Hemoglobinopathies and Glycated Hemoglobin: Influence in non-diabetic and diabetic patients

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Abstract

This study was carried out to evaluate the effect of hemoglobinopathies (HbPs) on glycated hemoglobin (HbA1c) levels, both in diabetic patients and non-diabetics. It included 82 subjects, with normal HbA1c levels, 23 diabetics and 59 non-diabetics. HBPs were assessed using HbA1c determination performed by ion-exchange high performance liquid chromatography (HPLC). In both HbA1c and HbA1c levels, the difference was statistically significant (P<0.05). Among non-diabetic, no significant differences were observed in HbA1c levels between patient with HbPs and those with HbA1c (P>0.05). In diabetic patients with HbPs, the difference was statistically significant (P<0.05). The effect of HbPs on HbA1c level among non-diabetic was negligible. However, in diabetes with abnormal HbA1c variance, a sparsely high HbA1c values may be misinterpreted resulting in mismanagement of diabetes.

Key words: Hemoglobinopathies, diabetes, glycated hemoglobin.

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Introduction

Diabetes mellitus is one of the most important modifiable cardiovascular risk factors. It increases the risk of cardiac, cerebral and peripheral arterial disease 2-7 fold. Achievement of good glycemic control among diabetics is indispensable to prevent its complications.

Measurement of glycated hemoglobin (HbA1c) has been widely used for monitoring diabetic patients. It is a well established method for evaluating short-term as well as long-term glycemic control in diabetics. It has been confirmed that direct relationship exist between the degree of glycemic control and the development as well as the progression of long-term diabetic complications.

Hb glycation and hence HbA1c level depends on the mean blood glucose level. Since Hb glycation occurs gradually within 2-3 months of the red cell life span. Therefore, HbA1c level represent the mean blood glucose level during the last 2-3 months.

Hemoglobinopathies (HbPs) can influence Hb A1c assay. High or low HbA1c values have been reported among patients with abnormal Hb variants. The value of HbA1c as a retrospective indicator of glycemic control in diabetic patients is greatly weakened in case of HbPs. In addition, abnormal Hb variant increases the methodological difficulties due to interference with most assay methods, and also influence the normal process of HbA1c glycation to HbA1c.

This study was carried out to evaluate the effect of HbPs on HbA1c levels determined by ion-exchange high performance liquid chromatography (HPLC) both in diabetics and those with normal blood glucose levels.

Table 1: HbA1c levels in relation to Hb variants

<table>
<thead>
<tr>
<th>Group</th>
<th>Hb type</th>
<th>HbA1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-diabetic</td>
<td>HbA (n = 59)</td>
<td>4.9 (1.4)</td>
</tr>
<tr>
<td></td>
<td>HbP (n = 61)</td>
<td>4.7 (0.8)</td>
</tr>
<tr>
<td>Diabetic</td>
<td>HbA (n = 23)</td>
<td>9.3 (3.0)*</td>
</tr>
<tr>
<td></td>
<td>HbP (n = 8)</td>
<td>10.7 (3.3)*</td>
</tr>
</tbody>
</table>

Values are expressed as Mean (SD)
P<0.05 (HbA vs HbP in both groups).
*P<0.001 (Diabetics vs non-diabetics)

Results

Identification of abnormal HbA1c determination was performed by ion-exchange HPLC using the VARIAN™ HbA1c Program from BIO-RAD. Statistical analysis was carried out using t-test P<0.05 was considered statistically significant.

Table 1 presents HbA1c levels in the study groups. Diabetic patients, both in HbA and HbP groups, have significantly higher HbA1c levels in comparison to non-diabetes (P<0.001). Among non-diabetics, there were no significant differences in HbA1c levels between HbA subjects and those with HbPs (P>0.05). In the diabetic group, HbA1c levels was higher in patients with abnormal Hb variants compared to HbA diabetic patients, however, the difference was statistically not significant (P>0.05).

HbA1c levels in non-diabetics are shown in Table 2. No significant differences in HbA1c values reported neither among HbP types (P>0.05) nor between each type and HbA non-diabetic group (P>0.05).

Discussion

The effect of HbPs on HbA1c values is highly method dependent. It was suggested that HPLC methods lacked the resolution necessary to differentiate Hb variants and demonstrated additional peaks in chromatograms giving either too low or too high results. In addition there are some suggestions that these methods are unsuitable for HbA1c determination in patients with homozygous HbPs. Also, HbA1c determination by
HPLC methods may be influenced by abnormal Hb variants, and HbA1c level in HbPs does not reflect the glycaemic status when compared with reference population. In the present study, the effect of HbPs on HbA1c levels in non-diabetics was negligible. However, in diabetic patients, the effect of abnormal Hb variants on HbA1c determination was more obvious leading to a spuriously high result, though still not significant, and this could probably due to small number of diabetic patients with abnormal Hb variants. But this influence may have substantial implications in assessment of the long-term glycaemic control in diabetes resulting from incorrect HbA1c values. In this study, no significant differences in HbA1c levels reported among HbP types, and also, between each one and HbA1c type in non-diabetic subjects. On the other hand, it has been reported that HbAS had no effect on HbA1c determination, but β-thalassemia minor patients had falsely high HbA1c levels. Also, it has been shown that patients with high or low HbF values have no significant differences in glycaemic control. In fact, HbSS patients included in this study had high HbF values (mean and standard deviation of 12.3% ± 5.4), but these values had no effect on the degree of glycaemic control assessed by HbA1c determination.

References

Table 2: HbA1c levels in non-diabetics

<table>
<thead>
<tr>
<th>Group</th>
<th>Type</th>
<th>HbA1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbP</td>
<td>HbAS (n = 32)</td>
<td>4.9 (5.8)</td>
</tr>
<tr>
<td>HbP</td>
<td>HbSS (n = 13)</td>
<td>4.7 (1.2)</td>
</tr>
<tr>
<td></td>
<td>β-thalassemia minor (n = 16)</td>
<td>4.4 (0.9)</td>
</tr>
<tr>
<td>HbA</td>
<td>(n = 59)</td>
<td>4.9 (1.4)</td>
</tr>
</tbody>
</table>

Values are expressed as mean (SD).