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Higher Glycated Hemoglobin Level Is Associated with Increased Risk of Ischemic Stroke in Non-Diabetic Korean Male Adults (*Diabetes Metab J* 2011;35:551-7)

Seok Hong Lee, Jihyun Ahn, Jaetaek Kim

Division of Endocrinology and Metabolism, Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, Korea

Prospective observational and clinical trial data report a clear association between diabetes mellitus and vascular disease, which involves cerebrovascular disease. The benefits of lowering blood glucose on microvascular health are well known, but benefits on macrovascular, especially cerebrovascular, health are less apparent.

Oh et al. [1] recently reported that an elevated glycated hemoglobin level (5.8±0.5% vs. 5.5±0.5%, $P<0.01$) in non-diabetic Korean male adults had an association with increased risk for ischemic stroke. Diabetes is a known risk factor for cardiovascular diseases, and its relationship with the risk of stroke has also been reported. Previous cohort studies have found that diabetes nearly doubled the risk of stroke incidence and doubled or even quadrupled the risk of death from stroke, after adjustment for other risk factors [2,3]. Many cohort studies have also investigated the association between blood glucose level and stroke and revealed the relationships of fasting blood glucose level and postprandial blood glucose level with stroke [4,5]. However, previous studies of fasting glucose concentrations and incident stroke in non-diabetic populations have reported mixed results [4], possibly because a single glucose measurement has high intraindividual variation and is not a good measurement of chronic hyperglycemia, especially in people without overt diabetes.

Unlike fasting and postprandial blood glucose level, A1C is not affected by short-term lifestyle changes. Therefore, A1C can provide a more accurate glycemic status [6]. However, only a few trials have investigated the relationship between A1C and the risk of stroke incidence in the general population [7].

Observational analyses of data from the United Kingdom Prospective Diabetes Study (UKPDS) suggested that A1C is positively associated with the risk of stroke, and a cohort study revealed that elevated A1C could be an independent risk factor for ischemic stroke in people with and without diabetes [8].

Oh et al. [1] demonstrated that subjects in the highest A1C (A1C >6.0%) quartile showed a nearly 10-fold increased risk for ischemic stroke compared with those in the lowest A1C (5.3%<A1C≤5.6%) quartile after adjusting for confounding variables including age, smoking, body mass index, high density lipoprotein cholesterol, low density lipoprotein cholesterol, systolic and diastolic pressure.

However, the suggested use of A1C for evaluating the current blood glucose level may present several disadvantages, including the unsatisfactory correlation with fasting blood glucose, the risk of overestimation among patients with iron-deficiency anemia or among those predisposed to rapid glycosylation, and the underestimation in certain populations such as elderly persons, pregnant women, end-stage renal disease, and non-Hispanic blacks, people with increased red-cell turnover or in those with a history of alcohol abuse [9]. The potential

Corresponding author: Jaetaek Kim
Division of Endocrinology and Metabolism, Department of Internal Medicine, Chung-Ang University College of Medicine, 84 Heukseok-ro, Dongjak-gu, Seoul 156-861, Korea
E-mail: jtkim@cau.ac.kr

interference from hemoglobin variants is another possible disadvantage. Oh et al. [1] used a single baseline measurement of A1C and therefore cannot evaluate the effects of changes in this parameter over time.

This study by Oh et al. [1] is a clinically important work showing A1C is a predictive value for ischemic stroke in non-diabetic Korean male adults. These results suggest that chronic exposure to hyperglycemia could play a role in the development of stroke in people without diabetes, although this study only included male adults and was a cross-sectional, case-controlled study.

Interestingly, smoking rate in ischemic stroke patients was 10 times greater than that in control subjects (51.1% vs. 5.5%) in this study. Smoking decreased insulin-mediated glucose uptake and enhanced oxidative stress; these effects are suggested as mechanisms in smoking-related deterioration in glucose metabolism [10].

More large-scale, long-term prospective cohort studies directly evaluating the association of A1C and ischemic stroke morbidity including insulin sensitivity and insulin resistance in non-diabetic Korean adults are warranted. Finally, we greatly appreciate the effort of the study investigators to conduct such an important clinical study and wish them continued success in their future research.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article were reported.

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