Effects of Mood States, Smoking and Urinary Catecholamine Excretion on Hemoglobin A1c in Male Japanese Workers

Norito KAWAKAMI1,2, Shunichi ARAKI1, Hisashi OHTSU3, Takeshi HAYASHI4, Takeshi MASUMOTO5 and Kazuhito YOKOYAMA1

1) Department of Public Health, Faculty of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan
2) Department of Public Health, Gifu University School of Medicine, 40 Tsukasa-machi, Gifu, Gifu 500, Japan
3) Analysis Center, Hitachi Kyowa Kogyo Co., Ltd., 3-10-2 Benten-cho, Hitachi, Ibaraki 317, Japan
4) Hitachi Health Care Center, 4-3-16 Ohse-cho, Hitachi, Ibaraki 317, Japan
5) Keihin Health Care Center, NKK Corporation Hospital, 1-1 Minamitoda-cho, Kawasaki, Kanagawa 210, Japan

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Abstract: To know the association between psychological strain and glycosylated hemoglobin (HbA1c) and to examine roles of smoking and catecholamine excretion as a possible mediator in the association, we measured mood states (Profile of Mood States, POMS), urinary catecholamines (adrenalin, noradrenalin and dopamine) from urine sample in early morning, HbA1c and fasting plasma glucose (FPG) of 63 male employees on a rest day. After excluding 12 subjects who had diabetes or impaired glucose tolerance or had missing response to the questionnaire, data from 51 subjects were analyzed. The POMS anger-hostility score significantly and positively correlated with HbA1c (p < 0.05), while other scale scores did not (p > 0.05). Number of cigarettes smoked per day significantly and positively correlated with HbA1c (p < 0.05). Urinary excretion rate of any catecholamine did not significantly correlate with HbA1c (p > 0.05). Multiple linear
regression analysis indicated that the anger-hostility score significantly correlated with HbA1c after controlling for number of cigarettes per day (p < 0.05). It is suggested that, among mood states, anger-hostility is associated with increased HbA1c. However, our study failed to find a mediating role of urinary catecholamines or smoking on the association between the mood and HbA1c.

Key words: Mood states — Smoking — Urinary catecholamine excretion — Glycosylated hemoglobin

INTRODUCTION

Proportion of glycosylated hemoglobin (HbA1c) in total hemoglobin has been linked to chronic and acute stress1-3). Cesane et al.1) reported higher levels of HbA1c in blue-collar workers who engaged in stressful working condition and had lower job satisfaction than in clerical workers. Higher levels of HbA1c were also reported in medical students before a school examination2). The authors found a positive correlation between job dissatisfaction and levels of HbA1c in white-collar workers3). These studies have suggested that HbA1c is a potential physiological measure of psychological stress.

However, the psychological and physiological mechanisms of stress-associated increase in HbA1c are not clear. Hinkle and Wolf’s early work suggested that blood glucose changes vary with the type of emotions: anger increases blood sugar levels and anxiety decreases them4). Thus a hypothesis could be raised that anger mood is a major factor for stress-associated increases in HbA1c. However, no study has been conducted on the effects of mood states on HbA1c. Furthermore, two variables have been suggested as a possible mediator for the linkage between stress and HbA1c, i.e., catecholamine excretion5) and smoking5). Emotional reactions cause release of counterregulatory hormones including catecholamines6), which increase blood glucose7). Thus catecholamine excretion may explain stress-induced increase in HbA1c. Smoking is also associated with psychological distress8) and with increased blood glucose9) and HbA1c5). Although our previous study indicated an association between job dissatisfaction and HbA1c in non-smokers5), smoking may partly explain the association between stress and HbA1c.

To investigate the association between psychological stress and HbA1c further, we conducted a cross-sectional survey of male industrial workers in Japan. The aims of the study are: 1) to know which mood state is associated with increased HbA1c levels and 2) to clarify whether catecholamine excretion and smoking can explain the association between mood states and increased HbA1c levels.
SUBJECTS AND METHODS

Subjects
A total of 63 male employees in an electric company, aged 30–60 years, came to a multiphasic health examination from May 16 to 18 in 1989. They were asked to complete questionnaires concerning mood states, smoking and other covariates. HbA1c and fasting plasma glucose (FPG) were measured from their blood samples; and urinary excretion rates of catecholamines were assessed from their urine samples. Four subjects were omitted because they had been diagnosed as diabetes mellitus or had abnormal results in glucose tolerance test\(^1\). Eight had missing values on variables relevant to the study. Data from 51 subjects were analyzed.

