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Drug Therapy of Postprandial Hyperglycaemia

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Abstract

It is widely accepted that the most challenging goal in the management of patients with diabetes mellitus is to achieve blood glucose levels as close to normal as possible. In general, normalising postprandial blood glucose levels is more difficult than normalising fasting hyperglycaemia. In addition, some epidemiological studies suggest that postprandial hyperglycaemia (PPHG) or hyperinsulinaemia are independent risk factors for the development of macrovascular complications of diabetes mellitus.

Recently, several drugs with differing pharmacodynamic profiles have been developed which target PPHG. These include insulin lispro, amylin analogues, α-glucosidase inhibitors and meglitinide analogues.

Insulin lispro has a more rapid onset of action and shorter duration of efficacy compared with regular human insulin. In clinical trials, the use of insulin lispro was associated with improved control of PPHG and a reduced incidence of hypoglycaemic episodes.

Repaglinide, a meglitinide analogue, is a short-acting insulinotropic agent which, when given before meals, stimulates endogenous insulin secretions and lowers postprandial hyperglycaemic excursions.

Both insulin lispro and repaglinide are associated with postprandial hyperinsulinaemia. In contrast, amylin analogues reduce PPHG by slowing gastric emptying and delivery of nutrients to the absorbing surface of the gut. α-Glucosidase inhibitors such as acarbose, miglitol and voglibose also reduce PPHG primarily by interfering with the carbohydrate-digesting enzymes and delaying glucose absorption.

With the availability of agents which preferentially reduce postprandial blood glucose excursions, it is now possible to achieve glycaemic goals in a larger proportion of individuals with diabetes mellitus.

Over 60 years ago, Dr. Elliott P. Joslin believed that the goals of therapy for those with diabetes mellitus should include a serious effort to achieve blood glucose levels as close to normal as possible.[1] The validity of this approach was subsequently confirmed by a number of interventional studies. The most comprehensive of these studies was the Diabetes Control and Complications Trial[2] which demonstrated beyond doubt the benefits of achieving near normal blood glucose levels in individuals with type 1 (insulin-dependent) diabetes mellitus. However, in clinical practice, normalising blood glucose levels is a formidable challenge. Even more difficult is the control of postprandial surges of blood glucose levels. In 1 study, treatment of a group of individuals with type 2 (non–insulin-dependent) diabetes mellitus with either diet, a sulphonylurea or insulin, lowered fasting blood glucose levels substantially while postprandial blood glucose excursions continued to exceed 11.1 mmol/L (200 mg/dl).[3]

The pathophysiology of postprandial hyperglycaemia (PPHG) is illustrated in figure 1. The main determinants of postprandial blood glucose levels are the availability of insulin and the influx of glucose from the gut. However, disposition of glucose at peripheral tissues as well as reduced down-regulation of hepatic glucose output are also important contributors to PPHG.

