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ORIGINAL ARTICLE

Clinical significance of lipid profile in systemic lupus erythematosus patients: Relation to disease activity and therapeutic potential of drugs

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Abstract *Aim of the work:* To study the lipid profile in systemic lupus erythematosus (SLE) patients and correlate it with disease activity parameters. The effect of hydroxychloroquine (HCQ), steroids and azathioprine on the lipid profile was also determined.

Patients and methods: The study included 48 female SLE patients. Total cholesterol, triglycerides and high density lipoprotein cholesterol (HDL-C) were measured in plasma. Low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL) were calculated. Disease activity was assessed using the systemic lupus activity measure (SLAM).

Results: The mean age of the patients was 25.7 ± 7 years. Hypercholesterolemia was present in 23 (47.9%) patients and hypertriglyceridemia in 16 (33.3%). There was no significant difference in the lipid profile of SLE patients receiving 200 or 400 mg/day HCQ. No significant difference in the lipid profile was found among patients who did not receive steroids, those who received 10 mg/day and those who received >10 mg/day. A significant difference in cholesterol and LDL-C level was present between SLE patients with (243.1 ± 84.3 mg/dl and 166.1 ± 65.7 mg/dl) and without (192.7 ± 50.6 mg/dl and 115.7 ± 44.4 mg/dl) lupus nephritis (LN) ($p = 0.01$, $p = 0.002$ respectively). SLAM significantly correlated with triglycerides and VLDL and negatively with HCQ intake ($r = -0.3$, $p = 0.04$).

Conclusion: Disease activity of SLE patients affects the lipid level and its control can be helpful in treatment strategies. The use of HCQ through its reduction of disease activity added to low dose steroids may reduce the lipid profile of SLE patients. Control of hyerlipidemia can favourably affect SLE renal disease.

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1. Introduction

The improvement in survival rates of SLE patients has led to the recognition of premature atherosclerosis as an important cause of coronary artery disease in these patients. One of the important traditional factors contributing to premature atherosclerosis is dyslipoproteinemia [1,2]. This dyslipoproteinemia ranges between 30% and 73% of the adult SLE patients. Studies have shown that there are two patterns of dyslipoproteinemia [3–5]. The first is related to active disease where there are increased levels of triglycerides and high density lipoprotein (HDL) [6], while the second is related to high dose steroid therapy and not related to active disease [7,8]. Actually it is difficult to differentiate between the two patterns and there are no clear distinctive boundaries between them.

It has been shown that there is an association between elevated levels of triglycerides, small dense low density lipoprotein-cholesterol (LDL-C), low levels of HDL-C and atherosclerosis. Steroid therapy has been shown to alter lipid levels [9]. The administration of antimalarial drugs in SLE patients not only treats constitutional symptoms and mild to moderate organ involvement but it has lipid lowering properties. This is attributed to a decrease in cholesterol synthesis, inhibition of lysosomal hydrolysis, increased uptake of LDL and alterations in insulin resistance [10–13]. Antimalarials are particularly effective in reducing VLDL which is the lipid part affected by steroids. Therefore antimalarials are more efficient in reducing cholesterol levels in the presence of steroids [7].

The aim of the present study was to reveal the changes and clinical significance of the lipid profile in SLE patients and to correlate it with the disease activity parameters. Another aim was to study the effect of hydroxychloroquine (HCQ), steroid and azathioprine therapy on the lipid profile level.

2. Patients and methods

The present study included forty-eight female SLE patients attending the Rheumatology and Rehabilitation outpatient clinic of Cairo University Hospitals between September 2013 and July 2014. The patients fulfilled the updated American College of Rheumatology (ACR) revised criteria for the classification of SLE [14]. The patients had a mean age of 25.7 ± 7 years and a mean disease duration of 5.9 ± 4.8 years. The patients underwent full history taking and clinical examination including cardiopulmonary, neurological, gastrointestinal, renal, musculoskeletal and dermatologic examination. The protocol of the research was approved by the institution within which the work was undertaken and it conforms to the provisions of the world association's Declaration of Helsinki. All patients gave informed consent. Exclusion criteria included menopausal women and hypothyroidism. None of the patients received lipid lowering drugs, estrogen and progesterone containing agents or thyroid medication at the time of study or three months prior to it [15]. None of the patients were smokers or alcoholics.

