

## Editorial

### Postprandial hyperglycemia: Clinical significance and management

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Type 2 diabetes incidence is increasing in epidemic proportions throughout the world. Today 177 million people suffer from diabetes and this number will increase to at least 300 million in the next 20 years. The chronic complications of this disease have devastating consequences on quality of life and life expectancy and impose a great burden to individuals and society. About 4 million deaths in every year are attributable to diabetes complications, predominantly cardiovascular.

Macrovascular complications (especially ischemic heart disease, peripheral arteriopathy, ischemic cerebrovascular disease) are the leading cause of morbidity and mortality in type 2 diabetes.

As compared to non-diabetic individuals, people with type 2 diabetes have an increased (2 to 4 fold) risk of dying from a cardiovascular event (stroke or myocardial infarction), and a 10 fold increased risk for nontraumatic amputation of lower extremity.

Unfortunately, cardiovascular complications are already present in a significant number of newly diagnosed patients. There is evidence that the cardiovascular risk is increased long before the onset of clinical diabetes and cardiovascular complications may appear early, during the preliminary phases leading to clinical diabetes. These preliminary phases are characterized by clustering of cardiovascular risk factors as metabolic syndrome.

Elevated plasma glucose levels are independent risk factors for micro and macrovascular complications.

The current targets (HbA1c <7.0%) for glycemic control are based on epidemiological data and controlled clinical trials that have demonstrated that maintaining HbA1c levels under 7.0% is associated with prevention of microvascular complications.

Although, in patients with diabetes, a good glycemic control (hemoglobin A1c < 7.0%) can substantially reduce the occurrence of microvascular complications and prevent their

progression (neuropathy, nephropathy, retinopathy), multiple observations suggest that a more strict glycemic control is needed in order to prevent macrovascular complications.

Even slightly elevated plasma glucose levels associated to HbA1c levels within normal (<6.1%) levels such as isolated postprandial hyperglycemia are associated to an increased risk of cardiovascular complications and death.

The EPIC-Norfolk (European Prospective Investigation of Cancer and Nutrition) study (1) has measured HbA1c (at baseline: 1995-1997) in a cohort of 4662 men aged 45 to 79 years followed (up to December 1999) for mortality from all causes, cardiovascular disease and ischemic heart disease.

As compared to the group with lowest (< 5%) HbA1c concentrations, a 1% increase in HbA1c levels was associated with a 28% increase in risk of death. Remarkable, 82% of the excess mortality occurred in men with HbA1c levels between 6%-6.9%.

Glycated hemoglobin explained most of the excess mortality, independent of diabetes, age, blood pressure, serum cholesterol, cigarette smoking and BMI.

This study showed glycated hemoglobin (reflecting glycemic exposure) to be a continuous risk factor in the whole population.

Another important conclusion of this study, supported also by the well known Monnier study (2) is that normal HbA1c levels can be associated with a substantially increased risk of death from CV disease and that normal or slightly abnormal increased HbA1c levels may be due to postprandial hyperglycemia.

The Diabetes Epidemiology Collaborative Analysis of Diagnostic Criteria in Europe (3) study (DECODE) has found, in a 22514 individuals cohort, followed up for 8.8 years, an increased risk for death from all causes and cardiovascular events in people with IGT and type 2 diabetes. Remarkably, in people with IFG there was no increased risk.

An increased cardiovascular risk was also observed in people with IGT or elevated 2-hour postprandial plasma glucose levels during many population prospective studies (4-6) whereas the link between diabetic complications and fasting hyperglycemia was found inconsistent.

During Framingham Offspring study (7), the fasting glucose levels were not associated with cardiovascular risk whereas isolated postchallenge hyperglycemia (8,9) was a significant predictor for general mortality and fatal cardiovascular disease in two other studies.

Is postprandial hyperglycemia a risk factor or is it a marker of increased risk?

If it is a risk factor indeed, then targeting postprandial hyperglycemia would reduce the cardiovascular risk.

In a recent meta-analysis (10), incorporating seven randomized double-blind, placebo-controlled studies in 2180 type 2 diabetes patients, there was a 35% reduction in relative risk for total cardiovascular events with acarbose ( $\alpha$ -glucosidase inhibitor) treatment.

The effect of reducing postprandial hyperglycemia with acarbose treatment was

examined in a subgroup analysis of the study to prevent diabetes STOP-NIDDM trial (11). In patients with IGT treated with acarbose, as compared to those treated with placebo, the annual increase in carotid intima-media thickness (IMT) was halved. This study support the concept that treating postprandial hyperglycemia slows the evolution of atherosclerosis.

Similar results by control of postprandial hyperglycemia in type 2 diabetic patients were reported in another study (12).

Several mechanisms have been proposed to explain the link between postprandial hyperglycemia and cardiovascular risk.

The recent IDF guideline for postmeal glucose management present recommendations for the management of postmeal glucose in people with diabetes.

These recommendations, based on actual knowledge of the relationship between postmeal glucose and the development of diabetic complications, are intended to help clinicians to develop efficient strategies for management of postmeal hyperglycemia in patients with type 1 and type 2 diabetes.

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