**Blood Thiamine Levels in Outpatients with Diabetes Mellitus**

Noboru SAITO¹, Mieko KIMURA,² Akiko KUCHIBA,³ and Yoshinori ITOKAWA²

¹Department of Geriatrics, Kochi Medical University, Kochi 781-51, Japan
²Department of Hygiene, Faculty of Medicine, Kyoto University, Kyoto 606, Japan
³Department of Food Science, Faculty of Home Economics, Kyoto Women's University, Kyoto 605, Japan

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**Summary** In 46 diabetic outpatients consisting of 20 males and 26 females not given thiamine treatment, the blood thiamine level was 46.9±28.5 ng/ml (mean±SD) and only 23.9% of all cases had a value of more than the normal lower limit (50 ng/ml). Erythrocyte transketolase activity was 443.8±107.7 µg/ml/h and only 20.9% had a value of more than the normal lower limit (500 µg/ml/h), and the erythrocyte TPP effect was 16.6±13.2%. Moreover, there was a significant positive correlation ($r=0.97$) between the blood thiamine level and erythrocyte transketolase activity, and a significant inverse correlation ($r=-0.525$, $r=-0.576$) between blood thiamine level and/or erythrocyte transketolase activity and the erythrocyte TPP effect. In 24 diabetic outpatients consisting of 14 males and 10 females given thiamine treatment, the blood thiamine level was 96.5±44.5 ng/ml/h excluding one case (621.7 ng/ml), and it was higher than the normal lower limit in 83% of all cases. Erythrocyte transketolase activity was 513.9±133.4 µg/ml/h and it was higher than the normal lower limit in 58.3%. Erythrocyte TPP effect was 5.84±8.39%. There was also a significant positive correlation ($r=0.663$) between blood thiamine level and erythrocyte transketolase activity, and a significant inverse correlation ($r=-0.668$, $r=-0.834$) between blood thiamine level and/or erythrocyte transketolase activity and erythrocyte TPP effect. Blood thiamine level and erythrocyte transketolase activity were significantly higher in diabetic outpatients given thiamine treatment than in diabetic outpatients not given thiamine treatment, while the erythrocyte TPP effect was significantly lower in diabetic outpatients given thiamine treatment than in diabetic outpatients not given thiamine treatment. There was no direct
relationship between the lowered response of patellar tendon reflex and the biochemical status of thiamine. From the above findings it was concluded that diabetic outpatients tend to have a low blood thiamine level, with low erythrocyte transketolase activity and high erythrocyte TPP effect, and showed marginal thiamine deficiency.

**Key Words** blood thiamine level, erythrocyte transketolase activity, thiamine pyrophosphate (TPP) effect, patellar tendon reflex, aging in diabetes mellitus

Dietary treatment, especially energy restriction, is necessary and fundamental for control of diabetes mellitus. The appropriate dietary chart is prescribed to improve obesity, to maintain ideal body weight, and to attenuate diabetic impaired metabolism. However, all indispensable nutrients such as protein, vitamins and minerals should be sufficient in these diets. We measured the blood thiamine level, erythrocyte transketolase activity, and the TPP effect in diabetic outpatients to investigate their thiamine adequacy.

**MATERIALS AND METHODS**

**Subjects.** Group 1: 46 diabetic outpatients not given thiamine treatment were 57.5 ± 13.1 years old on average, and consisted of 20 males and 26 females (15 patients received oral hypoglycemic agents, 7 patients received subcutaneous insulin injections).

Group 2: 24 diabetic outpatients given thiamine treatment were 61.3 ± 9.3 years old on average, and consisted of 14 males and 10 females (16 patients received oral hypoglycemic agents and 3 patients received subcutaneous insulin injections).

**Blood collection.** Five ml of fasting (12-h fasting) blood was taken by a heparinized syringe in the morning. Determination of thiamine: Total thiamine concentration in blood was determined by the fluorometric thiochrome method (1, 2).

**Assay of transketolase.** Transketolase [EC 2.7.1.1] activity in erythrocytes was assayed as described by Brin et al. (3) and Itokawa (4). This assay was carried out in a set of 3 tubes. One tube served as zero time control, the second as original activity, and the third for thiamine pyrophosphate (TPP) effect; that is, a percentage stimulation of the enzyme activity produced by adding TPP to the sample before assay. The TPP effect therefore reflected the proportion of the apoenzyme which was not saturated with thiamine pyrophosphate.

**Determination of fasting blood sugar (FBS).** FBS was measured by the enzyme method.

**Calculation of nutrient intake from food.** The recommended dietary energy was 1,300 to 1,800 kcal per day for diabetic outpatients. Main nutrient intake was calculated from patients' dietary records by referring to the Japan Standard Foodstuff Table.
Data analysis. The Student's t-test for paired or un-paired data was used for statistical analysis.