Considering the multitude of factors that mod-

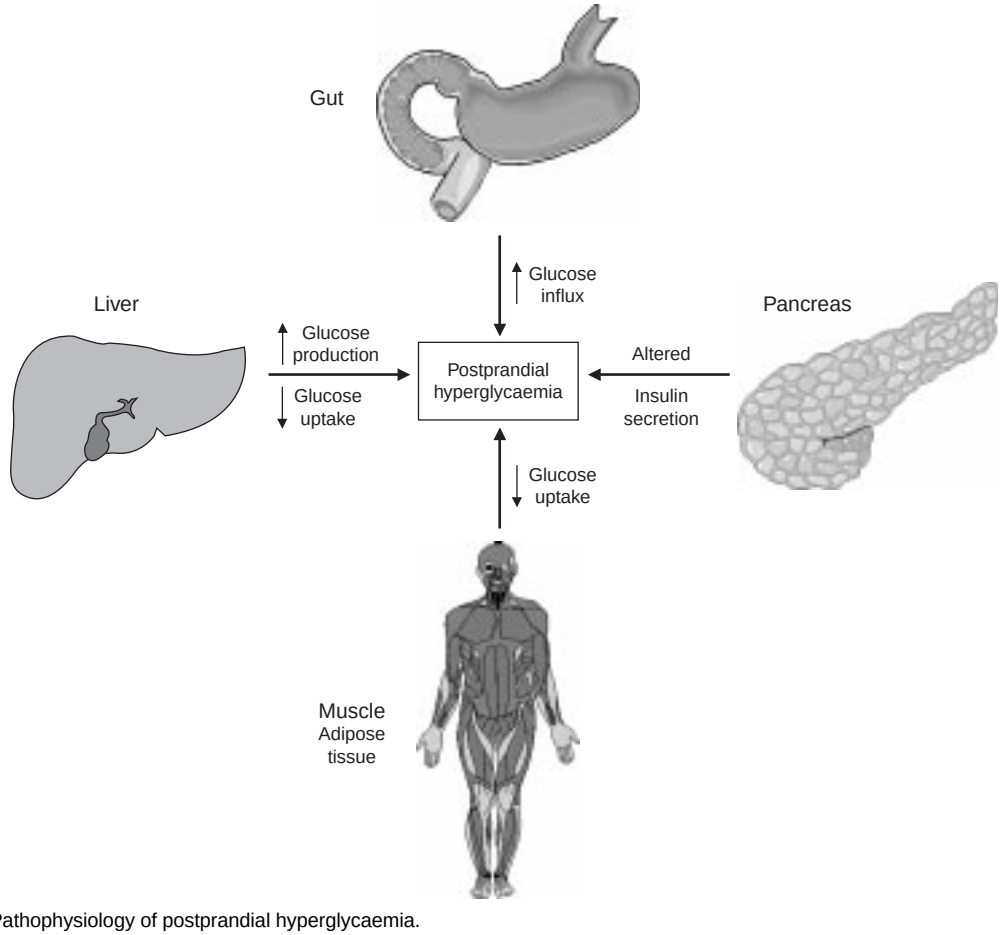

Fig. 1. Pathophysiology of postprandial hyperglycaemia.

ulate postprandial blood glucose levels, any therapeutic intervention aimed at lowering the blood glucose level in individuals with diabetes mellitus will have some ameliorating effect on PPHG, irrespective of its mechanism of action. More recently, however, several classes of agents have been developed which primarily target PPHG.

1. The Rationale for Treating Postprandial Hyperglycaemia

There are multiple rationales to justify the treatment of PPHG. Perhaps the most compelling reason to target PPHG is to achieve around-the-clock blood glucose control. The relative contribution of postprandial excursions of blood glucose to overall glycaemic control, as indexed by glycosylated haemoglobin (HbA_{1C}) levels, depends on the magnitude of fasting hyperglycaemia. It is likely that the higher the fasting blood glucose concentrations, the less the proportion of HbA_{1C} attributable to PPHG.

In a recent study of individuals with type 2 diabetes mellitus it was found that post-lunch plasma glucose levels at 2pm and 5pm were better predictors of glycaemic control and correlated better with HbA_{1C} than fasting plasma glucose.[4] It is noteworthy that PPHG, similar to HbA_{1C}, has been correlated with the presence of diabetic complications, notably retinopathy and nephropathy, in various epidemiological studies.[5-7] In addition, some data, especially in pregnant women with diabetes mellitus, indicate that normalising postprandial blood glucose levels is associated with better outcomes of pregnancy than normalising pre-prandial blood glucose levels.[8] Such observations underscore the potential dire consequences of PPHG.

Another important reason for treating PPHG is the fact that PPHG, even in the absence of marked fasting hyperglycaemia, is a recognised risk factor for coronary artery disease.[9-14] The Honolulu Heart Study evaluated the role of PPHG in the risk of fatal coronary heart disease (CHD) and total CHD. This study found that the risk of CHD increased significantly as 1-hour post-50gm glucose load serum glucose values increased.[9] The age-adjusted rate for fatal CHD in those with postprandial serum glucose values in the range of 8.7 to 10.5 mmol/L (157 to 189 mg/dl) was at least twice the rate in those where postprandial values were less than 6.3 mmol/L (114 mg/dl). In addition, the rate of sudden death per 1000 men who had 1-hour post-50gm glucose loads with serum glucose levels of <8.4 mmol/l (<151 mg/dl) was only 21; this rate more than doubled in those with post-load serum glucose levels of between 8.4 to 12.4 mmol/L (151 to 224 mg/dl).[10] This indicated that even mild PPHG increased the risk of CHD significantly.