Methods
The subjects came to the health examination center at 8:00–9:00 a.m. on a rest day after fasting overnight. A urine sample was collected after their arrival and blood sample was taken at about 9:00 a.m. Then other physical and medical examinations were conducted. While they waited for the next examination, they were asked to complete the questionnaires. The procedures were fully explained to the subjects before the survey and the written consent was obtained.

Mood states were measured by means of the Profile of Mood States (POMS)\(^1\). The POMS is a 65-item self-administered questionnaire designed to assess six mood states, i.e., tension-anxiety, anger-hostility, fatigue, depression, vigor and confusion. The Japanese version was developed by Yokoyama et al.\(^1\) and acceptable reliability and validity of the POMS scales have been reported. We asked the subjects to recall and answer their mood states within the past seven days.

HbA1c was measured by an automatic analyzer (Daiichi Kagaku Co., Kyoto) by means of high performance liquid chromatography\(^1\). Laboratory blood tests provided measures of FPG. A sample of complete urination was collected at the subjects’ arrival at the examination center between 8:00 and 9:00 a.m.; the urine volume was measured; the time of the previous urination was assessed by means of the questionnaire. A urine sample (10 ml) was collected in a small tube where the PH was adjusted to be about 3 with HCl to avoid oxidation, and frozen in \(-20^\circ\text{C}\) for a week. Adrenalin, noradrenalin and dopamine were measured by means of high performance liquid chromatograph auto-analyzer using fluorescent method\(^1\). Mean urinary excretion rates (ng/min) of catecholamines for the period between the previous urination and the collected urination were calculated. According to the methods proposed by Jenner et al.\(^1\), these excretion rates were normalized by taking log\(_{10}\) values and adjusted for urine volume, length of time of urine accumulation, time of collected urination by means of multiple linear regression.

Number of cigarettes currently smoked per day was assessed using the ques-
tionnaires. For those currently not smoking, 0 was assigned to the number of cigarettes. Other covariates included age, occupation, overtime hours per month, alcohol consumption, obesity and frequency of coffee/tea drinking with sugar. These covariates were also assessed using the questionnaire or from physical examination data. Occupation was further dichotomized into white- and blue-collar workers. Habitual alcohol consumption was assessed in ml of pure ethanol intake per week on the basis of type of alcohol beverages, frequency of consumption and amount of drinking at occasion which the subjects reported. The degree of obesity was measured using body mass index (BMI) determining a ratio of body weight (kg) to the square of height (m).

Analysis

Pearson correlation coefficients between the following variables and HbA1c or FPG were calculated: the POMS scales, number of cigarettes smoked per day, urinary excretion rates of catecholamines (adrenalin, noradrenalin and dopamine) and other covariates (age, overtime hours per month, alcohol consumption, BMI, frequency of coffee/tea drinking with sugar).

Multiple linear regression analysis of HbA1c was employed to know the unique effects of the POMS scales, smoking and catecholamines and the mediating effects of the latter two variables. To avoid multicollinearity due to strong correlations among the POMS scales, the analysis was conducted for each POMS scale. At the first step, age, occupation and the POMS scale were entered. At the second step, number of cigarettes per day was added. At the third step, we conducted total three regression analyses for each POMS scale: adrenalin was added for regression equation (a); noradrenalin for (b); and dopamine for (c). This was also in order to avoid the multicollinearity due to close correlations among the catecholamines. The partial correlations for the POMS scale were compared between the first and second steps or the second and third steps to know the mediating effects by smoking or the catecholamine, respectively. The analysis was conducted using SAS STAT ver 6.04 on a PC16).

RESULTS

Mean values for age, the POMS scale scores, number of cigarettes smoked per day, urinary excretion rates of catecholamines, HbA1c and FPG in 51 male workers were shown in table 1. The subjects consisted of 30 white-collar workers (four managers, seven technicians, 11 clerks and eight sales workers) and 21 blue-collar workers (six repair workers, 13 machine operators and two transportation workers).

The POMS anger-hostility score significantly and positively correlated with HbA1c (Fig. 1). Other POMS scores did not significantly correlate with HbA1c.
None of the POMS scales significantly correlated with FPG: Pearson r, 0.07, 0.07, -0.05, 0.01, 0.25 and -0.19 for tension-anxiety, anger-hostility, depression, fatigue, vigor and confusion scales, respectively (all p > 0.05).

