Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Serum albumin-adjusted glycated albumin as a better indicator of glycemic control in Type 2 diabetes mellitus patients with short duration of hemodialysis

Takahiro Yajima [a,*], *Kumiko Yajima* [b], *Makoto Hayashi* [b], *Hiroshi Takahashi* [c], *Keigo Yasuda* [b]

[a] *Department of Nephrology, Matsunami General Hospital, Gifu 501-6062, Japan*
[b] *Department of Internal Medicine, Matsunami General Hospital, Gifu 501-6062, Japan*
[c] *Division of Medical Statistics, Fujita Health University School of Medicine, Aichi 470-1192, Japan*

ARTICLE INFO

Article history:
Received 22 March 2017
Received in revised form
19 April 2017
Accepted 16 May 2017
Available online 9 June 2017

Keywords:
Glycated albumin
Serum albumin-adjusted glycated albumin
Type 2 diabetes mellitus
Hemodialysis
Continuous glucose monitoring

ABSTRACT

Aims: Serum albumin-adjusted glycated albumin (adjusted GA) is reportedly a better predictor of mortality than GA in patients with Type 2 diabetes mellitus (T2DM) on hemodialysis (HD). We compared how accurately GA and adjusted GA reflected glycemic control in these patients.

Methods: We enrolled 31 patients with T2DM on HD. They were divided into two groups according to duration of HD: ≤6 months (short HD group, $N = 16$) and >6 months (long HD group, $N = 15$). GA or adjusted GA and parameters of glycemic control obtained by continuous glucose monitoring were measured, and the correlations between these were analyzed.

Results: GA and adjusted GA were significantly correlated with mean glucose levels ($r = 0.400$, $P = 0.025$ and $r = 0.508$, $P = 0.0037$) in all patients. Similar results were obtained in the long HD group (GA: $r = 0.554$, $P = 0.032$; adjusted GA: $r = 0.604$, $P = 0.017$). However, in the short HD group, adjusted GA ($r = 0.502$, $P = 0.047$) but not GA ($r = 0.340$, $P = 0.20$) was significantly correlated with mean glucose levels.

Conclusions: Adjusted GA may be a better indicator than GA for evaluating glycemic control in T2DM patients with short duration of HD.

1. Introduction

For patients with diabetes mellitus (DM), glycemic control is important for the prevention of microvascular and macrovascular complications [1–3]. Glycated hemoglobin (HbA1c) has been widely used as a standard marker for evaluating glycemic control, but in patients with end-stage renal disease (ESRD) on hemodialysis (HD), it underestimates past levels of glycemia due to renal anemia [4,5]. Glycated albumin (GA) is not influenced by erythrocyte lifespan or erythropoietin therapy [6,7], and thus, it could provide an alternative marker for evaluating glycemic control in these patients. Indeed, some

* Corresponding author at: Department of Nephrology, Matsunami General Hospital, 185-1 Dendai, Kasamatsu, Gifu 501-6062, Japan.
E-mail address: yajima5639@gmail.com (T. Yajima).
http://dx.doi.org/10.1016/j.diabres.2017.05.020
0168-8227/

studies have shown GA to be a significant predictor of mortality in patients with Type 2 DM (T2DM) on HD [8,9].

Recently, serum albumin-adjusted GA (adjusted GA) has been reported to be a better indicator of glycemic control than GA for patients with T2DM and ESRD who are not on HD [10,11]. Furthermore, adjusted GA could reportedly predict mortality more accurately than GA in patients with T2DM and ESRD on HD [12]; however, it remains unclear how effectively it reflects glycemic control. In this study, we evaluated whether adjusted GA reflected glycemic control more accurately than HbA1c or GA in these patients using continuous glucose monitoring (CGM). Moreover, we divided them into two groups according to the duration of hemodialysis, and then evaluated the correlation between them.

2. Patients and methods

2.1. Participants

We enrolled 31 patients with T2DM and ESRD at the outpatient clinic of Matsunami General Hospital, who had been treated with the same regimen of insulin for more than three months. Patients with Type 1 DM were excluded. All of the enrolled participants underwent regular HD, stably, three times a week with standard bicarbonate dialysate containing 7.0 mmol/L of glucose. This study adhered to the principles of the Declaration of Helsinki, and all participants provided informed consent to participate. The study protocol was approved by the ethics committee of Matsunami General Hospital (No. 319).

