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Short Communication

Lipoprotein(a) and Lipids in Relation to Inflammation in Rheumatoid Arthritis

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Abstract: The aim of this study is to evaluate whether lipoprotein(a) (Lp(a)) acts as the acute phase reactant and whether changes of lipids are related to inflammation in rheumatoid arthritis (RA). Lp(a) and lipids were measured after an overnight fast, before and after 14 days use of antiinflammatory agents and correlated with laboratory findings in 21 untreated RA patients and 19 healthy controls. Nine (42.3%) of 21 RA patients and 6 (31.6%) of 19 controls had high Lp(a) levels (> 30 mg/dl) and the Lp(a) level was higher in RA patients compared with controls (27.1 ± 5.3 vs 19.0 ± 4.2 mg/dl) without significant difference ($p > 0.05$). There was no significant correlation between ESR and Lp(a) and lipids in RA patients except for HDL cholesterol ($r = –0.563$, $p = 0.008$). After antiinflammatory agent use for 14 days, change in ESR (ESRsample1–ESRsample2) was significantly and negatively correlated to changes in total and HDL cholesterols in RA patients. In conclusion, although Lp(a) tended to be higher in RA, we could not find a distinct acute phase pattern of Lp(a). But changes in total and HDL cholesterols were negatively correlated with inflammation in RA. Our data support the phenomenon that dyslipoproteinemia observed in RA is associated with inflammation.

Keywords: Lipid's; Lipoprotein(a); Rheumatoid arthritis

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Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with an increased mortality that is associated with cardiovascular and arterosclerosis [1–3]. Previous studies suggest that inflammation in RA might cause an altered lipid metabolism, which could be related to arterosclerotic disease [4,5].

Lipoprotein(a) (Lp(a)) is a plasma lipoprotein that consists of an LDL-like particle and the apolipoprotein(a) (apo(a)) linked to apoB-100 by a disulphide linkage [6]. From structural considerations it has been postulated that Lp(a) might have both proatherosclerotic and prothrombotic actions [7,8]. Although Lp(a) is also suggested to act as an acute-phase reactant in certain conditions, such as the period after acute myocardial infarction and surgery [9,10], this remains to be clarified. This study therefore sought to evaluate whether Lp(a) acts as the acute-phase reactant and whether a change of lipids is related to inflammation in RA.

Patients and Materials

Twenty-one untreated RA patients were recruited for this study in the rheumatology division at Korea University Hospital. All satisfied the RA diagnostic criteria of the American College of Rheumatology [11]. The mean age was 40.7 years (range 20–60). There were five men and 16 women. The mean disease duration was 23.8 months. The control group consisted of 19 people in good health. Their mean age was 44.8 years, with a range of 26–66 years. There were two men and 17 women. Neither the patients nor the controls had diabetes mellitus, renal disease or a history of cerebral or myocardial infarction, thrombosis, or any known familial hyperlipidaemia.

None was being treated with corticosteroids or non-steroidal antiinflammatory drugs on entry to the study.

Samples for Lp(a) and other laboratory tests were taken before and after 14 days' use of anti-inflammatory agents (40 mg piroxicam and 7.5 mg prednisolone daily). Serum Lp(a) levels were serially determined by nephelometry (Beckman, LPA, Denmark), with a measuring range from 2 to 128 mg/dl. The accuracy of the Lp(a) test showed a correlation coefficient of 0.994 compared to the ELISA. A level higher than 30 mg/dl was considered abnormal according to the manufacturer's instructions. Lipids such as total cholesterol, high-density lipoprotein (HDL) cholesterol and triglyceride were measured by routine methods. Low-density lipoprotein (LDL) cholesterol was calculated using a modified Friedewald equation, which corrects for the cholesterol present in Lp(a) [12]. In both patients and controls age, disease duration and body mass index (BMI, weight/height^2) were assessed before the therapy. Tender joint count, swollen joint count, morning stiffness and visual analogue scale (VAS) for pain were examined before the use of antiinflammatory agents in RA patients. White blood cells (WBC), platelets (plat), haemoglobin (Hb), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF) and fibrinogen were measured by routine methods.

The serum Lp(a) concentration in RA patients ranged from 3.5 to 85.0 mg/dl (mean $\pm$ SEM 27.2 ± 5.3 mg/dl); in the control group this was 2.0–48.6 mg/dl (mean ± SEM 19.0 $\pm$ 4.2 mg/dl). Nine (42.3%) of 21 RA patients and six (31.6%) of 19 controls had high Lp(a) levels (>30 mg/dl) but the difference was not significant. Lp(a) was not correlated to any clinical or laboratory findings, such as age, disease duration, BMI, ESR, CRP, lipids, fibrinogen, RF, WBC, Hb, plat, tender and swollen joint counts, morning stiffness or VAS. There were no correlations between ESR and Lp(a) and lipids in RA patients except for HDL cholesterol ($r = -0.563$, $P = 0.008$). After antiinflammatory agent use for 14 days, changes in ESR ($ESRsample_1 - ESRsample_2$) were significantly and negatively correlated to changes in total and HDL cholesterol, but not to changes in Lp(a) and triglyceride (Table 1).

In this study no significantly high level of Lp(a) or any relationship between Lp(a) and clinical and laboratory variables was found in RA patients, but a significant correlation was found between change of inflammation and change of lipids, including HDL and total cholesterols.

Table 1. Correlations between change in ESR and changes in Lp(a) and lipids in RA

Variables	*r*	Significance
Change in Lp(a)	0.172	NS
Change in total cholesterol	−0.489	0.046
Change in LDL cholesterol	−0.287	NS
Change in HDL cholesterol	−0.8866	0.001
Change in triglyceride	−0.068	NS

NS = not significant.

In conclusion, Lp(a) level was higher in RA than in control groups, but did not reach statistical significance and there was no relationship between Lp(a) level and clinicolaboratory findings in RA patients. However there was a significant correlation between change of inflammation such as change of ERS and changes of HDL and total cholesterols in RA patients.

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