New International Guidelines Focus on Post Meal Glucose Management

Control of post meal glucose should be a focus of management for all patients with diabetes, according to new evidence-based guidelines from the IDF. “Regimens that target both fasting and post meal glycaemia are needed to achieve optimal glucose control. Treatment of fasting and post meal hyperglycaemia should be initiated simultaneously at any HbA1c level.” Post meal glucose spikes are major contributors to overall glycaemia as well as directly harmful, Paul S. Jellinger noted. Post meal surges in blood sugar are toxic, or acutely harmful.

Since 2001, the AACE has recommended a 2-hour post meal glucose value of <7.7 mmol/l for all diabetic patients, while the ADA advocates a target of below 10 mmol/l at any non-fasted measurement. The IDF document, developed by an 18-member international committee, recommends the following:

• **Post meal hyperglycaemia is harmful and should be addressed.** The highest-level evidence for this comprises four epidemiologic studies that indicate post meal and post-challenge hyperglycaemia are independent risk factors for macrovascular disease. Other supporting evidence suggests that post meal hyperglycaemia is also associated with increased risks for retinopathy and cancer, and for impaired cognitive function in elderly with type 2 diabetes. Post meal hyperglycaemia has also been linked to greater carotid intima media thickness and decreased myocardial blood volume and flow. It has also been shown to cause oxidative stress, inflammation and endothelial dysfunction.

• **Implement treatment strategies to lower post meal glucose in people with post meal hyperglycaemia.** Although no completed studies have specifically examined the effect of controlling post meal glycaemia on macrovascular disease, there are data to support the use of both dietary and pharmacologic treatment. Among those are the findings that treatment with medications that target post meal plasma glucose reduces vascular events, and that targeting both post meal and fasting plasma glucose is important for achieving optimal glycaemic control. Data suggest that the relative contribution of postprandial glucose to overall glycaemic control varies with HbA1c: At levels below 7.3%, post meal glucose values contribute about 70%, compared with just 40% when HbA1c is > 9.3% (Diabetes Care 2003; 26: 881-5). In practical terms, “to achieve A1C levels below 7.3%, you need to target the post meal glucose.

• **A variety of both non-pharmacologic and pharmacologic therapies should be considered to target post meal plasma glucose.** Diets with a low glycaemic load have been shown beneficial in controlling post meal plasma glucose, while several pharmacologic agents are available that preferentially lower post meal plasma glucose. These agents include the alpha-glucosidase inhibitors acarbose and miglitol, the amylin analogue pramlintide, the dipeptidyl peptidase-4 inhibitor sitagliptin phosphate, the glinides nateglinide and repaglinide, the glucagon-like peptide-1 derivative exenatide, and rapid-acting, biphasic, and inhaled insulins.

• **Two-hour post meal plasma glucose should not exceed 7.8 mmol/l as long as hypoglycaemia is avoided.** Post meal plasma glucose levels rarely rise above 7.8 mmol/L in people with normal glucose tolerance, and typically return to basal levels within 2-3 hours after eating.

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**Self-monitoring of blood glucose (SMBG) should be considered.** It is currently the most practical method for monitoring post meal glucose. While there is controversy about the benefits of SMBG in people with type 2 diabetes who don’t use insulin, most diabetes organisations advocate its use. For patients with type 1 and type 2 diabetes who do use insulin, the IDF advises SMBG at least three times a day. The IDF does not call for patients to measure glucose levels after every meal. One can ask patients to perform one 2-hour post meal glucose test a day - after different meals, in addition to their usual premeal measurements. Also check patients’ nonfasted glucose levels when they’re in the office.

**Efficacy of treatment regimens should be monitored as frequently as needed to guide therapy toward achieving post meal plasma glucose targets.** But that doesn’t mean fasting levels should be ignored. Indeed, despite all the emerging data on postprandial glucose toxicity, it’s just more practical to start out treatment by targeting fasting and premeal glucose levels. The first target is the fasting plasma glucose. Don’t try to bring down post meal excursions until the patient has achieved waking euglycaemia and then premeal euglycaemia. It is very difficult to achieve effective 2-hour post meal control when the patient enters the meal with a high blood glucose. You may have to give such high doses of medication for the meal that you begin to risk hypoglycaemia.