In a study of 18 403 British men aged 40 to 60 years (The Whitehall Study),[11] it was found that CHD mortality was doubled in individuals with 2-hour post-50g oral glucose load levels of 5.3 to 10.9 mmol/L (96 to 196 mg/dl) compared with individuals with 2-hour post-glucose load levels of <96mg/dl. Similarly, in the Islington Diabetes Survey,[12] the prevalence of major CHD increased from 9% in patients with normal glucose tolerance to 17% in those with impaired glucose tolerance, defined as whole blood glucose levels of 6.7 to 10.0 mmol/L (120 to 180 mg/dl) 2 hours after a glucose load of 50g. The prevalence of CHD in individuals with diabetes mellitus was only 20%, a figure similar to the prevalence rate among those with predominantly PPHG. In addition, the Bedford Study[13] also found that the protection against CHD found in nondiabetic individuals was lost with the onset of PPHG.

In a recent study of individuals with newly diagnosed type 2 diabetes mellitus seen in 16 diabetes clinics (Diabetes Intervention Study),[15] it was found that PPHG, but not fasting hyperglycaemia, was an independent risk factor for myocardial infarction and total mortality.

It is evident that the risk of CHD is substantially increased with the onset of PPHG. It is not known if this risk is attributable directly to hyperglycaemia or is secondary to other risk factors such as associated postprandial hyperinsulinaemia. It is likely that the clustering of metabolic cardiovascular risk factors is more important than hyperglycaemia, a single component of the insulin resistance

syndrome.[16] The Paris prospective study[17] found that postprandial hyperinsulinaemia, like fasting hyperinsulinaemia, was a more sensitive predictor of fatal coronary disease than either hyperglycaemia or diabetes.[17] Similarly, in the Helsinki Policemen study,[18] the association of fatal and nonfatal CHD with 1 and 2 hour postprandial hyperinsulinaemia was stronger than the association with fasting hyperinsulinaemia.

The association between high but non-diabetic blood glucose levels and the risk of death was recently evaluated by Balkau et al.[19] Men in the upper 20% of the 2-hour glucose distributions had a significantly higher risk of all-cause mortality in comparison with men in the lower 80%.[19] This observation suggested that even a mild postprandial elevation of blood glucose levels was a risk factor.

Overall, there is strong evidence in the literature to suggest that CHD is associated either directly with PPHG independent of fasting serum glucose levels or that the association is the result of hyperinsulinaemia as an index of insulin resistance. Although direct experimental proof is still lacking, it is reasonable to expect that targeting PPHG with the currently available therapeutic agents would decrease the risk of CHD. In this regard, it is noteworthy that in an atherosclerosis-prone animal model, acarbose treatment was associated with reduced atherosclerotic lesions.[20] This could partially be attributed to a reduction in postprandial hypertriglyceridaemia.[21]

The recent revision of the diagnostic criteria for diabetes by the American Diabetes Association has allowed for the early identification of larger numbers of individuals at risk for macrovascular disease who otherwise would have been left undiagnosed.[22] However, these criteria de-emphasise any role of postprandial blood glucose testing in screening for diabetes mellitus primarily because of difficulties in the logistics of standardising such tests. Although at the present time there is no direct evidence to indicate that treatment of PPHG would reduce the risk of cardiovascular disease, the strong epidemiological association between PPHG and coronary disease suggests that targeting PPHG with dietary or pharmacological means would be prudent clinical practice.

There are other theoretical reasons why PPHG may pose an added risk to the patient with diabetes mellitus. One is that PPHG in some individuals may be associated with postprandial lipaemia.[21,23-25] Lipoprotein moieties with enhanced atherogenic potential have been identified during postprandial lipaemia. There is a correlation between postprandial triglyceride levels and carotid artery sclerosis.[26] In addition, postprandial triglyceride level, like plasma cholesterol, is a predictor of CHD.[27] It is theoretically possible that reduction of postprandial lipaemia associated with the amelioration of PPHG would have favourable effects on the progression of CHD.[15,17] However, such an association remains speculative at this time.

Another theoretical concern linking diabetic complications to PPHG is the enhanced lipid peroxidation associated with postprandial elevations of the blood glucose level.[28-30] It is tempting to speculate that amelioration of PPHG will result in a reduced post-meal oxidative load and perhaps decrease diabetic complications. More studies are needed to determine if indeed therapeutic targeting of PPHG results in a reduced rate of lipid peroxidation.

