

Glycated hemoglobin or glycated albumin for assessment of glycemic control in hemodialysis patients with diabetes?

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SUMMARY

This commentary discusses the findings of a study by Peacock *et al.*, who measured levels of glycated hemoglobin (HbA_{1c}) and glycated albumin in patients with diabetes who either were or were not on hemodialysis in an effort to determine which marker is the better indicator of glycemic control. They found that HbA_{1c} and glycated albumin levels are both independently associated with serum glucose level. However, HbA_{1c} level—unlike glycated albumin level—was also influenced by hemodialysis, hemoglobin level, and erythropoietin dose. Although we agree that glycated albumin level could be a better indicator of glycemic control than HbA_{1c} level in patients on hemodialysis who have diabetes and anuria, this conclusion might not be applicable to patients with massive proteinuria or to those on peritoneal dialysis. Further studies are required to confirm the target glycated albumin level that is necessary to ensure a good prognosis for patients with diabetes who are on hemodialysis because no clear consensus has yet been reached. In addition, more data are needed to determine at which stage of kidney disease measurement of glycated albumin levels becomes preferable to assessment of HbA_{1c} level.

KEYWORDS diabetes mellitus, glycated albumin, glycated hemoglobin, hemodialysis

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COMMENTARY

In patients with diabetes, strict glycemic control lowers the risk of cardiovascular events—which are the main cause of death in this setting¹—and improves prognosis among those with chronic kidney disease (CKD) who undergo regular hemodialysis;² therefore, the accurate assessment of glycemic control is important to optimize outcomes.

Glycated hemoglobin (HbA_{1c}) level, which indicates the percentage of circulating hemoglobin that has chemically reacted with glucose, reflects the blood glucose level over the 120 days preceding the test; glucose levels during the 30 days before the test have the biggest impact on HbA_{1c} level. The lack of specific guidelines for assessing glycemic control in patients who are receiving hemodialysis has resulted in the HbA_{1c} assay—which is widely used in the general population—being the test of choice in this setting. However, in patients with diabetes who are on hemodialysis, factors such as anemia (due to reduced erythrocyte life span or iron deficiency), recent transfusions, metabolic acidosis, and administration of

erythropoietin affect the accuracy of the HbA_{1c} assay.³ By increasing the proportion of young erythrocytes in the blood, both anemia and erythropoietin can falsely lower HbA_{1c} levels, which could in turn lead to a failure to diagnose hyperglycemia.⁴ Approximately 90% of patients on hemodialysis worldwide undergo erythropoietin treatment;⁵ therefore, HbA_{1c} might be an unsuitable marker for glycemic control in the hemodialysis setting.

On the basis of a study involving Japanese patients on hemodialysis,³ glycated albumin has been proposed to be a better marker of glycemic control than HbA_{1c}, as levels of glycated albumin in the blood are unaffected by changes in the survival time of erythrocytes. Peacock *et al.* have now sought to validate the measurement of glycated albumin as an alternative to HbA_{1c} quantification for the assessment of glycemic control in 307 American patients with diabetes, of whom 258 were undergoing hemodialysis and 49 did not have overt kidney disease.⁶ To quantify the level of glycated albumin, Peacock *et al.* utilized a new enzymatic assay that relies on an albumin-specific proteinase and, unlike the conventional assay, is not subject to interference

by endogenous glycated amino acids or changes in albumin concentration.

Multiple regression analysis confirmed that both HbA_{1c} and glycated albumin levels were independently associated with serum glucose concentration ($P < 0.0001$ for both). However, Peacock *et al.* found that the glycated-albumin:HbA_{1c} ratio was higher in the patients on hemodialysis than in the patients without kidney disease (2.72 vs 2.07; $P < 0.0001$). Thus, in patients on hemodialysis, HbA_{1c} measurements significantly underestimate blood glucose levels compared with glycated albumin values. In addition, HbA_{1c} values were independently associated with hemodialysis ($P < 0.0001$) and, in hemodialysis patients, with hemoglobin concentration ($P = 0.0027$) and erythropoietin dose ($P = 0.03$). By contrast, glycated albumin level was not significantly associated with hemodialysis, or with hemoglobin level or erythropoietin dose in patients on hemodialysis; therefore, the authors concluded that glycated albumin is a better indicator of glycemic control than HbA_{1c}.

The average glycated-albumin:HbA_{1c} ratio in the patients on hemodialysis in Peacock *et al.*'s study was slightly lower than that reported by Inaba *et al.* for the Japanese patients who were receiving hemodialysis (2.72 vs 3.81).³ This inconsistency might be due to differences between the two studies in the serum albumin assays used, the erythropoietin doses administered, the mean HbA_{1c} levels, or the patients' ethnicity. The mean erythropoietin dose given to the American patients on hemodialysis far exceeded that administered to their Japanese counterparts (22,876 U/week vs 5,385 U/week), and the mean HbA_{1c} level in the American patients on hemodialysis was higher than that in the Japanese participants (6.8% vs 5.85%). The contention by Peacock *et al.* that discrepancies between the two studies might be due to the large proportion of African Americans (63.6% of the hemodialysis population) in the US study is difficult to understand. African Americans have an increased risk of carrying the hemoglobin S and thalassemia genes, which are both associated with decreased erythrocyte survival and would, thus, be expected to increase, rather than decrease, the glycated-albumin:HbA_{1c} ratio.

Some issues remain to be clarified. In Peacock *et al.*'s study, glycated albumin values were measured only once. Measurement of glycated albumin level reflects glycemic control for only

the 1–2 weeks preceding the assay, so repeated measurements of glycated albumin (i.e. every 2 weeks or monthly) will be required in future studies. Furthermore, it will be important to determine the clinical stage at which these measurements should be initiated (i.e. at CKD stage 3, 4, or 5, at diagnosis of renal anemia, or upon initiation of erythropoietin therapy). The use of glycated albumin levels to assess glycemic control might be limited to patients with anuria or normoalbuminuria who are receiving hemodialysis. In patients on peritoneal dialysis and those with CKD who have massive proteinuria, glycated albumin levels can be falsely reduced because of the shorter exposure time of albumin to glucose in plasma. Further investigations are also required to establish the target glycated albumin level that predicts the best prognosis for patients with diabetes who are on hemodialysis. Moreover, no long-term, large-scale clinical trials have investigated the use of glycated albumin as an indicator of glycemic control. Thus, whether this parameter is an accurate predictor of morbidity and mortality in patients with diabetes who are on hemodialysis remains to be ascertained.

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PRACTICE POINT

In patients with diabetes who are on hemodialysis, glycated albumin level seems to reflect glycemic control more accurately than does glycated hemoglobin level. However, clinicians should be aware that optimal levels of glycated albumin have not yet been established and that whether glycated albumin levels reflect glycemic control in patients with proteinuria and in those undergoing peritoneal dialysis is unclear.

Competing interests

The authors declared no competing interests.