Should Postprandial Glucose Be Measured and Treated to a Particular Target? Yes.

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In August 2001, the American College of Endocrinology (ACE) published its recommendations for glycemic targets in the management of diabetes. Included in those recommendations was a target for 2-h postprandial glucose (PPG) of <140 mg/dl; current American Diabetes Association (ADA) guidelines do not include a PPG target, nor have they for several years. The European Association for the Study of Diabetes (EASD/IDF-Europe) have a postprandial target of <7.5 mmol/l (135 mg/dl) as well.

Ever since ACE presented its recommendations to the health care community, there has been considerable debate about the appropriateness of recommending a PPG target to the health care community and lay public. Should PPG be monitored and treated? If so, what should the goal be?

The purpose of this report is to answer some central questions regarding the evidence and rationale that support the use of a 2-h postprandial target of <140 mg/dl. The goal is to provide health care providers and other interested parties with the information they need to make informed decisions about patient care.

It is important to note that although this debate has been broadened to include issues regarding the frequency of testing, no organization has proposed any form of recommendation for “routine” PPG testing.

What is the relationship between PPG and overall glycemic control?
Postprandial hyperglycemia is one of the earliest detectable abnormalities expressed in diabetes (8) and may be a better predictor of progression to diabetes than measurements of fasting glucose. Furthermore, PPG is also a significant contributor to mean plasma glucose, which is the key predictor of glycemic control as measured by A1C (9–12).

Bonora et al. (10) showed that post-lunch plasma glucose and extended post-lunch plasma glucose was more reliable in predicting poor glycemic control than pre-breakfast or pre-lunch plasma glucose.

Whether PPG or fasting plasma glucose is the stronger predictor of overall glycemic control is certainly debatable; the fact that PPG is a strong contributor to glycemic control is not.

What is a normal PPG value?
According to the ADA consensus panel on PPG, PPG levels in nondiabetic individuals rarely rise above 140 mg/dl and then return to normal preprandial levels within 2–3 h (13). Therefore, given that normal postprandial levels are usually well below 100 mg/dl, the ACE 2-h PPG target of <140 mg/dl is quite reasonable, even generous.

The fact that glucose levels are maintained very tightly in nondiabetic individuals reflects the importance of PPG levels. Additionally, the ADA already recognizes that impaired glucose tolerance, a 2-h PPG between 140 and 200 mg/dl, is abnormal (13).

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This commentary was intended to be part of a Point/Counterpoint feature discussing the value of postprandial glucose measurements. (See the commentary by John Buse: Should postprandial glucose be routinely measured and treated to a particular target? No! Diabetes Care 26:1615–1618, 2003.)

Abbreviations: ACE, American College of Endocrinology; ADA, American Diabetes Association; PPG, postprandial glucose.

A table elsewhere in this issue shows conventional and International (SI) units and conversion factors for many substances.

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Does targeting postprandial hyperglycemia improve overall glycemic control?

Feinglos et al. (14) showed that using insulin lispro to target postprandial hyperglycemia in patients with type 2 diabetes not only improved PPG control but also reduced both fasting glucose and A1C levels from 9.0 to 7.1%.

Furthermore, a study by Bastyr et al. (15) showed that therapies that focused on lowering PPG versus fasting glucose are better for lowering glycated hemoglobin levels.

Finally, De Veciana et al. (16) clearly demonstrated that targeting treatment to 1-h PPG levels rather than fasting glucose significantly reduces A1C in pregnant women and improves neonatal outcomes. These outcomes lead to fewer C-sections and decreased admission of neonates to the intensive care unit. Clearly, PPG control in pregnancy results in a substantial economic benefit.

Is PPG an independent contributor to diabetes outcomes?

A study by de Vegt et al. (17) found that the degree of risk conferred by the 2-h PPG concentration was nearly twice that conferred by A1C level.

Other recent studies (18,19) have demonstrated that even moderate postprandial hyperglycemia (148–199 mg/dl) is not only more predictive of atherosclerosis than fasting glucose, but also may have direct adverse effects on the endothelium.

Although numerous epidemiological studies (17–21) have shown elevated postprandial/postchallenge glucose to be independent and significant risk factors for macrovascular complications and increased mortality risk, it is not known if PPG is an independent contributor to diabetes outcomes.

Is managing PPG safe?

Although the percentage of severe hyperglycemia in the Diabetes Control and Complications Trial (1) was high in the intensive treatment group, the number of patients who actually experienced hyperglycemia was small.

The VA Cooperative Study (22) showed severe hypoglycemic reactions to be extremely rare among intensively treated patients, and not significantly different from those among conventionally treated patients.

The Kumamoto study (2) showed no severe hypoglycemia >8 years in either the intensively or the conventionally treated group.

The U.K. Prospective Diabetes Study (3,23) did show severe hypoglycemia in intensively treated patients (0.1–2.3% per year). However, even patients treated with diet therapy alone also reported severe hypoglycemia. The reporting of severe hypoglycemia among patients treated nonpharmacologically (0.03% per year) raises some question about the actual incidence of true severe hypoglycemia.

Regardless of the differences in reported hypoglycemia in these studies (2,3,23), all of them have shown that the risk of severe hypoglycemia in type 2 diabetes is significantly less than in type 1 diabetes.

Is managing PPG even possible?

Today’s new pharmacological therapies, blood glucose monitoring technologies, and innovative treatment strategies make it possible to safely and effectively manage PPG.

In addition to new rapid-acting and long-acting insulin analogs (24–27), there are also rapid-acting oral secretagogues, such as repaglinide and nateglinide, that have been shown to be safe and effective in controlling PPG excursions (28,29). Other drugs such as α-glucosidase inhibitors also work by lowering PPG levels (30).

Many of the existing sensitizers also have a positive effect on postprandial hyperglycemia, in addition to lowering fasting glucose (31).

Furthermore, a recent study of non-insulin-treated patients with type 2 diabetes by Schwedes et al. (32) showed that meal-related self-monitoring of blood glucose not only improved overall glycemic control but also resulted in significant improvement of general well-being.

Why would we not set a goal for PPG?

How many clinicians did not strive to achieve near-normal glycemia in our type 1 diabetic patients before 1993 when results from the Diabetes Control and Complications Trial were announced? How many did not strive to achieve near-normal glycemia in our type 2 diabetic patients before announcement of the U.K. Prospective Diabetes Study’s results in 1998?

We already know that elevated glucose in the fasting state is harmful and that an elevated postprandial before diagnosis of diabetes increases the risk of cardiovascular complications. How, then, can we consider postprandial hyperglycemia to be of no significance once the diagnosis is made? It does not make sense to not monitor and manage PPG.

Managing diabetes is both an art and a science. It is an art in regard to the clinical judgment we use to make decisions about patient needs and therapies. The science provides the base knowledge in our research. Both clinical judgment and evidence-based knowledge are critical to our ability to effectively treat patients.

Science shows that postprandial hyperglycemia is a significant contributor to overall glycemic control and possibly an independent contributor to diabetes outcomes. Therefore, sound clinical judgment dictates that it should be managed. Furthermore, the ADA guidelines (13) clearly state PPG monitoring may be considered during pregnancy and when using medications that treat postprandial hyperglycemia. But as the saying goes, “You can’t manage what you don’t measure.” Clearly a 2-h PPG target of <140 mg/dl is both reasonable and responsible.

References


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