Hypothesis

Adiponectin represents an independent cardiovascular risk factor predicting serum HDL-cholesterol levels in type 2 diabetes

B. Zietz, H. Herfarth, G. Paul, A. Ehling, U. Müller-Ladner, J. Schölmerich, A. Schäffler*

Department of Internal Medicine I, University of Regensburg, D-93042 Regensburg, Germany

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Abstract Low levels of high-density lipoprotein (HDL)-cholesterol represent an independent cardiovascular risk factor and, besides reduced physical activity, mechanisms leading to decreased HDL-cholesterol levels are not known. We aimed to test the hypothesis, that adiponectin provides a missing link between type 2 diabetes and low levels of HDL-cholesterol, independent from common metabolic risk factors. 523 patients with type 2 diabetes were investigated for adiponectin serum levels and parameters of lipid metabolism. Even after correction for age, gender, BMI and fasting insulin concentration, serum levels of adiponectin were highly significant ($P < 0.0001$) and positively (regression analysis: $r = 0.86$) associated with HDL-cholesterol levels in type 2 diabetes. Conclusion: adiponectin seems to predict HDL-cholesterol levels in patients with diabetes mellitus type 2. Low levels of adiponectin are associated with low levels of HDL-cholesterol independently from common metabolic risk factors and therefore represent an independent cardiovascular risk factor in type 2 diabetes. Thus, adiponectin is a potentially new drug target in the treatment of dyslipidaemia.

Key words: Diabetes; Adiponectin; Adipocyte; High-density lipoprotein-cholesterol; Lipid metabolism

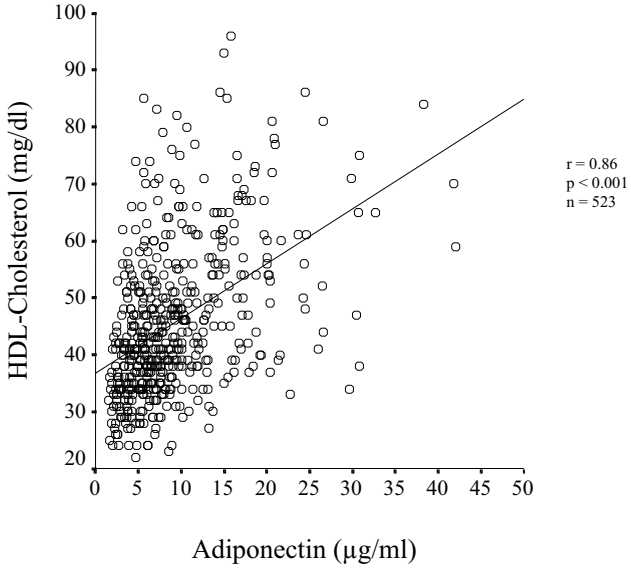

Fig. 1. Adiponectin serum levels (µg/ml) are highly significantly and positively associated with HDL-cholesterol levels (mg/dl) independent from age, gender, BMI and fasting insulin concentration ($P < 0.0001$, regression analysis: $r = 0.86$).

High-density lipoprotein (HDL)-cholesterol represents a common and independent protective cardiovascular risk factor. Cardiovascular risk increases with decreasing levels of HDL-cholesterol. While lipid lowering and antidiabetic drugs such as statins, fibrates, and PPARγ agonists as well as diet alone have only marginal effects on serum HDL-cholesterol levels, physical activity is able to elevate effectively HDL levels. Since type 2 diabetes mellitus and obesity are associated with low levels of HDL-cholesterol, a reduced physical activity has been regarded as the main mechanism standing behind these low levels. Adiponectin [1–4] represents a newly discovered adipocyte-specific secretory protein. Its expression is highly restricted to terminally differentiated adipocytes. Adiponectin is secreted into the plasma and represents a new member of the recently described C1q/TNF molecular superfamily [3]. Since adiponectin is the only known adipocyte-specific secretory protein in the human system, that is exclusively and paradoxically decreased in obesity and type 2 diabetes [1,4], we aimed to test the hypothesis that adiponectin might influence HDL-cholesterol levels. For that purpose, a large cohort of Caucasian patients with type 2 diabetes was investigated for serum adiponectin levels and parameters of lipid metabolism. Human adiponectin serum concentrations were measured by enzyme-linked immunosorbent assay (ELISA) according to the protocol provided by the manufacturer (human adiponectin ELISA kit, Biocat, Heidelberg, Germany). 523 subjects, 296 males (56.6%) and 227 females (43.4%), were included in the study. The main question was whether adiponectin serum levels may predict HDL-cholesterol levels after correction for age, gender, diabetes duration, HbA1c, BMI and fasting insulin levels. As depictured in Fig. 1, we were able to demonstrate a strong and highly significant ($P < 0.0001$) positive correlation between adiponectin and HDL-cholesterol levels (regression analysis: $r = 0.86$). Adiponectin serum levels were correlated to HDL-cholesterol even if factors such as age, gender, BMI and fasting insulin concentration were excluded.

Adiponectin seems to predict HDL-cholesterol levels in patients with diabetes mellitus type 2 independent from common

*Corresponding author. Fax: (49)-941-944 7019.
E-mail address: andreas.schaeffler@klinik.uni-regensburg.de (A. Schäffler).

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metabolic factors. Low levels of adiponectin are associated with low levels of HDL-cholesterol and might represent an independent cardiovascular risk factor, whereas high levels of adiponectin are associated with high levels of HDL-cholesterol indicating a protective risk profile. Adiponectin is therefore discussed as a potentially new drug target in the treatment of dyslipidaemia and investigating the mechanism standing behind the observed associations might provide the basis for the development of 'adiponectin agonists' as HDL-enhancing drugs.

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