Smaller and ‘Herniated’ HDL in patients with type 2 diabetes mellitus

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CONTEXT AND OBJECTIVES

• Concerns have recently been raised regarding the use of the amount of HDL cholesterol (HDL-C) to predict cardiovascular events. The search for new suitable biomarkers such as the number of particles, the ratio between large and small particles or their cholesterol efflux capacity continues.

• In the present study, we hypothesized that the lipid distribution within HDL particles modulated by their size modifies their function, which is compromised in metabolic disorders with abnormal lipoprotein particle sizes such as type 2 diabetes mellitus (DM2).

MATERIALS AND METHODS

Study population

In this study we analyzed the HDL fraction of 26 controls and 29 DM2 patients (with atherogenic dyslipidemia) before and after two different interventions with niacin and fenofibrate. The HDL fractions were isolated and their cholesterol, triglycerides, protein and phospholipids content was quantified.

NMR analysis

HDL fractions were analyzed by NMR to obtain the size, the balance of large, medium and small particles and their spatial lipid distribution.

Fluorescence Analysis

Prodan fluorescence experiments were performed to evaluate the polarity of the probe microenvironment: a more hydrophobic microenvironment produces a blue shift on the emission maximum.

RESULTS

Shen Lipoprotein Model Modification

We modified the classical spherical model of lipoproteins to obtain the best agreement between the biochemical composition and the measured size.

\[
\frac{V_{\text{Shell}}}{V_{\text{Core}}} = \frac{4}{3} \pi R^3 - \frac{4}{3} \pi (R - 2)^3
\]

We characterized the spatial lipid distribution of the three major subfractions of HDL (large, medium and small). The percentage of core lipids located in the external shell increased as the radius decreased.

Particle distribution and biochemical composition

Our results showed an abnormal lipid distribution within smaller HDL particles, accentuated in the DM2 group, which presented a higher concentration of the small HDL subclass. The mean size of the HDL fraction corroborated this distribution.

Neither Niacin nor Fenofibrate reverted the pathological condition, characterized by smaller HDL particles and increased levels of TG in the lipoprotein core.

CONCLUSIONS

The reduction in particle size forced the hydrophobic lipids (cholesterol and triglycerides) to emerge from the lipoprotein core to the surface of the same, changing its polarity. The changes in surface polarity and composition of the hydrophobic lipids can modify the interactions between HDL particles and their environment, and might explain the dysfunctional behavior of the pathological group before and after the pharmacological interventions.

REFERENCES


We have no potential conflicts of interest to report

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