Finally, the relationship between postprandial hyperinsulinaemia and deterioration of cognitive function in older individuals is intriguing.[31] However, at this time, there is no evidence to suggest that amelioration of postprandial hyperinsulinaemia with pharmacological means would enhance cognitive function.

2. Management of Postprandial Hyperglycaemia

Both dietary and pharmacological tools are now available for the management of PPHG. The pharmacological agents with the greatest effect on PPHG include insulin lispro, amylin analogues and α-glucosidase inhibitors. Dietary modifications or use of supplements such as guar gum are also helpful and will be discussed briefly.

2.1 Dietary Modifications and the Use of Supplements

Several dietary modifications can be made which would potentially reduce PPHG. The main dietary determinant of postprandial blood glucose levels is the carbohydrate (CHO) content.[32-35] In order to avoid marked postprandial blood glucose excursions, multiple small portions of meals rather than the traditional 2 or 3 large meals a day has long been recommended as a prudent dietary habit. In addition, the reduction in CHO content of the diet in some hypertriglyceridaemic individuals would also be helpful. In these individuals, CHO can be substituted with monounsaturated fatty acids.[36]

The possible benefit of modest CHO restriction in the diet of those with gestational diabetes was recently reported.[37] In addition to reducing the CHO content of the diet, the use of poorly digestible CHO instead of refined, easily digestible CHO would also ameliorate PPHG.[38,39] Individualisation of diet based on an assessment of the glycaemic index of foods has been suggested.[38,39]

Another approach has been diet supplementation with soluble fibre such as guar and oat gums and some hemicelluloses. The effect of these modifications on PPHG is usually modest.[40]

If dietary modifications are not sufficient in ameliorating PPHG, then drug therapy is indicated.

2.2 Pharmacological Therapy

2.2.1 Insulin Lispro

The development of insulin lispro was in response to the realisation that new insulins were needed to mimic the physiological insulin response to meals. Insulin lispro differs from human insulin only in the order of 2 amino acids in the β-chain. The proline and lysine at positions B28 and B29 of human insulin, respectively, were inverted in the insulin lispro compound. This inversion in amino acid sequence allowed the hexamer-structure of insulin lispro at the subcutaneous injection site to dissociate to dimers and monomers at a faster rate, and with less variability.[41,42] This accounts for the faster onset of insulin activity. Unlike human insulin, where increasing doses are associated with a time shift in peak action, insulin lispro pharmacokinetics appear to be less variable with changes in dose.[41] Of note is that the serum concentrations of insulin and glucose after the intravenous administration of human insulin and insulin lispro are identical, indicating that the insulin analogue and human insulin have equal bioavailability and potency when administered intravenously. In addition, the binding characteristics of these 2 insulins to insulin receptors or insulin-like growth factor-1 receptors are identical.[41]

Large clinical studies in patients with both type 1 and type 2 diabetes mellitus have shown that the primary efficacy parameter of insulin lispro is a reduction in postprandial glucose excursions.[43-45] However, the overall glycaemic control, as measured with HbA_{1C}, was not improved when patients were given insulin lispro instead of regular human insulin. In general, patients with type 1 diabetes mellitus randomised to receive insulin lispro tended to have less hypoglycaemia, especially during the night.[43,44] This latter advantage was also apparent in patients with type 2 diabetes mellitus who were usually less predisposed to having severe hypoglycaemic reactions.[45]

Overall, it is evident that the main advantage of insulin lispro is improved control of PPHG with the added advantage that it can be used within 10 to 20 minutes of initiation of food intake, allowing more flexibility in insulin dose scheduling.

2.2.2 Amylin Analogues

Amylin is a pancreatic β-cell hormone co-secreted with insulin in response to various insulin secretagogues. Since its discovery in 1987, a host of studies have been performed in order to determine the physiological role of amylin.[46-49] The mechanisms of action include: (i) the regulation of gastric emptying, thereby limiting the rate of delivery of nutrients to the absorptive surface of the gut;[49-51] (ii) suppression of postprandial glucagon secretion;[52] and (iii) replenishment of hepatic glycogen stores.