2.2. Study protocol

All participants were hospitalized, and their insulin therapy was continued according to the same regimen. A blood sample was obtained in the morning before breakfast on a non-HD day. HbA1c was measured by high performance liquid chromatography (ADAMS-A1c HA8170; Arkray Inc., Kyoto, Japan); at the same time, GA was measured by an enzymatic method (Lucica GA-L, Asahi Kasei Pharma, Tokyo, Japan) using a JCA-BM8000 series analyzer (JEOL Ltd., Tokyo, Japan). A CGM device (iPro2; Medtronic MiniMed, Fridley, MN, USA) was attached on a non-HD day when blood sample was obtained. Glucose levels were continuously recorded every 5 min for 4 days; calibration was performed four times a day by a self-monitoring blood glucose device (One Touch Ultra; LifeScan Inc., Milpitas, CA, USA). Mean and standard deviation (SD) of glucose levels were obtained for HD (2nd day) and non-HD days (3rd day). As glycemic variability makaers, mean amplitude of glycemic excursions (MAGE) and percentage coefficient of variation (%CV) were also calculated using CGM data. Adjusted GA was calculated using the formula previously reported by Yajima et al. [12] as follows:

$$\text{adjusted GA } [\%] = \text{GA } [\%] \times 21.1/(0.298 \times \text{Alb } [\text{g/L}] + 10.1),$$

where Alb is the serum concentration of albumin.

2.3. Statistical analysis

Normally distributed variables are presented as mean ± SD, and non-normally distributed variables as median and interquartile range (IQR). Pearson's product-moment correlation coefficients were calculated to analyze the correlations between HbA1c, GA, or adjusted GA and parameters of glycemic control obtained by CGM on each HD day, non-HD day, and overall. In addition, the participants were divided into two groups according to whether they had been on hemodialysis for more (the "long HD" group, $N = 15$) or less (the "short HD" group, $N = 16$) than the median period of 6 months. Differences between the two groups were evaluated by Mann–Whitney test or Student's two sided t-test for continuous variables and by chi-square test for categorical variables. All statistical analyses were performed using the SPSS version 21 software program (IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered statistically significant.

3. Results

The clinical characteristics of the participants are summarized in Table 1. All were treated only with insulin (12 with insulin lispro, 6 with insulin lispro with insulin glargine, 11 with insulin lispro with insulin degludec, and 2 with insulin glargine). The median total daily dose of insulin was 12 (9–24) U/day. Comparisons between the long and short HD groups showed that the levels of hemoglobin, HbA1c, GA, and adjusted GA were significantly lower in the short HD group than in the long HD group. However, the levels of Alb tended to be lower in the short HD group than in the long HD group (Table 1). Adjusted GA was significantly higher than GA (20.5 ± 3.5 versus 19.2 ± 3.9, $p = 0.029$) in the short HD group, but no significant difference was found between adjusted GA and GA (23.9 ± 4.3 versus 23.7 ± 4.9, $p = 0.80$) in the long HD group.

The CGM was successfully performed for all of the participants, and there were no missing data. The mean values for all the participants of their individual mean glucose levels, SD of glucose levels, MAGE, and %CV were shown in Table 2. There were no significant differences in mean glucose levels, SD of glucose levels, MAGE, and %CV between the short and long HD groups (Table 2).

Table 3 shows the correlation coefficients for HbA1c, GA, and adjusted GA with parameters of glycemic control on days with and without HD, and overall. GA and adjusted GA but not HbA1c showed significant correlations with mean glucose levels on days with and without HD, and overall. On the other hand, HbA1c was significantly correlated with SD of glucose levels only on HD days, but was not correlated with MAGE and %CV. GA and adjusted GA was significantly correlated with SD of glucose levels on HD and non-HD days, and overall. GA was significantly correlated with MAGE on HD days and overall days, and with %CV only on overall days. Adjusted GA was significantly correlated with MAGE on HD days and overall days, but was not correlated with %CV.

Table 4 shows the correlation coefficients for HbA1c, GA, and adjusted GA with parameters of glycemic control obtained by CGM in the long HD group. HbA1c, GA, and adjusted GA were significantly correlated with mean glucose levels overall. HbA1c was significantly correlated with mean glucose levels on HD days and tended to be correlated with those on non-HD days ($p = 0.053$). GA was significantly