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International Journal of Diabetology & Vascular Disease Research (IJDVR)
ISSN 2328-353X

Glycated Albumin: A More Sensitive Predictor of Cardiovascular Disease than Glycated Hemoglobin?

Editorial

Saisho Y

Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan.

Keywords: Glycated Albumin, Glycated Hemoglobin, Cardiovascular Disease, Type 2 Diabetes.

***Corresponding Author**:
Yoshifumi Saisho
Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan.
Tel: +81-3-3353-1211 Extn: 62383 ; Fax: +81-3-3359-2745
E-mail: ysaisho@z5.keio.jp

Received: October 06, 2013
Published: October 31, 2013

Citation: Saisho Y (2013) Glycated Albumin: A More Sensitive Predictor of Cardiovascular Disease than Glycated Hemoglobin?. Int J Diabetol Vasc Dis Res. 1(4e), 1-2. **doi: http://dx.doi.org/10.19070/2328-353X-130004e**

Type 2 diabetes is an established risk factor for cardiovascular disease (CVD). Compared to non-diabetic subjects, patients with type 2 diabetes have a 2 to 4-fold increased risk of development of CVD [1]. Intensive glycemic control aiming at HbA1c below 7% has been shown to reduce the risk of development of microvascular disease in patients with type 2 diabetes; however, its effect on CVD was rather modest [2]. Moreover, recent trials aiming to achieve near-normal glycemic control (i.e., HbA1c below 6%) to improve CVD outcomes in patients with type 2 diabetes failed to show a reduction of the primary endpoints (death from CVD, non-fatal myocardial infarct and non-fatal stroke) by intensive glycemic control compared to standard care [3-5]. The findings revealed a modest effect of glycemic control on CVD outcome, and underpinned the importance of avoiding hypoglycemia in the treatment of type 2 diabetes, but also suggested the limitation of HbA1c as a predictor of therapeutic effect on CVD outcome.

Glycated albumin (GA) is a ketoamine which is formed by binding of albumin and glucose by nonenzymatic glycation reaction. Since the turnover of albumin is relatively short, GA reflects the average glucose value in the previous 1 to 2 weeks, whereas HbA1c reflects the average glucose value in the previous 1 to 2 months [6]. Moreover, it has been reported that albumin is more rapidly glycated compared to hemoglobin [7]. Therefore, glycated albumin may reflect glycemic control more sensitively than does HbA1c. A recently-developed enzyme method for measurement of GA has allowed GA to be more rapidly and easily determined [8]. Recent studies have shown that GA is more strongly correlated with postprandial glycemic excursion compared with HbA1c [9-12]. Since postprandial glycemic excursion has been shown to be a risk factor for CVD [13-14], GA may predict CVD outcome more sensitively than does HbA1c. This was shown to be the case. It has been reported that GA was more strongly associated with coronary atherosclerosis [15-16]. It has been also reported that GA and GA to HbA1c ratio but not HbA1c predicted the pro ression of carotid intima-media thickness (IMT) [17]. These findings suggest the usefulness of GA for prediction of CVD. Recently, the usefulness of GA as a predictor of diabetic complications compared with HbA1c was examined in two large-scale studies; the Atherosclerosis Risk in Communities (ARIC) Study and the Diabetes Control and Complications Trial (DCCT). In these studies, GA was significantly associated with microangiopathy; however, its association was comparable to that of HbA1c [18-19]. In DCCT, GA showed no significant association with CVD, whereas HbA1c did [19]. Further prospective study examining the correlation between GA and CVD is warranted. Although the association between GA and atherosclerosis is explained by postprandial glucose excursion, the underlying mechanism of the association between GA and atherosclerosis remains unclear. It has also been reported that GA itself promotes atherosclerosis through induction of reactive oxygen species and inflammatory chemokines, endothelial damage and vessel wall hypertrophy [20]. To clarify the association between GA and atherosclerosis, further studies to explore the underlying mechanism are also needed. Another issue with GA is the existence of factors other than plasma glucose level that affect GA level. As HbA1c level is affected by various factors such as anemia and hemoglobinopathy, GA level is also affected by various factors [6,21]. It has been reported that GA level is decreased with obesity and nephrotic syndromend increased with liver cirrhosis and hypothyroidism [6,22] In clinical settings, since obesity and proteinuria are also associated with increased risk of CVD, the predictive value of GA in those patients needs to be clarified. Nonetheless, in hemodialysis patients, it has been reported that GA more sensitively reflects plasma glucose level and all-cause mortality than does HbA1c [23-24]. In conclusion, GA is a novel glycemic marker which more sensitively reflects postprandial glucose excursion compared with HbA1c. Although GA has been shown to more strongly correlate with atherosclerosis compared with HbA1c in some studies, GA is also affected by various factors other than plasma glucose level, as is HbA1c. Therefore, further studies are warranted to clarify the usefulness of GA in the treatment of type 2 diabetes. Hopefully, a combination of GA and HbA1c would increase the predictive value for CVD, and reducing the GA level would lead to a reduction of CVD in patients with type 2 diabetes.

Acknowledgement

The author has no conflict of interest.

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