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Glycated albumin is superior to glycated hemoglobin for glycemic control assessment at an early stage of diabetes treatment: A multicenter, prospective study

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ABSTRACT

Aims: This study was to determine whether serum glycated albumin (GA) was a better indicator of glycemic control than hemoglobin A1c (HbA1c) when starting a new treatment regimen for type 2 diabetes.
Methods: Newly diagnosed type 2 diabetes patients, or patients who had poor glycemic control with oral hypoglycemic agents, were enrolled at 10 hospitals in Beijing. Serum GA, HbA1c, fasting blood glucose (FBG), and C-peptide were assayed on Days 0, 14, 28, and 91 after treatment.
Results: Four hundred ninety-nine patients were enrolled. Mean FBG, GA and HbA1c decreased significantly in patients at Days 14, 28, and 91. In patients with improved glycemic control, the reduction of GA and HbA1c levels was 10.5 ± 13.3% vs. 5.1 ± 5.4% on Day 14, 16.0 ± 13.4% vs. 9.0 ± 7.0% on Day 28, and 18.0 ± 16.7% vs. 18.3 ± 9.4% on Day 91, respectively, compared with baseline values. Changes in GA on Day 14, 28 and 91 were all closely correlated with changes in HbA1c on Day 91. Change in GA on Day 14 was correlated with treatment effectiveness evaluated by HbA1c on Day 91.
Conclusions: GA may be a useful marker for assessing glycemic control at an early stage of new diabetes treatment and assist in guiding adjustments to treatment and therapy.

1. Introduction

Accurate glucose monitoring in diabetes is needed to guide treatment and adjust therapy. Measurement of glycated proteins is an option for monitoring routine glycemic control in people with diabetes. Among various glycated proteins, glycated hemoglobin, hemoglobin A1c (HbA1c), i.e., the percentage of hemoglobin that is bound to glucose, is widely used as the gold standard parameter for assessment of glycemic control. Moreover, previous studies in diabetes patients have used the mean HbA1c level or changes in HbA1c level to evaluate development or progression of diabetic complications (Lind, Oden, Fahlen, & Eliasson, 2009). However, HbA1c has some limitations as marker of average blood glucose levels. HbA1c is affected by a variety of conditions, such as hemolytic anemia, recent blood loss or blood transfusion, chronic renal failure, use of erythropoietin or other drugs that affect erythropoiesis, and the presence of variant hemoglobins (Bry, Chen, & Sacks, 2001; Lapolla, Mosca, & Fedele, 2011). In addition, HbA1c represents the average blood glucose level over the previous 2–3 months. It does not provide information on glycemic control before that time or on rapidly occurring changes in glycemic control. Thus, HbA1c is not a good indicator for patients who are starting or changing diabetes treatments because its level changes too slowly to guide near-future treatment.

Conflict of interest: There is no conflict of interest.

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Glycated albumin (GA), expressed as the percentage of serum GA to total serum albumin, is also used to monitor glycemic control. Serum albumin has a shorter half-life (approximately 17–19 days) than that of hemoglobin. As a result, GA reflects a shorter-term (2–3 weeks) glycemic control status than HbA1c (Lee et al., 2013). Therefore, GA is likely to be more sensitive than HbA1c for monitoring glycemic control when rapid treatment responses are evaluated, in rapidly developing diabetes for example (Juraschek, Steffes, & Selvin, 2012). In addition, GA is not strongly influenced by disorders of hemoglobin metabolism, such as anemia and erythropoietin injection (Koga & Kasayama, 2010).

We evaluated GA as an indicator of glucose control compared with HbA1c in type 2 diabetes patients who were beginning or changing diabetes treatment. The main comparison was change in GA at 2 weeks after the initiation of treatment versus changes in HbA1c at 3 months.

2. Methods and subjects

2.1. Patients

Patients with type 2 diabetes were enrolled at ten hospitals in Beijing between 3 November 2010 and 28 November 2011. The patients were diagnosed with diabetes according to the 1999 World Health Organization (WHO) criteria (Alberti & Zimmet, 1998). Eligible patients were 1) 20–70 years of age; 2) newly diagnosed with type 2 diabetes or needing a change in regimen because of poor glycemic control with one or two oral hypoglycemic agents. Poor glycemic control was defined as an HbA1c level of 7–11% after treatment with oral hypoglycemic agents for at least 2 months. These patients with 1) diabetes of more than 15 years duration (n = 0); 2) current insulin treatment (n = 0); 3) severe microvascular or macrovascular complications (n = 0); 4) severe liver and kidney dysfunction (n = 0); 5) hematological abnormalities or anemia (n = 0); 6) thyroid diseases (n = 0); 7) current systemic corticosteroid treatment (n = 0); 8) pregnant women or 9) unwillingness to participate or poor adherence (n = 20) were excluded, based on their medical history, physical examination and laboratory tests. In addition, another 12 patients were excluded due to the loss of basal blood samples.