Number of cigarettes currently smoked per day significantly and positively correlate with HbA1c (Table 2). The following variables did not significantly correlate with HbA1c or FPG (p > 0.05): age, occupation, overtime, alcohol consumption, BMI, sleeping hours, frequency of coffee and tea drinking (data not shown). Urinary excretion rate of adrenalin marginally correlated with HbA1c, while noradrenalin and dopamine did not significantly correlate with HbA1c. Number of cigarettes per day or urinary excretion rate of any catecholamine did not significantly correlate with FPG. No significant correlations between any POMS scale and number of cigarettes per day were observed.

Number of cigarettes per day significantly and positively correlated with the urinary excretion rate of adrenalin (Pearson r, 0.29, p < 0.05); and weakly with noradrenalin and dopamine (r, 0.22 and 0.20, respectively, p > 0.05). Urinary excretion rates of three catecholamines significantly and positively correlated each other (r, 0.63–0.90, p < 0.01).

Multiple linear regression analysis indicated that the anger-hostility score significantly and positively correlated with HbA1c before and after controlling for number of cigarettes per day and urinary excretion rate of any catecholamine (Table
3). Number of cigarettes smoked per day significantly and positively correlated with HbA1c, independent of the anger-hostility. The correlation coefficients for the anger-hostility score and number of cigarettes per day were almost same at every steps. Other POMS scales did not significantly correlated with HbA1c in any regression equation (p > 0.05).

Mean wake-up time and urine collection time for the subjects were 6:34 a.m.
Table 2. Pearson correlations of age, number of cigarettes per day and urinary excretion rates of catecholamines with POMS scale scores, HbA1c, and fasting plasma glucose (FPG).

<table>
<thead>
<tr>
<th></th>
<th>POMS scalea</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>HbA1c</th>
<th>FPG</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>TA</td>
<td>AH</td>
<td>D</td>
<td>F</td>
<td>V</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.15</td>
<td>-0.21</td>
<td>-0.14</td>
<td>-0.15</td>
<td>-0.07</td>
<td>-0.09</td>
<td>0.05</td>
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<tr>
<td>Number of cigarettes per day</td>
<td>0.13</td>
<td>0.22</td>
<td>0.01</td>
<td>0.12</td>
<td>0.16</td>
<td>0.17</td>
<td>0.42**</td>
</tr>
<tr>
<td>Urinary excretion rate of catecholamine:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenalin</td>
<td>0.18</td>
<td>0.03</td>
<td>0.05</td>
<td>0.04</td>
<td>0.04</td>
<td>0.14</td>
<td>0.25</td>
</tr>
<tr>
<td>Noradrenalin</td>
<td>0.10</td>
<td>-0.06</td>
<td>-0.06</td>
<td>0.01</td>
<td>-0.02</td>
<td>0.12</td>
<td>0.14</td>
</tr>
<tr>
<td>Dopamine</td>
<td>0.10</td>
<td>-0.02</td>
<td>-0.10</td>
<td>0.03</td>
<td>-0.08</td>
<td>0.13</td>
<td>0.18</td>
</tr>
</tbody>
</table>

a: The scale was indicated in abbreviated forms: TA, tension-anxiety; AH, anger-hostility; D, depression; F, fatigue; C, confusion.

* p < 0.05, ** p < 0.01.

Table 3. Multiple linear regression of HbA1c on age, the POMS anger-hostility score, number of cigarettes per day, urinary excretion rates of catecholamines: partial correlation coefficients.

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3a</th>
<th>(a)</th>
<th>(b)</th>
<th>(c)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(a)</td>
<td>(b)</td>
<td>(c)</td>
</tr>
<tr>
<td>Age</td>
<td>0.151</td>
<td>0.160</td>
<td>0.165</td>
<td>0.150</td>
<td>0.147</td>
<td></td>
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<tr>
<td>Occupationb</td>
<td>-0.123</td>
<td>-0.231</td>
<td>-0.247</td>
<td>-0.232</td>
<td>-0.225</td>
<td></td>
</tr>
<tr>
<td>POMS anger-hostility</td>
<td>0.336*</td>
<td>0.284*</td>
<td>0.293*</td>
<td>0.289*</td>
<td>0.288*</td>
<td></td>
</tr>
<tr>
<td>Number of cigarettes per day</td>
<td>0.424**</td>
<td>0.376**</td>
<td>0.399**</td>
<td>0.397**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary excretion rate of catecholamine</td>
<td>0.185</td>
<td>0.084</td>
<td>0.113</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Multiple R</td>
<td>0.345</td>
<td>0.526</td>
<td>0.548</td>
<td>0.529</td>
<td>0.533</td>
<td></td>
</tr>
</tbody>
</table>

a: One of the three catecholamines was added to the equation: (a) for adrenalin, (b) for noradrenalin or (c) for dopamine.
b: Coded as white-collar = 0, blue-collar = 1.

