

Physicians' Corner

Advancing Change—Perspectives on Postprandial Glycemia

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One of the most fascinating and challenging aspects of diabetes mellitus (DM) for the interested practitioner is the apparently endless complexity of this disease and its treatment. Sir William Osler wrote in 1901, in the 4th edition of *The Principles and Practice of Medicine*,¹ that he had personally reviewed each of the 161 cases of DM seen at The Johns Hopkins Hospital and Dispensary. All his insights are priceless, and many are timeless. He expressed discouragement, though, that it appeared unlikely that attempts to treat the disease with extracts from the pancreas would ever prove beneficial. Opium alone seemed to be the most effective therapy.¹ As we now know, treatment options certainly have changed!

Not so long ago, the Diabetes Control and Complications Trial (DCCT) found that intensive control in patients with type 1 DM significantly reduced microvascular complications.² On the strength of this news, the treatment strategy for type 1 DM changed. The United Kingdom Prospective Diabetes Study³ and the Kumamoto Study⁴ demonstrated that intensive therapy of type 2 DM, with insulin used as needed, also significantly reduced microvascular complications. These results led to modifications in how we treat this population. Change appears to be inevitable in DM management, and it seems to lead to better and better outcomes.

It is my impression that most primary care providers, largely as a result of the studies mentioned above, are aware of the existence of established glycosylated hemoglobin (A1C) goals, and, on some level, strive to achieve them. Certainly, one of the forces that has carried us toward better control is the development of relatively simple oral or basal-oral treatment strategies (basal insulin and oral antidiabetic drugs [OADs]) to lower A1C values. Analogue basal insulins are simple to add to OADs and quite easy for patients to self-titrate toward an A1C goal. Such simple regimens make it attractive and feasible for busy primary care providers to institute insulin therapy targeted at lowering the risk of DM complications.

I met an older family physician in rural South Carolina recently who related the ease with which he was achieving established A1C goals in his busy practice. His strategy in newly diagnosed patients with an A1C level <8.5% is to implement lifestyle changes plus an oral agent at the time of diagnosis and add basal insulin as the second agent if the A1C goal is not reached within 3 to 4 months. If the A1C level is $\geq 8.5\%$ at the time of diagnosis, he starts an oral agent and basal insulin concomitantly. His method obviously closely mimics the American Diabetes Association/European Association for the Study of Diabetes consensus algorithm for type 2 DM.⁵ He says this strategy has been effective because it is simple for him to use and widely applicable from patient to patient.

The question that hung in the room and fed our further discussion, however, was whether achieving a good A1C level alone is enough. Is achievement and maintenance of an A1C goal the end of our therapeutic road? It would certainly be convenient if that were all we had to do. Several years ago, after a quick review of the literature, I briefly convinced myself that achieving and maintaining A1C goal was the end point for my patients with DM. Now, however, I think I was wrong. There are clear signs on the horizon that reducing diabetic complication risk involves more than just A1C control. The way we manage DM may, once again, be in for a change.

We have known all along that the A1C value is something of an average and, as such, is related to both the fasting blood sugar and the postprandial blood sugar. In an article exploring the relative contribution of each of these sugars to the A1C, Monnier et al⁶ demonstrated that below an A1C level of $\sim 7.5\%$, the postprandial blood sugar becomes the most significant contributor, rather than fasting blood sugar, to A1C outcome. We must couple that information with the fact that the most recent glycemic goal recommendation by the American Diabetes Association calls for an A1C for “individual patients” to be “as close to normal as possible (<6.0%) without significant hypoglycemia.”⁷ This means that the practitioner committed to excellent A1C control will be paying regular attention to postprandial blood sugar to achieve lower A1C levels. But this attention to postprandial control is still aimed at achieving good A1C levels and does not really address the question I posed earlier—that is, is there more to reducing risk of DM complications than just A1C control?

A fascinating body of evidence is emerging which proposes that the risk of DM complications can be lowered by mechanisms independent of A1C. Such an occurrence was suggested in the DCCT data, which revealed less retinopathy in the intensively treated group (presumably with less postprandial glycemic excursions) despite having A1C values identical to the controls.⁸ A recent article by Monnier et al⁹ reported a linear relationship between markers of oxidative stress and the magnitude of glucose fluctuations, independent of A1C level. This would suggest that postprandial glycemic variations may be independently stimulating harmful by-products (eg, oxidative radicals) that could contribute to endothelial damage. For an excellent in-depth discussion of this concept, the reader is referred to an editorial comment by Brownlee

and Hirsch¹⁰ on the article by Monnier et al and to the recorded lectures given by Brownlee and Hirsch on this topic during the recent Insulin Congress held in Washington, DC (November 2006).¹¹

So, what does all this really mean to primary care providers, such as myself, who are managing 90% of the type 2 DM in the population? First, it in no way diminishes the importance of achieving A1C goals in all of our patients. As discussed earlier, it is likely that postprandial blood sugar will have to be routinely addressed to achieve lower ranges of A1C levels, which are desirable. What is new and somewhat changed is the concept that, beyond the best levels of A1C control, we ought to analyze and address issues of postprandial glycemic excursion and seek to maintain these variations within established guidelines just as we seek to maintain lower A1C levels (Table).¹² To accomplish such goals will likely require considerably more attention being given to prandial therapy.

Does this mean everything just got way too complicated? I think not, actually. Admittedly a new step in our management paradigm may need to be added, but it does not necessarily have to be a complicated one. Just as we have crafted strategies for basal insulin use that are simple, reproducible, and relatively free of hypoglycemia, we must begin to do the same for prandial control. Obviously, the first step is understanding the tools and techniques available to us. The articles in this issue of *Insulin* should be a valuable resource as we start the process of routine targeted management of postprandial glycemia.

Table. Recommended treatment targets for patients with type 2 diabetes mellitus.¹²

	ADA	AACE
A1C	<7.0%	≤6.5%
Preprandial plasma glucose	90–130 mg/dL	<110 mg/dL
Peak postprandial glucose	<180 mg/dL*	<140 mg/dL
Blood pressure	<130/80 mm Hg	
Lipids		
LDL	<100 mg/dL	
Triglycerides	<150 mg/dL	
HDL	>40 mg/dL (male)	>50 mg/dL (female)

ADA = American Diabetes Association; AACE = American Association of Clinical Endocrinologists; A1C = glycosylated hemoglobin; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

*One to 2 hours after the beginning of the meal.

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