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Action of Heparin on Lecithin:Cholesterol Acyltransferase Activity in Normal Subjects

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The triglyceride decrease and free fatty acid increase by lipoproteinlipase post-heparin effect does not modify the Lecithin:Cholesterol Acyltransferase activity *in vitro*, using homologous substrate, in normal subjects. These findings agree with the unmodified proportion of esterified cholesterol and relative proportion of phospholipids on thin layer chromatographic fractioning after heparin. The conclusion is reached that heparin has no action on Lecithin:Cholesterol Acyltransferase activity in normal subjects.

The Lecithin:Cholesterol Acyltransferase (LCAT) is synthesized in the liver and catalyses the formation of cholesterot esters and lysolecithin from unesterified cholesterol and lecithin substrate (2). Norum and Gjone (4) described in 1967 the first family with LCAT deficiency. Lipoprotein-X (LP-X), an anomalous low density lipoprotein of cholestasis is also found in the serum of patients with familial LCAT deficiency (9). We have described that LP-X is apparently cleared by a lipoprotein-lipase postheparin effect, and this is associated in some cases with a lecithin/lysolecithin ratio decrease after heparin in patients with cholestasis (5). Recently Ritland *et al.* (6) describe that the synthesis of LCAT was decreased during acute phase of myocardial infarction. Because some of patients with heart attack would receive heparin as treatment, is not only of theoretical interest but also of practical significance to investigate the effect of heparin on LCAT activity in normal subjects.

Materials and Methods

The study was carried out on twelve healthy male subjects (medical students and hospital staff) whose ages ranged from 19 to 32. The first blood sample was taken between 8 and 9 a.m. after overnight fast, and a second sample was taken 20 minutes after 25 mg of sodium heparin was given intravenously. Blood samples were processed immediately. LCAT activity was measured according to the meth-

od of GLOMSET and WRIGHT (3) using an excess of homologuos substrate (1). Inactivated plasma from a pool of normal subjects served as substrate for all analyses. It has been also investigated: total lipids, total cholesterol, triglycerides, lipid electrophoresis on cellulose acetate, and thin layer chromatographic fractioning of neutral lipids, cholesterol esters and phospholipids.

Results

All subjects showed a significant decrease in triglycerides after heparin ($p < 0.001$). In the lipid electrophoresis there was a decrease of prebetalipoproteins with an increase of prealphalipoproteins after heparin. The triglycerides/free fatty acids ratio (TG/FFA) on neutral lipids chromatographic fractioning fell significatively after heparin ($p < 0.001$). Total lipids, total cholesterol, esterified cholesterol, lecithin/lysolecithin ratio, and LCAT activity did not show significant variation after heparin. Figure 1 shows the results of LCAT activity in basal conditions and after heparin administration, and its relationship with TG/FFA ratio.

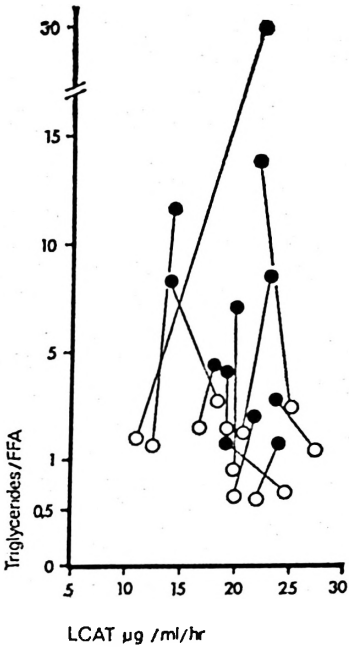

Fig. 1. *Relationship between LCAT activity and triglycerides/FFA ratio in basal conditions and after heparin* (●–○) *in twelve normal subjects.*
Triglycerides/FFA, $p < 0.001$; LCAT activity, p = N.S.

Discussion

In a previous study we suggested that heparin could have a LCAT-like effect because LP-X was cleared after heparin administration, and this was associated in some cases with a raised lecithin/lysolecithin ratio in basal conditions which diminished to normal values after heparin (5). At present it has not yet been established if LP-X acts directly as a substrate for LCAT (7, 10). Furthermore SODHI and KUDCHODKAR (8) have suggested that the presence of triglycerides in hypertriglyceridemic subjects inhibits the activity of LCAT *in vitro*. In our study the absence of modification neither on the proportion of esterified cholesterol, nor on the lecithin/lysolecithin ratio strongly suggest that heparin does not increases the LCAT activity *in vivo*. This seems to be in agreement with the absence of modification on LCAT activity *in vitro* when homologous substrate is used.

Resumen

El descenso de los triglicéridos y el aumento de los ácidos grasos libres después de la administración de heparina en sujetos sanos no modifica la actividad Lecitin:colesterol aciltransferasa. Estos resultados concuerdan con la ausencia de modificación en la proporción de colesterol esterificado y en la proporción relativa de fosfolípidos separados por cromatografía en capa fina. Se concluye que la heparina no tiene ningún efecto sobre la actividad Lecitin:colesterol aciltransferasa en los sujetos normales.

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