Usefulness of Glycated Albumin for Diabetes Screening


Background In recent years, the measurement of glycated albumin (GA), a glycation product of albumin, has been used widely in clinical practice in Japan. Since the half-life of albumin is shorter than that of Hb and its rate of glycation is 10 times faster, GA is a more sensitive indicator than HbA1c in evaluating therapeutic effects. An easy-to-use reagent has been developed to measure GA using biochemical analyzers. Thus, the measurement of GA, conducted in the same panel such as total cholesterol for health examinations, is expected to improve efficiency and reduce costs in primary screening for diabetes mellitus (DM).

Methods We measured the serum GA value in 970 subjects receiving comprehensive health examinations to determine the optimal cut-off value of GA for diabetes screening. We also investigated the correlation among GA, fasting plasma glucose (FPG), and 2h or peak values of the 75 g oral glucose tolerance test (OGTT). The subjects were divided into four groups, i.e., DM group, impaired fasting glycemia (IFG) group, impaired glucose tolerance (IGT) group, and normal glucose tolerance (NGT) group.

Results The cut-off value for GA was determined to be 14.5%, at which detection sensitivity for DM was 78.5% and non-DM specificity was 69.3%. DM and IGT detection sensitivity of GA were similar to those of HbA1c.

Conclusion We would like to recommend GA for the detection of diabetes together with blood glucose determination. (Ningen Dock 2007; 21: 11-13)

Key Words: glycated albumin (GA), screening, diabetes mellitus (DM), oral glucose tolerance test (OGTT)

Diabetes is a disease of peace and prosperity1-2. Everyone hopes peace and prosperity, and so diabetes will continue to increase worldwide. Hyperglycemia leads to numerous sequelae, such as microangiopathy and other disorders, which will impose many limitations on daily life and activity. The most simple and widely supported way to reduce diabetes is the early detection of a hyperglycemic tendency. Among the various detection methods, the interest has been focused on HbA1c and also glycated albumin (GA) because of their stability, being less influenced by food intake. Recently, GA can be measured by an enzymatic method using an ordinary biochemical analyzer3-5. The present study was carried out to assess whether HbA1c and GA can be used in diabetes screening.

Methods

The subjects were persons who visited to receive comprehensive health examinations at either Tohoku Kosei Nenkin Hospital, Sendai Shakai Hoken Hospital, or Tohoku Kosai Hospital, and had consented to the use of their samples for research purposes. After an overnight fast, blood samples were collected from the cubital vein and used to measure plasma glucose (PG), GA, and HbA1c, followed by 75 g oral glucose tolerance test (OGTT). None of the subjects had abnormal Hb.

GA was measured with an enzymatic method using Lucica® GA test reagents (Asahi Kasei Pharma Corporation, Tokyo, Japan) on a Toshiba TBA80FR Neo II autoanalyzer (Toshiba Medical Systems Corp., Tochigi, Japan) at the Tohoku Kosei Nenkin Hospital with serum that was stored frozen. PG was measured by the electrode method, and HbA1c was by high performance liquid chromatography (HPLC).

Results

Among the 970 subjects, 64 were classified in the diabetes mellitus (DM) group with a 2h OGTT value of 200 mg/dl or greater, and 251 were classified in the impaired glucose tolerance (IGT) group with a 2h OGTT value of 140-199 mg/dl (Table 1). The IGT group was subdivided into an impaired fasting glycemia (IFG) group of 58 subjects with a fasting plasma glucose (FPG) level of 110-125 mg/dl and a normal fasting glucose (NFG)/IGT group of 182 subjects with an FPG level of less than 110 mg/dl. The IFG group consisted of 47 subjects with an FPG level of 110—
125 mg/dl and 2h OGTT values of 140 mg/dl or less. The normal glucose tolerance (NGT) group consisted of 604 subjects with FPG concentrations of less than 110 mg/dl and 2h OGTT values of less than 140 mg/dl. The aggregate profile of the subjects was: age 52.2±8.71, BMI 24.2±3.08, FPG 100.0±16.38 mg/dl, HbA1c 5.3±0.55%, and GA 14.2±1.73% (mean±SD).

A receiver operating characteristic (ROC) curve to determine DM was plotted for GA and HbA1c measurement, as shown in Fig. 1, and the optimal cut-off value was 14.5%, at which sensitivity and specificity were 79.7% and 79.7%, respectively. The cut-off value for HbA1c, calculated in the same manner, was 5.5%, sensitivity 85.9%, and specificity 93.6%, respectively.

The detection sensitivity in each group is shown in Table 2 for GA, HbA1c, FPG, and combinations thereof. Detection sensitivity in the IGT group was 34.3% for GA, 36.7% for HbA1c, and 27.5% for FPG. However, if GA and FPG were combined (GA≥14.5% or FPG≥110 mg/dl), IGT detection sensitivity increased to 49.0%, and if HbA1c and FPG (HbA1c≥5.5% or FPG≥110 mg/dl), IGT detection sensitivity increased to 48.6%, i.e., IGT detection sensitivity was higher in combination with FPG than with GA or HbA1c alone (p<0.05).

