Antimalarials and cholesterol profile of patients with systemic lupus erythematosus

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ABSTRACT

A beneficial influence of antimalarials on lipid profile of systemic lupus erythematosus (SLE) patients has been recently claimed. In this cross-sectional study, we evaluated the effect of chloroquine on cholesterol levels of a Brazilian population with SLE. Sixty patients were studied, 95% females. Mean age was 48.7 years (SD 13.3 years). Overweight or obesity was documented in 27 cases (45%). Thirty-four patients (56.6%) were using chloroquine in standard dosage, while 33 (55%) were on corticosteroids. Hypercholesterolemia was present in 26 patients (43.3%), while low HDL-cholesterol levels were seen in 18 cases (30%). Normal cholesterolemia was documented equally in users and non-users of antimalarials ($P > 0.20$). After adjustment for statin and corticosteroid intake by multivariate analysis, cholesterol and HDL-cholesterol levels did not significantly differ in users or non-users of chloroquine ($P > 0.05$). There was no association of chloroquine intake with low body mass index ($P = 0.314$). Our findings suggest that antimalarial intake by itself does not distinguish cholesterol profiles in SLE patients.

Keywords: systemic lupus erythematosus, antimalarials, cholesterol.

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Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by microvascular inflammation.[1] Chloroquine is widely used in SLE, and its early use in "incomplete" SLE is associated with delayed SLE onset.[2] The influence of antimalarials on lipid profile is of recent interest, owing to a supposed antilipemic effect of these drugs.[3] In this cross-sectional study, we evaluated the cholesterol profile of users and non-users of chloroquine.

SLE patients according to the 1997 criteria[4] of our reference center entered the study after written informed consent. Body mass index (BMI) above 24.9 was considered abnormal.[5] Cholesterol and high-density lipoprotein (HDL)-cholesterol levels[6,7] were obtained by chart review in non-users and current users of antimalarials (hydroxychloroquine 400 mg daily, or chloroquine diphosphate 250 mg daily for at least six months). Those patients on lower doses of any of the antimalarials were excluded of the study. Triglycerides and low-density lipoprotein (LDL) levels were not included in the study due to incomplete information in medical records. Chi-square analysis was used for comparison of categorical variables, and the Student's *t* test was utilized for comparison of continuous variables. A level of 5% ($P < 0.05$) was considered significant. Data were adjusted for statin and corticosteroid intake by multivariate analysis. The association of chloroquine intake with BMI changes was also evaluated. All analyses used procedures of the SPSS for Windows, version 13 Chicago, IL. The study was approved by the local ethics committee (protocol number 07/04067).

Sixty patients were studied. Females strongly predominated (57 patients, 95%). The global mean age was 48.7 years. The white race largely predominated (53 patients, 88.3%). Mean duration of disease was 9 years. Twenty-seven patients (45%)

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showed BMI above 24.9. The mean BMI was 25.5 for females, and 24.5 for males. Thirty-four patients (56.6%) were using antimalarials in standard dosage, while 33 (55%) were on corticosteroids. Nineteen patients (31.7%) were using both drugs. Statins were being utilized by 19 patients (31.7%). Twenty-six patients (43.3%) had increased cholesterol levels (above 200 mg/dL),[7] while 18 patients (30%) showed low HDL levels (less than 40 mg/dL).[7]

Mean cholesterol levels for non-users of chloroquine were 203.9 mg/dL (SD 29.5), while users had mean levels of 200.8 mg/dL (SD 63.4); these data did not significantly differ (P = 0.799). As to HDL, mean levels were of 55.8 mg/dL (SD 12.8) for non-users and 57.8 mg/dL (SD 13.8) for users (P = 0.571). Normal cholesterol levels were seen in 46.2% of non-users and in 64.7% of chloroquine users (P = 0.240). Normal HDL levels were detected in 69.2% of non-users and in 70.6% of the users (P = 1.000). After adjustment for statin intake, cholesterol (P = 0.428) and HDL (P = 0.964) levels did not differ in users and non-users of chloroquine. After adjustment for corticosteroid intake, chloroquine intake again did not relate to cholesterol (P = 0.139) or HDL (P = 0.909) variations. Antimalarials intake did not associate to BMI < 20 (P = 0.314).

As a whole, nearly half of our SLE population was overweight or obese. It is well known that BMI is increased in SLE, and obesity behaves as an independent contributor to functional incapacity and inflammatory changes in SLE patients.[8] Of note, weight excess and an increased prevalence of metabolic syndrome were recently reported in a large cohort of SLE patients.[9]

In our study, mean levels of cholesterol and HDL did not significantly differ in non-users and users of chloroquine. Normal cholesterol levels were more frequently seen in chloroquine users, but this finding lacked statistical significance. Normal HDL, in turn, occurred equally in both groups. After adjustment for statin and corticosteroid intake, cholesterol and HDL levels again did not significantly differ in users and non-users of antimalarials.

Chloroquine has been claimed as an antilipemic agent in SLE.[10] In a survey of 18 SLE patients controlled for daily steroid intake, those on hydroxychloroquine had 35%-54% lower total triglyceride, cholesterol and apolipoprotein CIII levels as compared to non-users.[11] The influence of a 3-month chloroquine treatment on lipid metabolism was assessed in 34 SLE patients; total cholesterol, LDL cholesterol and triglycerides levels were significantly lowered at the end of the study, but data were not adjusted for statin and steroid intake.[12] In patients with rheumatoid arthritis and SLE, therapy with hydroxychloroquine was associated with low cholesterol, LDL-cholesterol and triglycerides, irrespective of concomitant steroid administration.[13]

In concordance with our results, chloroquine had no significant effect on the serum lipid profile of Chinese patients with SLE.[14] In a recent systematic review, evidence supporting an effect of antimalarials on lipid levels of SLE patients was weak.[15]

The study of nutritional and lipid profiles in SLE can be of difficult interpretation, given the heterogeneity of clinical findings, duration and activity of disease, and the wide range of therapeutic agents utilized in these patients. Prednisone dose, for instance, varied greatly in our survey, so that dose stratification would be inappropriate for statistical purposes. Lipid profile was not adjusted for disease activity in our study, and a bias towards higher disease activity in chloroquine users has to be considered. Sample size may also limit our conclusions.

Globally, our SLE population showed a considerable prevalence of overweight. After adjustment for statin and steroid intake, chloroquine utilization did not distinguish cholesterol profiles in our SLE survey, neither related to BMI changes. The effect of antimalarials on lipid profile of SLE patients has to be clarified in further, and preferentially longitudinal, studies.

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