the therapy used, should actually be a routine in the follow-up of those patients. It is worth knowing that lower serum levels of HDL-cholesterol are detected in SLE, and are inversely related to the inflammatory process.<sup>2</sup> Indeed, the lipoprotein levels vary over the course of the disease, as has recently been demonstrated in the prospective study by the Toronto group,<sup>3</sup> involving the cholesterol assessment of 1,260 SLE patients and a total of 26,267 measurements over  $9.3 \pm 8.5$  years. The relevant conclusion of that study is that almost two thirds of those patients (64.7%) had an increase in total cholesterol over time, and that the variation of its levels was directly related to age, activity of disease, and use of corticosteroids and lipid lowering drugs. Another equally important result of that large longitudinal study was identifying that the use of antimalarials was negatively correlated with total cholesterol levels ( $P < 0.0001$ ).<sup>3</sup>

In addition to that study, a recent review of the literature<sup>4</sup> has identified seven other studies (cohort and prospective

ones) that conclude that the antimalarial therapy for SLE determines a significant reduction in the serum lipid levels, including total cholesterol and LDL-cholesterol, when compared with other drugs. Three out of those seven studies have aimed at assessing the effect of antimalarials on SLE patients undergoing corticotherapy. They have also identified a reduction in LDL-cholesterol and total cholesterol levels, in addition to an increase in HDL-cholesterol levels, when compared with those of patients undergoing exclusive corticosteroid therapy.<sup>4</sup> On the other hand, only two other studies (Chinese and Iranian) have not detected significant alterations in the lipid profile with the use of chloroquine in SLE,<sup>4</sup> as reported in this study.<sup>3</sup>

The mechanism of the effect of antimalarials on the metabolism of lipoproteins has been the object of a previous study of our group.<sup>5</sup> The *in vivo* evaluation of the LDL-cholesterol metabolism in SLE patients using or not chloroquine, as compared with healthy controls, was carried out by using a nanoemulsion of LDE (radioisotope-labeled LDL). This methodology enabled identifying that antimalarials actually interfere with the function of the LDL receptor, increasing the plasma removal of that lipoprotein, and leading to a reduction in its serum levels, and, consequently, in total cholesterol.<sup>5</sup>

In fact, further studies confirming that mechanism of action on the metabolism of lipoproteins are required to evidence one more beneficial effect of antimalarials on SLE.

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