Importance of postprandial hyperglicemia to controlling diabetes

Importância da hiperglicemia pós-prandial no controlo da diabetes

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Abstract

Many studies have demonstrated a strong relationship between postprandial hyperglycaemia and the development and progression of diabetes related macrovascular diseases, retinopathy, nephropathy and neuropathy. Therefore, therapies targeting elevated after meals glucose seem to be beneficial, although this has not yet been confirmed by randomized controlled trials. The International Diabetes Federation recommends the following goals for the diabetes clinical management: HbA_{1c} < 6.5 %, before meals (fasting) glycaemia 5.5 mmol/l (< 100 mg/dl), and 2-hour after meal glycaemia 7.8 mmol/l (<140 mg/dl). This short communication examines all these aspects.

Key words: diabetes, fasting glycaemia, postprandial glycaemia, haemoglobin HbA_{1c}, vascular consequences of diabetes, diabetic neuropathy.

Resumo

Muitos trabalhos têm demonstrado uma relação próxima entre a hiperglicemia pós-prandial e o aparecimento e a progressao das complicações da diabetes, tais como as doenças macrovasculares, a retinopatia, a nefropatia e a neuropatia. Terapias com o fim de melhorar a glicemia após as refeições parecem ter vantagem, embora a sua eficácia ainda não tenha sido confirmada por estudos randomizados e controlados. Segundo a Federação International de Diabetes os valores seguintes indicam um bom controlo da diabetes: HbA_{1c} < 6,5 %, glicemia pré-prandial (em jejum) 5,5 mmol/l (< 100 mg/dl), glicemia às 2 horas pós-prandial 7,8 mmol/l (< 140 mg/dl). Esta comunicação breve examina todos estes aspectos.

Palavras-chave: diabetes, glicemia em jejum, glicemia pós--prandial, hemoglobina $HbA_{1c,}$ consequências vasculares da diabetes, neuropatia diabética.

INTRODUCTION

Diabetes is, due to its related macrovascular and microvascular diseases, and neuropathy, a leading cause of death all over the world.[1,2,3] There is a strong association between poorly controlled diabetes and the development and progression of above mentioned diabetes complications.[1,3] Intensive glucose control in individuals with impaired glucose tolerance or type 1 diabetes reduces the risk for cardiovascular disease.[1] It seems that lower the glycated hemoglobin (HbA1c) is, the lower the risk for microvascular or macrovascular complications in types 1 and 2 diabetes will be.[1]

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Traditionally, diabetes control has predominantly focused on reducing HbA1c levels and fasting or pre--prandial glycemia.[1,3] However, studies have further demonstrated the importance of determining postmeal glucose since it has been suggested that lowering postprandial glucose is more important for achieving HbA1c goals; these studies support the notion of a relationship between postmeal hyperglycaemia and the risk of diabetic complications.[1,3]

The present article is mainly based on the International Diabetes Federation (IDF) guideline for management of postmeal glucose, 2007.

DEFINITION, PATHOGENESIS AND EFFECTS

Postprandial glycaemia in subjects with normal glucose tolerance

In people with normal glucose tolerance, glycemia generally increases no higher than 7.8 mmol/L (140 mg/dL) in response to meals and returns to premeal levels within two to three hours; the World Health Organization (WHO) defines normal glucose tolerance as < 7.8 mmol/L (140 mg/dL) two hours following ingestion of a 75-g glucose load; postmeal

hyperglycemia is defined as a glycemia > 7.8 mmol/l (140 mg/l) two hours after a meal.[1,3,4]

Postprandial hyperglycaemia in types 1 and 2 diabetes

Elevated postmeal glucose levels are frequently found in type 1 and type 2 diabetes, even when metabolic control appears to be adequate as assessed by HbA1c.[1,3] During 72-h continuous monitoring, subjects with type 1 diabetes show postprandial hyperglycaemia in 77 % of cases.[1,3] In a study involving 218 subjects with type 2 diabetes, about 74 % of individuals had postmeal hyperglycemia, although 39 % of those had a HbA1c < 7.0 %.[1,3]

In type 2 diabetes, prior to clinical manifestation, increases in postprandial glucose levels were found; these result mainly from a decrease of insulin sensitivity in peripheral tissues, the loss of first-phase insulin secretion, a reduction of late-phase insulin secretion, and consequent decrease of suppression of hepatic glucose output after meals, because of insulin deficiency; fasting hyperglycaemia is due to a defect in hepatic insulin sensitivity and first-phase insulin secretion.[1,3,5]

Fasting glycemia, postprandial glycemia and HbA_{1c}

Studies have demonstrated that targeting postmeal hyperglycemia contributes to optimize HbA_{1c}; diabetic individuals achieving a target HbA1c equal to or lower than 7.0 % have significantly lower postprandial glycemia after a 3-month intensified therapy compared with those who did not; fasting glycemia is not significantly different between the two groups; these findings suggest that, although control of fasting glucose is necessary, it is not sufficient for achieving HbA1c target.[1,3]

Postprandial hyperglycaemia and macrovascular diseases

According to a recent meta-analysis, the relative risk for myocardial infarction (MI) and stroke is increased by almost 40 % in type 2 diabetes population compared with non-diabetic people; the increased risk in subjects with impaired glucose tolerance (IGT) is nearly one-third of that observed in individuals with type 2 diabetes.[1,3] Studies have demonstrated that postmeal hyperglycaemia is an independent risk factor for developing carotid intima-media thickness (CIMT), a marker of atherosclerosis[1,3], and also an independent risk factor for macrovascular diseases.[1,3] The risk of incidence of cardiovascular events is higher after elevated postmeal glucose than after fasting hyperglycemia, especially in women with type 2 diabetes.[1,3] There is no difference in fasting myocardial flow velocity (MFV), myocardial blood volume (MBV) and myocardial blood flow (MBF) between diabetic population and control group; in the postmeal state, MBV and MBF are significantly decreased in individuals with type 2 diabetes compared with non-diabetic control group.[1,3] A causal association was found between postprandial hyperglycemia and oxidative stress, inflammation, endothelial dysfunction and adhesion molecules.[1,3]

