

Postprandial lipemia and exercise in type 2 diabetes mellitus

M. Castro Cabezas

Department of Vascular Medicine. University Medical Center Utrecht. Países Bajos.

Diabetes mellitus is becoming one of the major problems of healthcare in Western Society¹. In the Netherlands, with a population of 17 million inhabitants, there are at least 260,000 recognized type 2 diabetes patients². It has been estimated that at least a similar number of patients with type 2 diabetes has not been detected yet, and therefore the estimated prevalence is 17 patients per 1,000 inhabitants³. National programs are being set up to identify those patients who have not been diagnosed yet and several organizations are involved in this case-finding program, partly subsidized by the National Health Institute and the Dutch Diabetes Association.

In addition to the early identification of type 2 diabetes, an even major challenge is the appropriate treatment of these patients. There is no doubt that adequate control of glucose metabolism is of paramount importance to reduce the risk for microvascular complications⁴. However, reduction of the disproportionately high risk for cardiovascular mortality in patients with type 2 diabetes is still a challenge for clinical practice. In the landmark UKPDS study, intensive treatment directed to optimize the regulation of carbohydrate metabolism was not enough to reduce cardiovascular mortality significantly⁴. It is well accepted that the modulation of other risk factors will be obligatory⁵. The well-known risk factors in diabetics, such as fasting dyslipidemia (high triglycerides, low HDL-C) and the presence of small-dense LDL, may well be treated with classical lipid-lowering drugs (statins and/or fibrates)⁶. However, concealed risk factors like postprandial dyslipidemia are difficult to assess, and even more difficult to manage^{7,8}. The

cumbersome oral fat loading tests used to establish the diagnosis of postprandial hyperlipidemia are not a practical tool to be used by clinicians^{7,8}. Even more difficult is the follow-up after initiation of therapy, as responses to interventions aimed to improve postprandial lipemia can not be evaluated. This is a major problem because type 2 diabetes is closely linked to postprandial hyperlipidemia⁶. For the purpose of simplification, it may be said that all patients with type 2 diabetes have postprandial hyperlipidemia and that fasting normolipidemia does not exclude the presence of this important risk factor. In our department, a novel method has been developed which estimates postprandial lipemia using repeated self-measurements of capillary triglycerides on fixed time-points in an uncontrolled, out-of-hospital situation^{9,10}. In this way postprandial lipemia is calculated as the area under the diurnal triglyceride profile (cTG-AUC). This parameter correlates well with postprandial lipemia assessed by standardized oral fat loading tests¹⁰. Moreover, in patients with normal fasting plasma lipids and premature atherosclerosis, cTG-AUC is the strongest lipid-associated parameter, with a positive predictive power of almost 80%, and cTG-AUC is modifiable by aggressive lipid lowering therapy¹¹. In patients with type 2 diabetes and obesity, cTG-AUC is higher than in lean controls¹². These data suggest that diurnal triglyceridemia may be used as practical tool for the detection and optimal management of patients at high risk for atherosclerosis, such as those with type 2 diabetes.

Besides pharmacological interventions to improve the metabolic regulation in type 2 diabetes mellitus, life-style interventions have been applied by several investigators^{13,14}. However, there are not many reports on life-style changes in type 2 diabetes which are aimed to improve postprandial lipemia and are applicable in clinical practice. The paper by Sánchez Juan et al¹⁵ is a fine example of an attempt to improve postprandial lipemia in overweight, type 2 diabetes patients by introducing a

Correspondencia: Dr. M. Castro Cabezas.
Department of Vascular Medicine F02.126.
University Medical Center Utrecht.
P.O Box 85500. 3508 GA Utrecht. Países Bajos.
Correo electrónico: m.castrocabezas@azu.nl