For all 970 cases, the regression equation and correlation coefficient were as follows:

\[ Y (GA) = 1.83 \times (HbA1c) + 4.57 \] and \[ r=0.581 \]

From this regression, the GA value derived from the regression equation for GA and HbA1c was 14.6%, if HbA1c was 5.5%, which is primary cut-off value for DM screening under the Japan Health and Medical Service Law for the Aged. The GA value was the equivalent to the optimal cut-off value obtained from the ROC curve.

**Discussion**

Diabetes is one of the most rapidly increasing diseases in the world, and its prevention is a most urgent

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**Table 1. Distribution of oral glucose tolerance test (OGTT) 2h in the 970 examinees**

<table>
<thead>
<tr>
<th>2h OGTT value (mg/dl)</th>
<th>Normal &lt;140</th>
<th>IGT 140-199</th>
<th>Diabetic ≥200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal &lt;110</td>
<td>604</td>
<td>182</td>
<td>17</td>
</tr>
<tr>
<td>FPG</td>
<td>IFG</td>
<td>47</td>
<td>58</td>
</tr>
<tr>
<td>110-125</td>
<td>47</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Diabetic ≥126</td>
<td>4</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>655</td>
<td>251</td>
<td>64</td>
</tr>
</tbody>
</table>

IFG: impaired fasting glucose, IGT: impaired glucose tolerance, FPG: fasting plasma glucose.

**Table 2. Detection sensitivities for glucose intolerance by combination of fasting plasma glucose (FPG), glycated albumin (GA) and HbA1c**

<table>
<thead>
<tr>
<th>Group Fast PG (No. of case)</th>
<th>NGT (2h&lt;140)</th>
<th>IGT (2h 140-199)</th>
<th>DM (2h≥200)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NFG (n=604)</td>
<td>IFG (n=47)</td>
<td>Total (n=655)</td>
</tr>
<tr>
<td>FPG≥110 mg/dl</td>
<td>0</td>
<td>47</td>
<td>51</td>
</tr>
<tr>
<td>GA≥14.5%</td>
<td>175</td>
<td>17</td>
<td>196</td>
</tr>
<tr>
<td>HbA1c≥5.5%</td>
<td>81</td>
<td>21</td>
<td>106</td>
</tr>
<tr>
<td>FPG≥110 mg/dl or GA≥14.5%</td>
<td>175</td>
<td>47</td>
<td>226</td>
</tr>
<tr>
<td>FPG≥110 mg/dl or HbA1c≥5.5%</td>
<td>81</td>
<td>47</td>
<td>132</td>
</tr>
</tbody>
</table>

Fig. 2. Relation between glycated albumin (GA) and HbA1c. For all 970 cases, the regression equation and correlation were $Y(GA) = 18.3x + 4.57$ and $r = 0.581$.

problem. The most simple, exact, and economical test for diabetes screening is being sought worldwide. HbA1c has been applied for screening because it reflects the mean blood glucose level over the past several weeks.

HPLC and Latex methods are used to measure HbA1c. Regarding the HPLC method, you need to purchase an analyzer, which is time-consuming to measure a lot of samples and expensive in terms of maintenance. Regarding the Latex method, only the Bio Majesty 9030 autoanalyzer (JEOL Ltd., Tokyo, Japan) performs automatically from pre-treatment for hemolysis to measurement, although centrifugation to separate erythrocytes is required.

Recently a reagent that enables the simple measurement of GA, a glycation product of albumin, has been developed and is becoming widely used for diabetes management in Japan. Since the half-life of albumin is shorter than that of Hb and its rate of glycation is 10 times faster, GA is often used to evaluate diabetes treatment because it is more sensitive than HbA1c. The greatest merit of GA measurement is that it can be made with a usual automated biochemical analyzer which can deal with more than 800 samples per hour. GA can be measured simultaneously with other parameters such as serum cholesterol, enabling a tremendous saving of time. Also, since samples are stable for 1 week under refrigeration or for 1 month at $-20^\circ C$, they can be stored so that multiple samples can be assayed simultaneously.

In order to confirm the usefulness of GA in primary screening for diabetes at health examinations, we measured GA in serum obtained from 970 persons receiving comprehensive health examinations. The results showed that no conclusive difference was obtained between them. However, from an economical point, the GA test is cheap and able to rapidly process more than 800 samples per hour on widely available analyzers. On the contrary, HbA1c measurement is more expensive and time-consuming than that for GA. For these reasons, we would like to recommend GA for the detection of diabetes together with blood glucose determination.

Acknowledgements

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References