It is clear that a major determinant of post meal glucose is premeal glucose. The point is that you don’t stop when the premeal glucose’s are under control, which is the old thinking. Now start looking at post meal glucose values and start targeting therapy toward that parameter.

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**Nearly All Adolescents With Type 1 Diabetes Omit Insulin to Control Weight**

More than 90% of all teenagers with type 1 diabetes omit insulin doses at least occasionally in order to prevent weight gain, according to the results of an international observational study presented by Soren E. Skovlund at the European Society for the Study of Diabetes. Of concern, the practice is associated with significantly poorer glycaemic control. “Screening for and dialog with adolescents about omission of insulin injections may be particularly warranted in those who exhibit concern about their weight or engage in weight-reducing activities,” said Skovlund, of Novo Nordisk, Denmark.

A total of 2,062 adolescents aged 11-18 years with type 1 diabetes of at least 1 year’s duration completed the survey, conducted in 2005 by the Novo Nordisk. Respondents were from 21 centres in Europe, Australia, Japan, and North America (Los Angeles).

The study group was 49.4% female and 50.6% male. Both genders had a mean age of 14.5 years, and mean diabetes duration of 6.3 years for the females and 5.9 years for the males. Mean BMI was 22.8 kg/m² for the females and 21.7 kg/m² for the males, and mean HbA1c levels were 8.3% for the females and 8.1% for the males.

Each adolescent completed an extensive questionnaire covering topics such as lifestyle, self-management and health behaviours, treatment goals, family dynamics, well-being and quality of life, diabetes burden, and weight perception/dieting. Also included was the question: “How often do you miss insulin to control your weight?” Possible responses were “never,” “once a month,” “once a week,” or “every day.”

The majority - 91.7% of the females and 93.0% of the males - checked “once a month.” “Never” was a distant second, reported by 5.1% of females and 4.2% of males, followed by “once a week” (2.5% female/1.9% male) and “every day” (0.7% female/0.9% male). This was not just in general, but specifically to avoid weight gain. Clearly, people are connecting the two aspects, Skovlund commented.

The nearly equal proportion of males and females is striking. “A lot of the insulin omission literature has focussed on this being a female phenomenon. But we certainly also see it in boys.” Not surprisingly, those who reported omitting insulin doses either daily or weekly (“high omitters”) had poorer metabolic control, and averaged a significant difference of half a percentage point in haemoglobin A1c values, compared with the “low omitters,” those who omitted never or monthly (8.99% female/8.61% male vs. 8.24% female/8.08% male). Insulin omission remained significantly correlated with HbA1c after controlling for age and diabetes duration, but not gender.

Insulin omission also was highly correlated with other weight-loss behaviours, such as fasting, restricting certain food groups, vomiting, and use of diet pills / laxatives, as well as reduced well-being and quality of life. None of the associations significantly differed by centre. Insulin omission was reported both by patients on multiple daily injections as well as those on insulin pumps (who made up approximately 20% of the overall group).

The findings are not all that surprising to paediatric endocrinologist Francine R. Kaufman. “Kids miss doses all the time. The question is why.” Her adolescent patient population with type 1 diabetes, like many others, tends to be well educated and aware that insulin omission can control weight via glycosuria. In fact, in the US the practice of omitting insulin by young people with type 1 diabetes in order to control weight has been dubbed “Diabulemia” and is currently a hot topic in the lay press.
But the thought process may not always be so straightforward. Rather, teens might rationalise to themselves that perhaps they didn’t eat as much as they did, or that they don’t need as much insulin as they actually do. Often, it’s not a case of completely omitting a dose but simply not taking enough for the amount of food consumed. “A lot of it is not totally wilful, but kind of miscalculating the dose,” she remarked.

