Extended abstract title: EDMC 2019: Effect of Comprehensive Diabetes Care on HbA1C, Blood Glucose and Body Mass Index in Type II Diabetes Patients: A Retrospective Study- Rahul Mandole, Madhavbaug Cardiac Care Clinics and Hospital

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Abstract

In 2017, the numbers of adults with diabetes mellitus were estimated to be 425 million worldwide and over 7.2 million in Japan. Of the two principal types, approximately 95% of all diabetes cases were classified as type 2 (T2D). Adults with T2D have a higher risk of cardiovascular (CV) mortality than those without T2D. Many observational studies have reported an association between an increase in glycated hemoglobin (HbA1c) and CV risk in patients with T2D, which is why professional society guidelines have historically recommended strict control of blood glucose, assessed using HbA1c, in patients with T2D. In addition, regulatory authorities have approved medicines for the treatment of T2D on the basis of the use of HbA1c as the primacy therapeutic endpoint. However, data from large randomized trials have questioned the value of intensive glycemic control. As a result, recent revisions to such guidelines have moved away from the use of uniform intensive glycemic control as a target and toward individualized HbA1c goals, but the ideal target, which optimally balances benefits and risks, requires further clarification. Some of the published guidelines recommend standard glycemic control, with HbA1c targets of 7% or 8%, whereas those from the American Association of Clinical Endocrinologists (AACE), the American Diabetes Association (ADA), and the Japan Diabetes Society recommend intensive glycemic control, with HbA1c targets of below 7% or 6.5%.

The American College of Physicians (ACP) has reviewed these guidelines and five large randomized controlled trials comparing standard and intensive glycemic control. In their guidance statement issued in March 2018, the ACP recommended that clinicians should aim to achieve standard control, with an HbA1c between 7% and 8%, instead of intensive control in most adult patients with T2D. However, the ADA, AACE, the American Association of Diabetes Educators (AADE), and the Endocrine Society immediately issued a joint statement that strongly repudiated the ACP guidance, causing confusion among healthcare professionals.

Controversial conclusion not only questioned the efficacy of intensive glycemic control, but rekindled the long-standing debate about the usefulness of HbA1c targets in the treatment of T2D. Three problems can be identified. First, hypoglycemia and low HbA1c concentrations are associated with higher CV risk. Second, the use of either conventional or newer anti-diabetic agents is associated with a higher risk of heart failure. Third, recent CV outcome trials (CVOTs) have shown that drugs that lower HbA1c to similar concentrations are associated with differing CV outcomes. As a result, a recent survey showed that stakeholders in drug development considered HbA1c as an imperfect target. In this review, we aim to assess the usefulness of HbA1c as a therapeutic target and to discuss measures that could be implemented to improve the performance of HbA1c as a therapeutic target in T2D.

Glycated hemoglobin, a minor fraction of adult hemoglobin, is formed slowly and continuously by the non-enzymatic chemical modification of hemoglobin molecules. The glycation reaction is essentially irreversible, and the rate of formation of HbA1c is directly proportional to the ambient glucose concentration. The concentration of HbA1c therefore reflects glycemic history, that is, the time-weighted mean glucose over the preceding 8-12 weeks, which is determined primarily by red blood cell (RBC) lifespan. HbA1c has been proven to provide a superior estimate of mean glycemic than routine determinations of blood glucose concentration. Therefore, the use of HbA1c is endorsed for screening and the diagnosis of diabetes, because its concentration increases well in advance of the clinical development of diabetes. The International Expert Committee recommended the use of an HbA1c ≥6.5% for the diagnosis of diabetes in 2009, and this recommendation was subsequently adopted by the ADA, the World Health Organization, and other professional groups.

Glycated hemoglobin concentration can be affected by a variety of genetic, hematologic, and disease-related factors, but the specific effects depend on the specific hemoglobin variant or derivative and the HbA1c assay used. This is because structural variants of hemoglobin in patients with hemo-globinopathies, such as thalassemia or sickle-cell disease, interfere with some HbA1c assays. Even when the effect of carbamylated hemoglobin is excluded, high HbA1c values in non-diabetic patients are still associated with chronic kidney diseases.

Glucose-independent racial differences in HbA1c concentrations have been observed in people both with and without diabetes. Black people have been reported to have 0.4% (95% CI, 0.2-0.6) higher HbA1c than white people at comparable mean glucose concentrations. However, the implications of this ethnic difference in HbA1c for both the diagnosis and treatment of T2D have been debated, and it does not appear to affect CV outcomes in people without diabetes.

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