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SHORT COMMUNICATION

Plasma apolipoprotein C1 concentration is associated with plasma triglyceride concentration but not with visceral fat and liver fat content in people with type 1 diabetes

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Introduction

We have published previously an article entitled 'Plasma apolipoprotein C1 concentration is associated with plasma triglyceride concentration but not with visceral fat in patients with type 2 diabetes' [1]. After further research, we now have new data about the role of apolipoprotein C1 (apoC1) in triglyceride (TG) metabolism in people with type 1 diabetes (T1D).

ApoC1 is involved in the metabolism of triglyceride-rich lipoproteins by inhibiting the binding of very-low-density lipoproteins (VLDL) to VLDL receptors, to low-density lipoprotein receptors and to LDL receptor-related proteins by diminishing the activity of lipoprotein lipase and by stimulating the production of VLDL. All these effects lead to increased plasma TG in transgenic mice with an overexpression of human apoC1 [1]. ApoC1 might play a role in the regulation of fat mass because these mice experience a decrease in total adipose tissue stores [1] which is the result of lower uptake of fatty acids by adipocytes. In animal models, the role of apoC1 in steatosis is more uncertain. The results of two existing studies on mice are conflicting since both mice overexpressing apoC1 and mice deficient in apoC1 had increased levels of TG in the liver [1].

There is currently little published research about a possible association between apoC1, adipose tissue and liver fat content (LFC) in humans. In 2016, we conducted a study on people with type 2 diabetes (T2D), who are known to have abnormalities of adipose tissue, LFC and TG metabolism [2]. We found that there was a significant correlation between apoC1 and plasma TG, but no association between apoC1 and adipose tissue (mass, distribution) and LFC in our population [1]. We concluded that adipose tissue and LFC are not modulated by apoC1 in T2D.

Since the obesity epidemic affects adults with T1D and several recent studies have demonstrated a link between liver fat content and type 1 diabetes [3], it seems important to determine whether our results are similar in people with T1D, especially considering that the two major types of diabetes have a very different physiopathology.

Methods

We included 70 people with T1D and 56 normoglycaemic–normolipidaemic control subjects. The method was the same as in our previous study [1]. Briefly, all participants were > 18 years of age and not taking any treatment that could interfere with lipid metabolism. Alcohol consumption was less than 20 g/day. Fasting apoC1 was measured in total plasma by a specific ELISA using an anti-human apoC1 antiserum from rabbit. We obtained a single-slice axial T1-weighted image from the level of the L4/L5 intervertebral disc in order to evaluate the quantity of visceral adipose tissue and subcutaneous adipose tissue in the cross-sectional area. LFC was evaluated using MR imaging with a 3.0 Tesla Magnetom TRIO TIM whole-body system (Siemens, Erlangen, Germany). Hepatic steatosis was defined as LFC ≥ 5.5%. We obtained approval from our institutional review board before performing this cross-sectional single-centre study. Written informed consent was obtained from all included patients.

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Results

We report that plasma apoC1 concentration (100.9 ± 27.6 vs. 57.6 ± 5.2 mg/l, $P < 0.0001$) was significantly higher in people with T1D than in control subjects, whereas the plasma TG concentration was similar in the two groups. Visceral fat area (103.7 ± 58.3 vs. 75.7 ± 45.4 cm^2, $P < 0.004$) and the percentage of visceral fat (31.5 vs. 22.7%, $P < 0.0001$) were significantly higher in people with T1D than in control subjects, whereas the percentage of subcutaneous fat was significantly lower in people with T1D than in control subjects (68.3 vs. 77.3%, $P = 0.0008$) (Table 1). Liver fat content was significantly higher in people with T1D than in control subjects, but it was still in normal range.