In general, amylin secretion correlates with insulin secretion in healthy individuals and in those with type 1 diabetes mellitis where amylin

secretion, like insulin secretion, is profoundly impaired. In individuals with type 2 diabetes mellitus, the decline in amylin secretory response correlates with reduced pancreatic β-cell activity. However, it appears that decreased stimulated amylin release precedes the impairment of insulin secretion and that in some individuals with type 2 diabetes mellitus there is a dissociation in the insulin and amylin secretory responses to sulphonylureas.[53,54] It is tempting to speculate that the deterioration in amylin secretory capacity in patients with type 2 diabetes mellitus precedes the gradual loss of the insulin secretory response.

Another potential clinical condition associated with the dissociation between amylin and insulin production is physiological aging.[55] In one study of pancreatic islet cells of aging rats, it was found that, with age, there was a greater increment in amylin mRNA than insulin mRNA. This suggested that the proportions of insulin and amylin synthesised and secreted may change with age as appears to occur in other insulin resistant states.[56,57]

Pramlintide

The short half-life of amylin and its tendency to self-aggregate limits its therapeutic usefulness. These limitations have been surmounted with the advent of pramlintide. This is a human amylin analogue in which the amino acid residues at positions 25, 28 and 29 have been replaced with proline. These substitutions prevent self-aggregation of the molecule without diminishing its biological activity. Subcutaneous injections or intravenous infusions of pramlintide reduced post-meal glucose excursions significantly in healthy volunteers as well as in individuals with type 1 and 2 diabetes mellitus.[58,59] The drug also did not alter the disposition of intravenously administered glucose. These observations indicated that the main site of action of pramlintide was in the gut, presumably through reductions in the rate of gastric emptying and amelioration of the mismatch between nutrient delivery and insulin secretory response.

The clinical utility of pramlintide in the general population of people with diabetes mellitus remains to be demonstrated. Many patients with diabetes have delayed gastric emptying in the absence of clinical symptoms of gastroparesis[60] and in many individuals with diabetes mellitus glucagon secretion decreases over time and does not play a significant role in the aggravation of hyperglycaemia.[61] These realities cast doubt on the suitability of this agent for the majority of patients with diabetes mellitus.

However, recent reports from initial phase III trials have been encouraging. In a double-blind study of 477 patients with type 1 diabetes mellitus treated for 12 months with placebo or pramlintide 30μg or 60μg 4 times daily,[62] there was a significant net decrease in HbA_{1C} of 0.30% without an increased frequency of hypoglycaemia or increasing bodyweight gain.

In another study of 539 individuals with type 2 diabetes mellitus,[63] pramlintide treatment was associated with significant bodyweight reduction from baseline and improvement in HbA_{1C} by 0.38% compared with the placebo-treated group. Ongoing studies will further clarify the therapeutic role of pramlintide in the management of individuals with diabetes mellitus.

2.2.3 α-Glucosidase Inhibitors

At the present time, there are 3 glucosidase inhibitors that are available for the treatment of patients with type 2 diabetes mellitus. These include acarbose, miglitol and voglibose.[64-78] The inhibitory activity of voglibose on maltase and sucrase is 190 to 270 times greater than that of acarbose. However, voglibose has a much weaker inhibitory effect on pancreatic α-amylase compared with acarbose. Thus, at clinically useful doses, voglibose is a selective dissacharidase inhibitor. Miglitol also lacks inhibitory activity on α-amylase.[64,65,73,77]

Acarbose has been the most extensively studied and widely used agent of the α-glucosidase inhibitor class. Although there are some differences in the enzyme inhibitory profile of these agents, as a class their main mechanism of action is through inhibition of CHO digestion. Acarbose has a significant inhibitory effect on glucoamylase (90% inhibition), sucrase (65% inhibition) and maltase (60% inhibition).[64] Acarbose has produced 25 and

10% inhibition of isomaltase and lactase activity, respectively. Thus, lactose intolerance has not occurred during acarbose treatment.[64,79]

Glucosidase enzyme inhibition results in delayed CHO digestion. This has resulted in delayed glucose absorption with attenuation of postprandial hyperglycaemic excursions. It is noteworthy that although CHO absorption is delayed, the total amount of CHO absorbed is not altered and therefore there are no net nutritional caloric losses.[80] In addition, absorption in the gut of minerals such as copper or zinc have not been reduced when acarbose has been administered with meals.[81]

Acarbose treatment has been associated with increased secretion of glucagon-like peptide (GLP-1). When undigested CHOs reach the ileum, enteric glucagon cleavage increases, resulting in an increase in GLP-1 levels.[82] A similar effect has been found with voglibose treatment.[83] GLP-1 is an important incretin, which in addition to its insulinotropic properties, has inhibitory effect on glucagon secretion.[84] The relative contribution of these effects to the overall reduction in PPHG by these agents is not clearly defined.

