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HYDROXYCHLOROQUINE IMPROVED LIPID TRANSFER TO HIGH-DENSITY LIPOPROTEIN IN SYSTEMIC LUPUS ERYTHEMATOSUS: A POSSIBLE MECHANISM FOR THE REVERSAL OF ATHEROSCLEROSIS IN THE DISEASE

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BACKGROUND

The beneficial effect of hydroxychloroquine (HCQ) in decreasing LDL levels on systemic lupus erythematosus (SLE) is well defined. A probable influence of this drug on increasing HDL levels is still under debate and information about its possible effect on this lipoprotein function is scarce. Our objective was to evaluate the effect of HCQ on HDL levels and function in SLE.

MATERIALS AND METHODS

Nineteen premenopausal female SLE patients using HCQ (SLE WITH HCQ), 19 without any therapy (SLE WITHOUT THERAPY), and 19 age- and gender-matched healthy controls (CONTROL) were included. Demographical and clinical data were registered and lipoprotein plasma levels were evaluated. An *in vitro* transfer of four lipids (14C-phospholipid, 3H-cholesteryl ester, 3H-triglyceride, 14C-unesterified cholesterol) from a radioactively labeled donor nanoemulsion to HDL was performed.

RESULTS

All groups had similar mean age, weight, height, BMI and waist circumference as well as frequencies of Caucasian race ($p > 0.05$). SLE WITH HCQ had similar mean 2012 SLICC SLE criteria scores (6.11 ± 1.37 vs. 6.32 ± 1.73 ; $p = 0.68$), disease duration (12.1 ± 5.78 vs. 10.26 ± 7.93 years; $p = 0.42$) and SLEDAI-2K scores (0.47 ± 0.77 vs. 0.58 ± 1.60 ; $p = 0.52$) compared to SLE WITHOUT THERAPY, but had a lower SLICC/SDI score (0.37 ± 0.50 vs. 1.21 ± 0.98 ; $p = 0.002$). SLE WITH HCQ had a higher mean HDL levels compared to those without therapy (58.37 ± 14.04 vs. 49.79 ± 8.0 mg/dL; $p < 0.05$), but lower compared to controls (58.37 ± 14.04 vs. 68.58 ± 9.99 mg/dL; $p < 0.05$). Total cholesterol (TC) and LDL levels were significantly lower in SLE WITH HCQ compared to SLE WITHOUT THERAPY and CONTROL (148.16 ± 16.43 vs. 167.11 ± 30.18 vs. 174.11 ± 23.70 mg/dL; $p < 0.05$, 75.05 ± 22.52 vs. 96.05 ± 25.63 vs. 88.53 ± 20.24 mg/dL; $p < 0.05$). The *in vitro* lipid transfer to HDL revealed that mean transfer of unesterified cholesterol (UC) was significantly different among groups ($p = 0.002$), as can be seen in Table 1, and HCQ use promoted a higher transfer, since SLE WITH HCQ had a higher percentage of this transfer compared to SLE WITHOUT THERAPY ($p < 0.05$) but similar to CONTROL ($p > 0.05$). The percentage of transfer of triacylglycerol (TAG), esterified cholesterol (EC) and phospholipid (PL) were similar among groups ($p > 0.05$) (Table 1).

Table 1. Lipid transfers to HDL in all groups.

In vitro parameters	SLE WITH HCQ n = 19	SLE WITHOUT THERAPY n = 19	CONTROL n = 19	p
TAG transference (%)	4.93 ± 0.69	4.50 ± 0.69	5.14 ± 1.01	0.054
UC transference (%)	5.40 ± 1.05 ^b	4.44 ± 1.05 ^a	5.99 ± 1.71	0.002
EC transference (%)	5.24 ± 0.70	4.96 ± 0.89	5.69 ± 1.27	0.079
PL transference (%)	15.67 ± 1.03	15.34 ± 1.44	16.47 ± 1.89	0.066

ap < 0.05 compared with CONTROL. bp < 0.05 compared to SLE WITHOUT THERAPY.

CONCLUSION

Systemic lupus erythematosus had a negative impact on lipid profile by reducing HDL levels. The present study demonstrated that HCQ promoted a reversal of this deleterious effect since this drug enhanced the transfer of UC to HDL which is primarily responsible for transporting UC from tissues and endothelial cells thus preventing the formation of foam cells in atheroma.

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