Post-prandial Hyperglycaemia & Cardiovascular Disease: An Endocrinologist’s Perspective

Dr. Peter TONG

Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital

There is now a global epidemic of diabetes and obesity affecting more than 300 million people worldwide with Asia in the forefront. These silent conditions independently and collectively contribute to 50% of all causes of death mainly due to cardiovascular and renal complications. The major burden of diabetes is from the treatment costs of its complications, such as stroke, blindness, coronary artery disease, renal failure, amputation and infection. Diabetes is associated with approximately 2-fold increased mortality in most populations, with the risks decreasing with increasing age1,4. Cardiovascular disease is 76% more prevalent in subjects with diabetes. In particular, the prevalences of acute myocardial infarction and congestive heart failure are high in these subjects5. It is well established that the occurrence of vascular complications of diabetes is related to the duration of hyperglycaemia. With the earlier onset of type 2 diabetes, most patients will have increased risks of developing these devastating complications.

The UK Prospective Diabetes Study (UKPDS) showed that the lowering of fasting plasma glucose levels was associated with significant reductions in microvascular complications. However, such interventions were less effective in reducing the risk of macrovascular complications. In contrast, population studies showed that postprandial hyperglycaemia was a risk factor for cardiovascular and all-cause mortality in different ethnic groups6-9. Importantly, postprandial glucose levels were more strongly associated with all-cause mortality and cardiovascular risks than fasting glucose values10. The DECODE analysis demonstrated that 2-hour post-meal plasma glucose correlated with the risks of all-cause and cardiovascular mortality. There was a stepwise increasing relationship between the hazard ratio for mortality for cardiovascular disease and 2-hour plasma glucose, but not fasting plasma glucose levels 2. In a similar analysis of more than 6000 subjects in Asia (DECODA), the risks of both all-cause and CVD mortality significantly increased with increasing 2-hour post-meal plasma glucose levels. In contrast, there was no difference in the risk of mortality with increasing fasting plasma glucose values11.

Despite the strong relationship between abnormal glucose levels and cardiovascular risks, the prevalence of dysglycaemia in subjects with coronary artery disease (CAD) was not well documented. Of 4961 patients with CAD in the Europe Heart Survey, 31% were known suffering from type 2 diabetes. Following assessment by oral glucose tolerance test (OGTT) in the remaining patients, a further 21% had impaired fasting glucose (2%), impaired glucose tolerance (12%) or newly diagnosed type 2 diabetes (7%) 12. In the Glucose Tolerance in Patients with Acute Myocardial Infarction (GAMI) Study, 66% of subjects with no history of diabetes had dysglycaemia at discharge from hospital13. In the China Heart Survey, 33% of 3513 patients with CAD had type 2 diabetes at enrollment. Based on fasting plasma glucose values, 3% had newly diagnosed type 2 diabetes. Following OGTT in the remaining patients, 17% were found suffering from newly diagnosed diabetes and 24% had impaired glucose tolerance. Taken together, 77% of Chinese patients with CAD had abnormal glucose tolerance14.

These epidemiological studies suggested a close link between post-prandial hyperglycaemia and CAD. Several underlying mechanisms have been proposed to be involved in hyperglycaemia-induced vascular damage. These include activation of protein kinase C signalling pathway, oxidative stress and glycosylation of protein. The increase in free radicals from oxidative stress and the up-regulation of genes cause an increase in the proliferation of smooth muscle cells, the expression of adhesion molecules and growth factors. These changes lead to endothelial dysfunction with increased vessel wall thickness, vascular permeability and loss of elasticity15-17. Hence, glucotoxicity plays a key part in the development of generalised vascular dysfunction leading to retinopathy, albuminuria and accelerated atherosclerosis.

Among individuals with glucose intolerance, reducing the cardiovascular risks is a major unmet need. There is significant increase in the risks of cardiovascular morbidity and mortality in subjects in early stages of diabetes. To reduce macrovascular complications, both fasting and postprandial hyperglycaemia should be targeted. Interventions that focused on lowering fasting plasma glucose may not offer optimal risk reduction in cardiovascular complications. There are now therapeutic options available to address the issue of post-prandial hyperglycaemia. Pharmacological agents that specifically target post-prandial glucose include α-glucosidase inhibitors, glinides (rapid-acting insulin secretagogues) and insulin. New classes of therapies (glucagon-like peptide-1 [GLP-1] derivatives, dipeptidyl peptidase-4 [DPP-4] inhibitors) which address deficiencies in pancreatic and gut hormones also have beneficial effects on controlling post-prandial hyperglycaemia. Regarding the targets for post-prandial glycaemic control, the International Diabetes Federation recommended that 2-hour post-meal plasma glucose level of < 7.8 mmol/L using the self-monitoring of blood glucose approach18.
In conclusion, abnormal glucose tolerance is common among patients with coronary heart disease, but is often undiagnosed. Using the oral glucose tolerance test, the Euro Heart Survey and the China Heart Survey showed that nearly three-quarters of these patients had dysglycaemia, with one-third of these patients known to have type 2 diabetes. Postprandial hyperglycaemia contributes to increased cardiovascular risk. Efforts should be made to identify at risk subjects with oral glucose tolerance test, and to manage these high risk subjects with lifestyle modifications and appropriate pharmacologic therapy.

References