Although the gastric emptying rate is not altered with α-glucosidase inhibitors, the efficacy of voglibose is increased in those with rapid gastric emptying.[85]

The clinical efficacy of miglitol, voglibose and especially of acarbose, has been well established. Large clinical trials have indicated that acarbose, miglitol or voglibose, reduce, on average, postprandial plasma glucose levels by approximately 2.7 mmol/L (50 mg/dl) and fasting plasma glucose by 0.6 to 1.1 mmol/L (10 to 20 mg/dl).[65-75] HbA_{1C} levels are reduced by 0.5 to 1% when acarbose is used as monotherapy or as combination therapy with sulphonylureas, metformin or insulin. As with other antihyperglycaemic agents, the drop in HbA_{1C} with acarbose depends on baseline glycaemic control. In general, the higher the baseline HbA_{1C} level, the greater is the decrease in HbA_{1C} after acarbose treatment.[86,87]

Unlike the other oral antihyperglycaemic agents, where the primary failure rate has been approximately 15 to 20%, α-glucosidase inhibitors have been effective in all individuals who have consumed adequate amounts of dietary CHOs, irrespective of the duration of their diabetes mellitus or its severity.[73,88] However, the efficacy of this agent when used as monotherapy may not be sufficient to achieve the glycaemic goals in a large number of patients who would require concomitant therapy with additional classes of antihyperglycaemic agents.

α-Glucosidase inhibitors do not promote bodyweight loss. However, when used in combination with sulphonylureas, they have prevented sulphonylurea-associated bodyweight gain and have reduced postprandial serum insulin concentrations.[73]

Adverse Effects of α-Glucosidase Inhibitors

The main adverse effects of this class of agents are gastrointestinal in nature, notably flatulence and loose stools. Tolerance to the severity of these effects usually occurs with continued administration over 3 months.[88] Starting patients on lower doses has assisted in identifying those sensitive to these gastrointestinal adverse effects; these individuals therefore require a very slow titration regimen.

2.2.4 Meglitinide Analogues

Meglitinide is the nonsulphonylurea moiety of glibenclamide (glyburide) or its analogue S-3075.[89] Repaglinide, one of the several analogues of meglitinide which has recently been approved by the US Federal Drug Administration for the treatment of patients with type 2 diabetes mellitus, is an insulinotropic agent with a very short duration of action. Thus, its primary target is the amelioration of PPHG. Repaglinide augments glucose-induced insulin stimulation through a decrease in potassium conductance in islet cells.[89]

Meglitinide analogues do not significantly enhance insulin output of pancreatic islets incubated in the absence of nutrients.[90]

In a study comparing repaglinide with glibenclamide, the latter agent had a greater effect on fasting blood glucose levels while repaglinide significantly lowered PPHG.[91] In a recent randomised, placebo-controlled, double-blind, fixed dose study,[41] hypoglycaemic episodes increased with

increasing doses of repaglinide. The incidence of hypoglycaemic episodes was 11% in the placebo group, 27% in the group receiving repaglinide 1mg and 36% in those randomised to receive repaglinide 4mg daily. The high rate of hypoglycaemic episodes in this fixed-dose clinical trial was partly the result of a lack of gradual dose titration.[92] For oral antihyperglycaemic agent-naive patients, mean HbA_{1C} levels decreased from 9.3% at baseline to 7.6% and 7.6% at 24 weeks for the groups receiving 1 and 4mg repaglinide, respectively. For previously treated patients, mean HbA_{1C} levels did not significantly decrease following repaglinide treatment. However, in the placebo-treated group, HbA_{1C} increased from a baseline level of 8.4% to 10% by the end of the study.[92] Short term dose response studies have suggested that the mean blood glucose response to repaglinide levels off at doses greater than 1mg.[93]

3. Conclusions

Several therapeutic agents are now available which target PPHG. A comparative profile of these agents is summarised in table I. Of those, α-glucosidase inhibitors are currently the most commonly used oral agents for targeting PPHG. A suggested algorithm for the stepwise management of PPHG is shown in figure 2. The glycaemic goals should be individualised. However, it is desirable to limit postprandial excursions of blood glucose to less than 8.9 mmol/L (160 mg/dl).