Laboratory tests performed to the patients included complete blood count, erythrocyte sedimentation rate (ESR), liver function tests including aspartate aminotransferase (AST) and alanine aminotransferase (ALT), kidney function tests including blood urea nitrogen, serum creatinine and creatinine clearance as well as complete urine analysis. Antinuclear antibodies (ANA) and anti-deoxyribonucleic acid antibodies (anti-DNA) were performed by immunofluorescence and complement (C3 and C4) by radial immunodiffusion. Lipid profile was measured after an overnight fasting. Total cholesterol (TC) and triglycerides (TG) were measured by the calorimetric method using commercial assays. High density lipoprotein cholesterol (HDL-C) was measured using the direct HDL method (Hitachi 917) [16]. Low density lipoprotein cholesterol (LDL-C) was calculated using the formula LDL-C = TC–(TG/2.2 + HDL-C). Very low density lipoprotein cholesterol (VLDL) was calculated by multiplying TG by 0.45 [16]. Cholesterol levels were considered to be normal at less or equal to 200 mg/dl, triglycerides at less or equal to 150 mg/dl, HDL-C at more than or equal to 50 mg/dl and LDL-C at less or equal to 130 mg/dl [17]. Disease activity was assessed using the systemic lupus activity measure (SLAM) [18].

Chest X-ray, computed tomography of chest and echocardiography were performed for suspected cases of pleurisy, interstitial pulmonary fibrosis and pancarditis. Renal biopsy was performed for those cases of suspected lupus nephritis based on laboratory and clinical data.

All the patients were on oral steroids except for four patients at the time of the study, 15 patients were on a dose of 10 mg/day and 29 patients took more than 10 mg/day. The mean steroid dose was 15.8 ± 8.6 mg/day with a mean duration of 3 ± 2.7 years. Twenty-one patients did not receive antimalarials. Twenty-seven patients received hydroxychloroquine (HCQ) with a mean dose of 183.3 ± 179 mg/day and a mean duration of intake of 2.7 ± 2.76 years. Ten of these patients received a dose of 200 mg/day of HCQ with a mean duration of intake of 3.71 ± 3.41 years and 17 patients received 400 mg/day with a mean duration of intake of 2.18 ± 2.35 years. Twenty patients received azathioprine with a mean dose of 97.5 ± 30.24 mg/day and a mean duration of intake of 2.79 ± 2.62 years. Five patients received pulse cyclophosphamide monthly infusions of 0.5-1 g/m^2 for 6 months for lupus nephritis and vasculitis but all had finished the infusions at least 3 months prior to entry in the study. In this study, 4 patients did not receive any medications, 1 received HCQ only, 11 patients took only prednisolone, 13 patients received prednisolone + HCQ, 13 patients took prednisolone + HCQ + azathioprine (AZA) and 7 patients took prednisolone + AZA.

Statistical analysis: Data were recorded and analyzed using the statistical package SPSS version 12. Data were expressed as mean ± standard deviation. Comparison between 2 groups was by Student's *t*-test and more than two groups by analysis of variance (ANOVA). Correlation was done by Pearson's correlation coefficient. *P* values less than 0.05 were considered statistically significant.

3. Results

The study included 48 adult SLE female patients with an age range between 17 and 45 years and a mean of 25.7 ± 7 years. The disease duration ranged between 2 months and 18 years with a mean of 5.9 ± 4.8 years. Systolic blood pressure ranged between 100 and 200 mmHg with a mean of 133.5 ± 25 mmHg and diastolic blood pressure ranged between 60 and 150 mmHg with a mean of 88 ± 17 mmHg. SLAM score