In people with T1D, plasma apoC1 correlated with TG level ($P = 0.002$), with AST ($P < 0.001$) and with ALT ($P < 0.0001$). The TG level did not correlate with AST and ALT. Plasma apoC1 did not correlate with the area of visceral fat, the area of subcutaneous fat or with LFC. There was no correlation between plasma apoC1 and the percentage of visceral fat or subcutaneous fat. Plasma apoC1 concentration was not significantly different under and above the median value of total fat area (107.2 ± 29.2 vs. 95.9 ± 24.4 mg/l, $P = 0.15$). This result was similar in controls. In a multivariate analysis of the total population, plasma apoC1 was independently and positively associated with type 1 diabetes ($P < 0.0001$), TG levels ($P = 0.034$) and AST ($P = 0.022$). HDL concentration was higher in people with T1D than in controls, which is in accordance with the data of the literature [4]. Thus, we separated people with T1D and HDL < 1.6 mmol/l, in which mean HDL was 1.28 ± 0.25 mmol/l. ApoC1 concentration was still higher in people with T1D and HDL < 1.6 mmol/l than in controls, in which mean HDL was 1.27 mmol/l (99 ± 28.8 vs. 57.6 ± 15.2, $P < 0.0001$). As mean HbA1C was 8.7% in people with T1D, we separated people with HbA1C < 8%, in which mean HbA1C was 7 ± 0.7%. In this subgroup, apoC1 correlated with TG level ($P = 0.009$) and did not correlate with AST ($P = 0.05$), ALT, the area of visceral fat, the area of subcutaneous fat or with LFC.

Table 1 Characteristics of the study population

	Controls $n = 56$	People with T1D $n = 70$
Age	40.6 ± 14.3	42.1 ± 15.9
Gender M [(*n* (%)]	24 (43)	39 (56)
Weight (kg)	72.5 ± 16.9	74.6 ± 16.5
BMI (kg/m^2)	25.4 ± 4.8	25.7 ± 5.3
Glycaemia (mmol/l)	4.9 ± 0.4	9.7 ± 4.4[b]
HbA1C (mmol/mol) (%)	ND	95.09 ± 19.7 8.7 ± 1.8
ASAT (Units/l)	22 ± 9	18.4 ± 22.9[b]
ALAT (Units/l)	19 ± 5	33.8 ± 40.3[b]
GGT (Units/l)	29 ± 15	38.1 ± 43.6
Total cholesterol (mmol/l)	4.87 ± 0.84	4.94 ± 1.26
HDL-C (mmol/l)	1.27 ± 0.31	1.62 ± 0.46[b]
LDL-C (mmol/l)	2.98 ± 0.61	2.84 ± 1.05
Triglycerides (mmol/l)	1.09 ± 0.36	1.16 ± 0.77
ApoC1 mass (mg/l)	57.6 ± 15.2	100.9 ± 27.6[b]
Visceral fat area	75.7 ± 45.4	103.7 ± 58.3[a]
% of total fat area	22.7	31.5[a]
Subcutaneous fat area (cm^2)	270.1 ± 136.6	242 ± 122.8
% of total fat area	77.3	68.5[a]
Total fat area (cm^2)	345.8	345.7
Liver fat content (%)	2.3 ± 3.8	2.8 ± 3.5[b]
Steatosis (LFC > 5%) *n* (%)	6 (10.7)	6 (8.6)

Data are mean ± SD unless otherwise indicated

Total fat area = visceral fat area + subcutaneous fat area

AST aspartate aminotransferase, *ALT* alanine aminotransferase, *GGT* gamma-glutamyl transferase; *LFC* liver fat content; *T1D* type 1 diabetes

[a,b] Significantly different from controls, $P < 0.05$, $P < 0.001$, respectively

Conclusion

In the current study, apoC1 was increased in people with T1D and associated with plasma triglycerides. On the contrary, no correlation was found between apoC1 and the area of adipose tissue (visceral and subcutaneous), adipose tissue distribution (visceral vs. subcutaneous) or with liver fat content. Our findings were similar in a subgroup of people with good metabolic control. Our results suggest that the increased apoC1 concentration in people with T1D is not explained by the higher HDL concentration in people with T1D. While the physiopathology of type 1 diabetes and type 2 diabetes is dissimilar, our findings are consistent with our previous study of T2D. As in T2D, apoC1 is probably not a significant determinant of adipose tissue storage and liver fat content in people with T1D. As some studies have shown that the Mediterranean diet has a favourable effect on TG level [5], it could be interesting to determine the effect of this type of diet on apoC1 concentration. Because people with T1D develop abnormalities in fat mass distribution and triglyceride metabolism, and because apoC1 is strongly involved in the metabolism of triglyceride-rich lipoproteins, our results contribute to the current understanding of how apoC1 influences lipid metabolism. Further studies are necessary, especially in humans, to determine the precise role of apoC1 in lipid metabolism.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Human and animal rights disclosure All procedures performed in the study were in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from all included patients.

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