It’s important to routinely ask teens about insulin omission in a non-threatening way. If they admit to doing it, then try asking why they think they’re missing doses, and include enquiring about weight concerns. “You have to let them confess as much as they can, rather than giving them the third degree,” Kaufman advised.

But occasional insulin omission or under dosing doesn’t necessarily lead to disaster in all teens, particularly those with reasonably normal haemoglobin A1c levels and those who aren’t experiencing frequent ketoacidosis or severe hypoglycaemia. That’s what we need to find out from the data - of all those kids, what’s the spectrum? Maybe there’s some cut-off or characteristic that shows us the ones we really need to be concerned about.

Indeed, the findings that Skovlund presented are merely the initial descriptive data of the study population. Further analysis will yield more in-depth findings. Ongoing analysis is looking at various correlations between age, gender, psychosocial factors, and behaviours in order to guide development of clinical guidelines and tools to help clinicians address these issues in daily practice. It turns out to be rather complicated relationships.

Office-Based Management of Low-Carbohydrate Diet Effective in Teens

Overweight teens assigned to a 6-month low-carbohydrate diet experienced significant weight loss, decreased body mass index, and improved self-esteem while being managed in an office-based setting, Robert Siegel reported at the annual meeting of the Pediatric Academic Societies.

“The question asked is can a low-carbohydrate diet be practically implemented in the office setting,” said Siegel of Cincinnati Children’s Hospital. Siegel also is the medical director of the Cincinnati Pediatric Research Group, a network of 47 practise-based paediatricians in the Cincinnati area committed to translating research into practise.

Interestingly enough, fat intake by self-report did not significantly increase in these subjects. Increased fat intake is a concern with low-carbohydrate diets, he said.

A total of 63 healthy children 12-18 years of age and with a body mass index (BMI) greater than the 95th percentile for age were put on a low-carbohydrate diet (LCD) of less than 50 g of carbohydrate daily. Subjects were seen regularly by a dietician and counselled on good nutrition and physical activity along with specific LCD recommendations.

A total of 38 teens (60%) finished the 6-month study. The mean age of the study group was 15 years; 79% were female. Of participants, 22% were African American, 74% were white, and the ethnicity of the rest was unspecified.

Overall caloric intake and carbohydrate intake both dropped significantly during the 6-month study period. At baseline, average carbohydrate intake was 324 g daily and dropped precipitously to 62 g/day at 6 months. Fat and protein intake did not, however, differ significantly between baseline and 6 months.

Average body weight dropped from 93.4 kg to 88.3 kg, BMI fell from 34.9 to 32.5, and BMI percentile fell from 98.4 to 97.1.

A total of 32 of 38 teens lost at least some weight during the study period; the greatest loss was 23.9 kg of body weight. Average weight loss was 5.1 kg.

There also was a significant improvement in Rosenberg Self Esteem Scale scores, from 16.6 at baseline to 15.0 at 6 months. At study end, 54% of teens felt that the LCD was easier to follow than previously tried diets, and 38% said they planned to remain on the diet beyond 1 year.

“We tried to in our study mirror what goes on in practises,” said Siegel. However, not all practises have access to a dietician, and the study wasn’t randomised. “We might have just identified a highly motivated group of kids.”

“BMI Falls for Teens on Low-Carb Diet”
Metformin is an option for selected patients at high risk for the development of type 2 diabetes, according to the ADA in a new consensus statement. The document emphasises lifestyle modification as key to management of IFG and IGT. Metformin may be considered for patients who have both IFG and IGT, with at least one other risk factor, according to the ADA expert panel (Diabetes Care 2007;30:753-9). The statement specifies that screening for IFG / IGT should be undertaken in the same population that is currently screened for diabetes, using the FPG and the 2-hour OGTT. Both tests must be done, on separate days, in order to confirm both IFG and IGT, and to decide whether to start a patient on metformin. Patients treated with metformin should be monitored with a HbA1c semi-annually. However, lifestyle is more important.