In this study, patients received a single hypoglycemic agent or combination treatment with two or three agents, including sulfonylurea, metformin, or an alpha-glucosidase inhibitor. The Ethics Committee of the Chinese PLA General Hospital approved the study, and all patients provided written informed consent prior to participation.

2.2. Assay of serum GA and HbA1c

Blood samples were collected for measurement of serum GA, HbA1c, fasting blood glucose (FBG) levels on days 0, 14, 28, and 91 and stored at −80 °C in ultra-low temperature freezers until use. All blood samples were measured in the central laboratory. Serum GA was measured on an automatic biochemical analyzer (Hitachi 7600, Tokyo, Japan) by an enzymatic method (Lucica GA-L; Asahi Kasei Pharma Corp., Tokyo, Japan) following the assay kit manufacturer's instructions. The assay precision was evaluated by multiple measurements of GA at different serum concentrations. Specifically, serum samples with high and low concentrations of GA were measured for 10 times each, and the average values of GA were 36.8 ± 0.3% and 12.7 ± 0.1% with coefficients of variation of within-day reproducibility 0.7% and 0.9%, respectively. Similarly, serum samples with high and low concentrations of GA were measured for 8 times each, and the average values of GA were 37.9 ± 0.4% and 13.2 ± 0.2% with coefficients of variation of inter-day reproducibility 0.94% and 1.49%, respectively. HbA1c was measured by high-performance liquid chromatography (HPLC) using an automated system (HPLC Variant II; Bio-Rad Laboratories, Munich, Germany); the within-day and inter-day reproducibility coefficients of variation of HbA1c were 0.55–1.77% and 1.48–1.86%, respectively. FBG, C-peptide and blood lipids were assayed by an automatic biochemical analyzer (Hitachi Ltd., Tokyo, Japan).

2.3. Statistical analysis

Statistical analysis was performed using SAS 8.2 (SAS Institute Inc., Cary, NC, USA). Patient demographic and clinical data were expressed as means ± standard deviation (SD) or medians (range), as appropriate. Categorical variables were reported as numbers and/or percentages. Differences between patient groups were compared and tested for significance using analysis of variance (ANOVA). Correlations between variables were tested by logistic regression analysis. All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant.

3. Results

3.1. Patient clinical and biochemical characteristics

The final study population included 499 patients (228 men and 271 women) with a mean age of 54.8 ± 9.4 years. Of the 499 patients, 233 (46.7%) were using a single hypoglycemic agent, 237 (47.5%) were on combination regimens with two agents, and 29 (5.8%) were being treated with three agents. The clinical and biochemical characteristics of the study subjects are shown in Table 1. There were no statistically significant differences in body weight, serum albumin, serum total protein, systolic blood pressure, diastolic blood pressure, or heart rate before (day 0) or after (day 91) treatment.

3.2. FBG, C-peptide, HbA1c and GA levels before and after treatment

As shown in Fig. 1, the mean FBG, C-peptide, GA and HbA1c levels were significantly lower in all patients on days 14, 28, and 91, compared with the baseline (day 0) values. HbA1c and GA levels were 6.1% and 8.5% lower on day 14, 6.9% and 13.8% lower on day 28, and 13.5% and 14.6% lower on day 91, respectively, than on day 0. In addition, FBG, GA and HbA1c levels were significantly lower in all patients on days 28, and 91, compared with the baseline (day 14).

Of the patients with complete data, 332 achieved improved glycemic control on day 91, defined as a decrease in HbA1c of ≥0.5% compared with the baseline level. Twenty-six patients with improved glycemic control had some missing data and were not included in the analysis. Of the other patients, 141 had poor glycemic control, i.e., a

Table 1
Clinical and biochemical characteristics of the study subjects.

Characteristic	Day 0	Day 91
Gender (male/female, n)	228/271	–
Age (years)	54.8 ± 9.4	–
Body weight (kg)	71.6 ± 12.4	70.88 ± 12.0
Height (cm)	164.6 ± 8.2	–
BMI (kg/m^2)	26.4 ± 3.4	26.0 ± 3.3
Serum albumin (g/L)	46.6 ± 3.3	45.2 ± 3.1
Serum total protein (g/L)	74.3 ± 5.0	72.5 ± 4.6
SBP (mmHg)	128.9 ± 16.1	125.0 (13.3)
DBP (mmHg)	80.2 ± 9.0	78.2 (9.5)
Heart rate (beats/min)	76.0 ± 8.6	74.4 ± 7.2
HbA1c (%)	8.3 ± 1.1	7.2 ± 0.9
Glycated albumin (%)	19.8 ± 4.7	16.9 ± 2.4
Use of hypoglycemic agents		
Single agent (*n*)	233	
Two agents (*n*)	237	
Three agents (*n*)	29	

Data are expressed as means ± SD. All P values are >0.05 between day 0 and day 91.
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

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