physical activity program. This elegant study included a small number of patients and a well-matched control group of healthy controls. Patients were randomized to a moderate physical activity program or a control group. The authors were able to confirm that postprandial hyperlipidemia is present in type 2 diabetes compared to non-diabetic subjects, probably related to the higher fasting concentrations of triglyceride-rich particles in the patients. Although the intervention did not result in a significantly lower postprandial area under the triglyceride curve compared to baseline, postprandial lipemia was significantly improved compared to the control patients (who did not exercise). In addition, the postprandial peak values of triglyceride-rich lipoproteins were almost reduced by 50%, although the fasting concentrations were similar. These data represent a significant improvement by non-pharmacological intervention of this concealed risk factor of postprandial hyperlipidemia. This study is important since the results clearly underscore the usefulness of a multiple risk factor intervention approach in type 2 diabetes in a multidisciplinary setting. In the future, the use of self-measurements of diurnal triglyceridemia by patients with type 2 diabetes may help to enhance their awareness of risk-profiles and the impact of relatively simple daily measures like half an hour of brisk walking.

Bibliografía

1. Grundy SM, Benjamin IJ, Burke GL, Chait A, Eckel RH, Howard BV et al. Diabetes and cardiovascular disease. A statement for healthcare professionals from the American Heart Association. *Circulation* 1999; 100: 1134-1146.
2. Ruwaard D, Feskens EJM. Suikerziekte. En: Rijksinstituut voor Volksgezondheid Toekomst Verkenning 1997. I. De Gezondheidstoestand: een actualisering. Rijksinstituut voor Volksgezondheid en Milieu. Bilthoven, 1997; 269-280.
3. Mooy JM, Grootenhuys PA, Vries de H, Valkenburg HA, Bouter LM, Heine RJ. Prevalence of determinants of glucose intolerance in a Caucasian population. The Hoorn Study. *Diabetes Care* 1995; 18: 1270-1273.
4. UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; 352: 837-853.
5. Lehto S, Ronnema T, Pyorala K, Laakso M. Cardiovascular risk factors clustering with endogenous hyperinsulinaemia predict death from coronary heart disease in patients with type II diabetes. *Diabetologia* 2000; 43: 148-155.
6. Van Wanrooy F, Stolk R, Castro Cabezas M, Erkelens DW. Diabetic dyslipidemia: metabolic and epidemiological aspects. En: Betteridge DJ, editor. *Current perspectives in diabetes*. Londres: Martin Dunitz Ltd., 1999; 125-139.
7. Castro Cabezas M, Erkelens DW. The direct way from gut to vessel wall: Atheroinitiation. *Eur J Clin Invest* 1998; 28: 504-505.
8. Castro Cabezas M, Erkelens DW. Triglycerides and atherosclerosis: To feast or fast. *Neth J Med* 2000; 56: 110-118.
9. Van Oostrom AJHHM, Castro Cabezas M, Ribalta J, Masana LL, Twickler ThB, Remijnse TA et al. Diurnal triglyceride profiles in healthy normolipidemic male subjects are related to insulin sensitivity, body composition and diet. *Eur J Clin Invest* 2000; 30: 964-971.
10. Castro Cabezas M, Van Oostrom AJHHM, Erkelens DW. Gender differences in diurnal triglyceride profiles in healthy normolipidemic subjects. *Atherosclerosis* 2001; 155: 219-228.
11. Halkes CJM, Van Wijk J, Erkelens DW, Castro Cabezas M. Diurnal triglyceridemia: a novel risk factor for premature atherosclerosis? *Eur J Clin Invest* 2001; 31 (Supl 1): 29-30.
12. Halkes CJM, Castro Cabezas M, Van Wijk JPH, Erkelens DW. Diurnal triglyceridemia and insulin resistance in mildly obese subjects with normal fasting plasma lipids and lean subjects. *Intern J Obesity* 2001. En prensa.
13. Ligtenberg PC, Hoekstra JBL, Zonderland ML, Erkelens DW. Physical activity and diabetes mellitus: a review. *Eur J Intern Med* 1995; 6: 95-108.
14. Ligtenberg PC, Hoekstra JBL, Bol E, Zonderland ML, Erkelens DW. Effects of physical training on metabolic control in elderly type 2 diabetes mellitus patients. *Clinical Science* 1997; 93: 127-135.
15. Sánchez Juan C, Cucó Alberola A, Ascaso JF. Influence of moderate physical exercise on postprandial lipemia in non-obese, type 2 diabetes patients. *Clin Invest Arterioscler* 2001; 13: 139-147.