The ADA document notes that up to 70% of individuals with the ‘prediabetic’ states of IFG or IGT will eventually develop diabetes. The risk for CVD is only moderately elevated with IFG and IGT, but that risk increases sharply with the onset of type 2 diabetes along with other complications.

Increasing data have shown that it is possible to prevent or delay the onset of type 2 diabetes using lifestyle modification, with or without medications. Strong evidence supports efforts to prevent or delay the onset of diabetes, although the evidence is conflicting as to whether such efforts will improve cardiovascular outcomes.

To delay diabetes is to delay the risk for microvascular disease - this is known for sure. We don’t have enough evidence to say that we’re preventing CVD by preventing diabetes. But it’s possible, because we know that people who do get diabetes have a two- to fourfold increase in CVD”.

The ADA document takes into account data from eight major clinical trials published between 1997 and 2006, all of which showed reductions in the development of diabetes, ranging from 25%-60%. The largest reductions (about 60%) were achieved in studies that tested lifestyle interventions aimed at a 5%-10% weight loss and moderate physical activity for about 30 minutes a day, and treatment with thiazolidinediones. Lesser degrees of reduction (about 25%-30%) were achieved with other medications.

On the basis of the available data, the panel recommended lifestyle modification alone for patients who have either IFG or IGT. Metformin, 850 mg twice a day, may be added to the same lifestyle prescription for patients who have both IFG and IGT, as well as one or more of the following:

- Younger than 60 years of age.
- Body mass index of at least 35 kg/m².
- Family history of diabetes in first-degree relatives.
- Elevated triglycerides.
- Reduced HDL cholesterol.
- Haemoglobin A1c greater than 6.0%.

The data supporting lifestyle intervention come primarily from two trials, the Diabetes Prevention Program (N. Engl. J. Med. 2002; 346: 393-403) and the Finnish Diabetes Prevention Study (N. Engl. J. Med. 2001; 344: 1343-50). In the DPP, the benefit of metformin therapy was only about half that of lifestyle intervention, but substantially greater benefit was seen in younger and more obese individuals. The low cost of generic metformin and its relatively low rate of gastrointestinal side effects (5-10%) also factored into the recommendation.

In other studies, the oral drugs acarbose and orlistat were about as effective as metformin. However, both are poorly tolerated, and acarbose is also costly. Although orlistat is now generic and therefore less expensive, the trial showing its effectiveness wasn’t designed as a diabetes prevention trial, the ADA authors explained.

More recently, the Diabetes REDuction Assessment with ramipril and rosiglitazone Medication (DREAM) study showed that rosiglitazone was as effective in delaying or preventing the onset of diabetes as was lifestyle modification in the DPP and the Finnish trials. However, rosiglitazone is costly and was associated with a sevenfold increase in heart failure (Lancet 2006;368:1096-1105).

For its part, the American Association of Clinical Endocrinologists plans to issue a response to the ADA document later this year, AACE president Richard Hellman said in an interview. In 2003, the AACE issued a broader statement on the insulin resistance syndrome, in which it advocated individualisation of treatment based on risk factors and co-morbid conditions, aiming therapy at an even earlier stage than IFG / IGT (Endocr. Pract. 2003; 9: 237-52). “Our position has been that we should identify people at risk with insulin resistance and begin making lifestyle changes then, rather than wait until the patient has IFG or IGT,” said Hellman, at Kansas City.

“The use of metformin and other drugs should be individualised. In some, it may be appropriate very early, such as in a patient with severe insulin resistance, with or without IGT, or a young woman with hyperandrogenism,” he added.

The ADA statement is a good one, although it doesn’t go far enough, he said. “It’s not particularly radical to say that a person with IGT would be put on metformin,” he said, noting that the progression from insulin resistance to IFG / IGT to diabetes is a continuous one. “We think there are probably more options where it would be appropriate than just the ones the ADA included, but we think it’s a good first step.”