Postprandial hyperglycemia, microangiopathy and neuropathy

Elevated postmeal glucose is associated with increased risk of diabetic retinopathy, nephropathy and neuropathy. A recent study demonstrated that postmeal hyperglycaemia is a better predictor of diabetic retinopathy than HbA1c in type 2 diabetes; a multiple regression analysis revealed an independent correlation between elevated postprandial glucose and the incidence of diabetic retinopathy and neuropathy; also, it was found that postprandial hyperglycemia is associated, although not independently, with the incidence of diabetic nephropathy.[1,3]

Postprandial hyperglycemia and increased cancer risk

It appears that postmeal hyperglycaemia has an association with the development of cancer of the pancreas, endometrium, urinary tract, and colon; many prospective studies found a strong correlation between pancreatic cancer mortality and elevated postprandial glucose levels; the relative risk for developing pancreas cancer was 2.15 in individuals with postmeal glucose >11.1 mmol/L (200 mg/dL) compared with individuals with postprandial glycemia < 6.7 mmol/L (121 mg/dL); this association was stronger in males than females; in some studies, however, this association was found only for women; further trials are necessary.[1,3]

Postprandial hyperglycemia and cognitive dysfunction

Postmeal hyperglycemia may negatively affect cogni-

tive function in elderly individuals with type 2 diabetes; it has been reported that significantly elevated postprandial plasma glucose excursions > 200 mg/dL (11.1 mmol/L) were related with a disturbance of global, executive and attention functioning.[1,3]

TREATMENT

Although no randomized controlled studies have specifically examined the effect of controlling postprandial glycemia on diabetic macrovascular, microvascular and neuropathic risk, there is some evidence which supports therapies targeting postmeal hyperglycemia.[1,3]

Alpha-glycosidase inhibitors and metformin, that delay carbohydrate absorption following meals, reduce postprandial hyperglycaemia, risk of MI and other cardiovascular events in subjects with type 2 diabetes and IGT;[1,3,6] these drugs lead also to reduction of CIMT.[1,3]

Glinides (repaglinide, nateglinide), rapid-acting insulin secretagogues, have similar effect on postmeal glucose; and a positive effect of repaglinide on CIMT has been observed.[1,3]

Rapid-acting insulin analogues decrease postmeal hyperglycemia showing a positive effect on surrogate markers of cardiovascular disease, such as nitrotyrosine, endothelial function and methylglyoxal (MG) and 3-deoxyglucosone (3-DG).[1,3]

A trial with intensive insulin therapy in individuals with type 2 diabetes suggests that both reduced postprandial hyperglycemia and decreased fasting hyperglycemia are strongly related to reductions in retinopathy and nephropathy; there was neither development nor progression of retinopathy or nephropathy with fasting glycemia < 6.1 mmol/L (110 mg/dL) and postmeal glycemia <10 mmol/L (180 mg/dL).[1]

Glucagon-like peptide-1 (GLP-1) derivatives and dipeptidyl peptidase IV (DPP-4) inhibitors, that increase endogenous insulin levels and inhibit glucagon secretion, are other options for decreasing postmeal hyperglycemia, lowering HbA_{1c} and reducing cardiovascular risk factors.[1,7,8]

Some dietary changes may improve postprandial glucose and risk for diabetic complications; there is an increasing evidence that alterations in the macronutrient composition of the diet, like decreasing carbohydrate and increasing unsaturated fats and/or protein, play a role that facilitates weight loss, increases insulin sensitivity and glucose tolerance, and improves blood pressure, blood lipid profile, and inflammatory markers; foods with low-energy density, such as soups, fruits, vegetables, oatmeal, and lean meats are recommended; diet should also contain more dietary fibre; it is suggested a daily fiber intake of 38 g (men) and 25 g (women) for persons over 50 years of age and 30 g (men) and 21 g (women) for those under 50; the use of foods with lower glycemic index, like eg legumes, pasta and most fruits, provide an additional benefit in controlling postprandial glycaemia.[1,9,10,11]

RECOMMENDATIONS

Recommendations for postprandial glucose control in diabetes[3] and glycemic goals for clinical management of diabetes[1] are outlined in Table I and Table II, respectively; all glucose parameters should be lowered to as near normal as safely possible; glycemic targets should be individualized; these goals are not appropriate for children and pregnant women.

CONCLUSIONS

Postprandial hyperglycaemia occurs early in the development of type 2 diabetes. It is frequently found in type 1 and type 2 diabetes. Control of fasting glucose is necessary, but usually insufficient for achieving HbA_{1c} goals; therefore, postmeal glucose should be controlled, in addition. Postprandial hyperglycemia is related to oxidative stress, inflammation and endothelial dysfunction; it is an independent risk factor for the development and progression of macroangiopathy; and it may be linked to diabetic retinopathy, cognitive dysfunction in older people with type 2 diabetes and certain cancers. Several nutritional and pharmacological interventions specifically target postprandial hyperglycaemia. Regimens, targeting fasting and postprandial hyperglycemia, and HbA1c are needed to achieve an optimal metabolic control. Thus, it may be possible to reduce the morbidity and mortality due to poorly controlled diabetes.

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