The cornerstone of management is lifestyle modifications including exercise and dietary changes, notably reducing meal portions and gradually increasing the fibre content of meals. If, after a 3 month trial, the glycaemic goal has still not been achieved, then an α-glucosidase inhibitor can be started at low doses and gradually increased until either the goal is achieved or intolerance to the agent develops. At the 3-month follow-up, if the patient continues to have postprandial blood glucose values consistently over 8.9 mmol/L (160 mg/dl), then repaglinide should be added before each meal. If the combination of dietary changes, glucosidase inhibitor and repaglinide fail to achieve the glycaemic goal at another 3 month follow-up, the oral agents should then be discontinued and insulin lispro started if the patient is a candidate for insulin therapy. In such patients an intermediate or long acting insulin preparation is usually needed to achieve glycaemic goals.

Because of the lack of a hypoglycaemic threat, and more importantly the prospect of blood glucose control without hyperinsulinaemia and bodyweight gain, α-glucosidase inhibitors should be the therapeutic agents of first choice. It is noteworthy that there have not been therapeutic trials demonstrating the efficacy of the combination therapy of repaglinide and an α-glucosidase inhibitor. In addition, it is not yet known whether repaglinide has a clear clinical advantage compared with short-acting sulphonylureas such as tolbutamide. The algorithm presented in figure 2 is a suggested approach and patient management should be highly individualised. It should be borne in mind that other antihyperglycaemic agents are also quite useful in controlling postprandial blood glucose levels and should be tried before resorting to insulin therapy.

Table I. Comparative profile of agents available for managing postprandial hyperglycaemia

	Injectable			Oral	
	regular insulin	insulin lispro	pramlintide[a]	α-Glucosidase inhibitors	repaglinide
Potency	+++	+++	+	++	++
Hyperinsulinaemia	Yes	Yes	No	No	Yes
Bodyweight gain	Yes	Yes	No	No	Yes
Hypoglycaemia	Yes	Yes	No	No	Yes
Gastrointestinal adverse effects	No	No	Yes	Yes	No

a Currently in phase III trials.

+, ++, +++ indicate the range of potency with + being least potent and +++ being most potent.

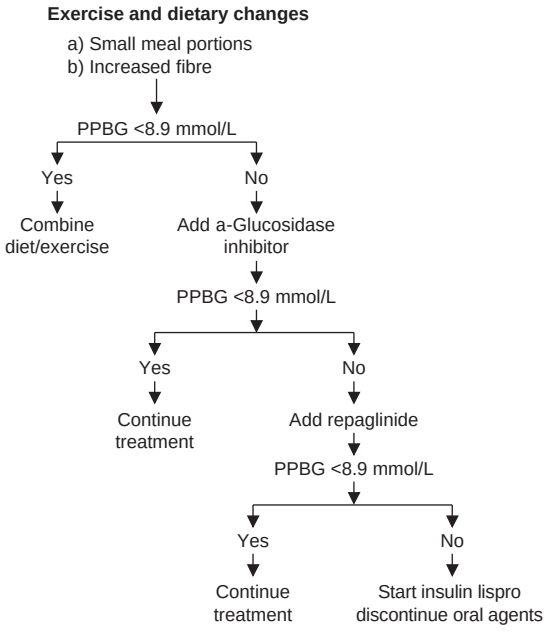

Fig. 2. A suggested algorithm for the stepwise approach to the management of postprandial hyperglycaemia. **PPBG** = postprandial blood glucose.

The recently published results from the United Kingdom Prospective Diabetes Study (UKPDS) reaffirm the need for optimising blood glucose control in patients with type 2 diabetes.[94,95] However, at the present time, it has not been established if PPHG contributes to diabetes-related complications independent of its contribution to overall glycaemic control. However, common clinical experience indicates that it is more difficult to control PPHG than to achieve normal fasting or pre-prandial glucose levels. Thus, the availability of agents which preferentially reduce postprandial blood glucose excursions enhances our ability to achieve the glycaemic goals in a larger proportion of individuals with diabetes mellitus.

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