* p < 0.05, ** p < 0.01.
were not statistically different between these two groups (p > 0.05), while the urinary excretion rates of three catecholamines were significantly higher in those who had their last urination after waking up than in those who had before sleeping (p < 0.05). When the same analyses were conducted for those who had their last urination before sleeping, similar results were obtained. Correlations of the anger-hostility score and number of cigarettes smoked per day with HbA1c were 0.28 (p = 0.08) and 0.33 (p < 0.05), respectively; urinary excretion rate of any catecholamine did not significantly correlate with HbA1c (p > 0.05).

When we omitted one subject with the lowest level of HbA1c (i.e., 4.5%) from the analysis, correlations of the POMS scales with HbA1c changed only slightly; the anger-hostility score significantly correlated with HbA1c (pearson r = 0.28, p = 0.05). Omitting this subject did not influence the results of multiple regression analysis.

**DISCUSSION**

Our study indicated that the anger-hostility score significantly and positively correlated with HbA1c. Hinkle and Wolf suggested that anger increases blood sugar level and anxiety decreases it4~. Our findings are consistent with the previous findings. Since we selected subjects who did not have impaired glucose tolerance or clinical diabetes, the findings are less likely due to increased anger-hostility caused by diabetes mellitus. It is suggested that, among the mood states, anger-hostility is a factor for increased HbA1c. Job stress, such as job dissatisfaction, might increase HbA1c levels through increased feeling of anger-hostility.

Our study failed to find mediating effect by urinary excretion rates of catecholamines. Since our urine samples were taken in an early morning on a rest day and were overnight urine samples for most of the subjects, the urinary excretion rates of catecholamines in our study are considered to mainly reflect resting levels of catecholamine excretion. Despite our expectation, urinary excretion rates of catecholamines only weakly correlated with HbA1c. It is suggested that catecholamine excretion does not explain the effects of anger-hostility on increased HbA1c. However, urine samples were collected two hours after wake-up on average. For one fourth of the total subjects, urine catecholamines were measured from urine samples after they woke up and had urination. Although the analysis indicated similar results for those who had the last urination before sleeping, the catecholamine excretion rates could be to some extent contaminated by those by early morning activities. These methodological problems in assessment of urinary catecholamines might cause random measurement errors and result in less clear associations between urinary catecholamines and HbA1c. Another possibility is that catecholamine excretion in daytime might be more associated with HbA1c, mediating the effects of anger-hostility. Assessment of resting and daytime excretions of catecholamines from a 24-hour urine sample might be useful to answer this
question.

Number of cigarettes currently smoked per day significantly and positively correlated with HbA₁c. Smoking is known to stimulate release of the counterregulatory hormones (7) and consequently cause temporal elevation in blood glucose (9). As in a previous study (18), we found a significant correlation between amount of smoking and urinary excretion rate of adrenalin. However, smoking explained only small part of the association between anger-hostility and HbA₁c as indicated by little change in the partial correlation before and after entering smoking into the regression equation. Thus, our study failed to indicate a mediating role of smoking between anger-hostility and increased HbA₁c. The association between anger-hostility and HbA₁c might be not attributable to smoking induced by anger-hostility.

Since we failed to indicate a mediating role of resting levels of catecholamines and smoking, other possible explanation should also be examined in future research on the effects of anger-hostility on HbA₁c. Emotional reactions cause frequent release of other counterregulatory hormones than catecholamines, such as cortisol and growth hormone (6), which could lead to a subsequent rise in blood glucose (7). These other stress-related hormones should be investigated. Increased alcohol drinking due to anger-hostility is one possibility. However our study found a nonsignificant correlation between alcohol consumption and HbA₁c. Thus it is unlikely. Changes in dietary habits by anger-hostility is another possibility. However, BMI and frequency of coffee and tea drinking with sugar were not significantly associated with HbA₁c in our study. Our previous study found that several serum indicators of nutritional states, such as total cholesterol, triglyceride and uric acid, did not significantly correlate with HbA₁c (3). Thus it is also unlikely. Other behavioral changes which leads to frequent and temporal elevations of blood glucose should be considered in a further study.

As a conclusion, our study demonstrates that anger-hostility is associated with increased HbA₁c, although we failed to clarify possible explanations. Our findings are also consistent with recent evidence on stress and diabetes (9). Further investigations on psychological and physiological mechanisms underlying stress-related increase in HbA₁c might be useful for establishing a stable physiological measure of psychological stress, as well as for clarifying the etiological roles of psychological stress on incidence of diabetes.

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