RESULTS

Blood thiamine level, erythrocyte transketolase activity, and the TPP effect in diabetic outpatients not given thiamine treatment

Blood thiamine level was 46.9±28.5 ng/ml (mean±SD), erythrocyte transketolase activity was 443.8±107.7 μg/ml/h, and the TPP effect was 16.6±13.2% in 46 diabetics not given thiamine treatment. Furthermore, a blood thiamine level higher than the normal lower limit (50 ng/ml) (2) was found only in 11 of the 46 diabetics (23.9%), while a lower level was found in 35 diabetics (76.1%), which indicates the trend of low blood thiamine level in diabetic outpatients. Erythrocyte transketolase activity was lower than the normal lower limit (500 μg/ml/h) (5) in 34 of the 43 diabetics (79.1%), showing the trend of thiamine deficiency in diabetics. Erythrocyte transketolase activity was 572.4±98.2 μg/ml/h in cases with a blood thiamine level over 50 ng/ml, while 389.7±66.6 μg/ml/h in the other cases, the difference between them being significant at p<0.001. Thiamine pyrophosphate (TPP) effect was 4.7±3.9% in cases with a blood thiamine level over 50 ng/ml, while 23.6±16.1% in the other cases, the difference between them being significant at p<0.001. There was a significant positive correlation (r=0.97) between blood thiamine levels and

Fig. 1. The correlation between blood thiamine level and erythrocyte transketolase activity (ETKA) in diabetic outpatients not given thiamine treatment.

(In Figs. 1–6: ●, male; ○, female.)

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Fig. 2. The correlation between blood thiamine level and thiamine pyrophosphate (TPP) effect in diabetic outpatients not given thiamine treatment.

Fig. 3. The correlation between erythrocyte transketolase activity (ETKA) and thiamine pyrophosphate (TPP) effect in diabetic outpatients not given thiamine treatment.

erthrocyte transketolase activity (Fig. 1), and a significant inverse correlation ($r = -0.525$, $r = -0.576$) between blood thiamine level and/or erythrocyte transketolase activity and the TPP effect (Figs. 2 and 3), showing the availability of these three measurements for evaluating thiamine adequacy.

Fasting blood sugar (FBS) was 145.3 ± 42.1 mg/dl in cases with a blood thiamine level over 50 ng/ml, while 164.8 ± 51 mg/dl in the other cases, but the difference between them was not significant.

The patients with a blood thiamine level over 50 ng/ml were 62.5 ± 13.2 years old, and those with a lower level were 57.1 ± 13 years old, but the difference was not significant. Thus no significant correlation was observed between blood thiamine level and aging.

**Blood thiamine level, erythrocyte transketolase activity, and the TPP effect in diabetic outpatients given thiamine treatment**

Blood thiamine level in diabetic outpatients given thiamine treatment was 96.5 ± 44.5 ng/ml except in one case showing 621.7 ng/ml. Erythrocyte transketolase activity was 513.9 ± 133.4 μg/ml/h, and the TPP effect was 5.84 ± 8.39% in 24 diabetic outpatients given thiamine treatment. A blood thiamine level higher than the normal lower limit was found in 20 of the 24 diabetics (83%), while it was lower than the normal limit in only 4 of the 24 diabetics (17%).

Erythrocyte transketolase activity was higher than the normal lower limit in 14 of 24 diabetics (58.3%) and the TPP effect was zero% in 15 of the 24 diabetics given thiamine treatment (62.5%). Therefore, blood thiamine level, erythrocyte transketolase activity, and the TPP effect were normal in cases of diabetic patients receiving thiamine treatment. There was a positive correlation (r=0.663) between blood thiamine level and erythrocyte transketolase activity (Fig. 4), and an inverse

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Fig. 4. The correlation between blood thiamine level and erythrocyte transketolase activity (ETKA) in diabetic outpatients given thiamine treatment.

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Fig. 5. The correlation between blood thiamine level and thiamine pyrophosphate (TPP) effect in diabetic outpatients given thiamine treatment.

Fig. 6. The correlation between erythrocyte transketolase activity (ETKA) and thiamine pyrophosphate (TPP) effect in diabetic outpatients given thiamine treatment.

correlation \( (r = -0.668, r = -0.834) \) between blood thiamine level and/or erythrocyte transketolase activity and the erythrocyte TPP effect (Figs. 5 and 6).

The blood thiamine level was \( 81.9 \pm 51.5 \text{ ng/ml} \) in diabetics given 3 to 10 mg of oral doses of thiamine per day, and \( 104 \pm 26.6 \text{ ng/ml} \) in diabetics given 50 to 80 mg per day, but the difference between them was not significant.

Table 1. The daily nutrient intakes calculated from dietary records in diabetic outpatients not given or given thiamine treatment.

<table>
<thead>
<tr>
<th>Case numbers</th>
<th>Diabetic outpatients without thiamine treatment</th>
<th>Diabetic outpatients with thiamine treatment</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Total cases Male cases Female cases</td>
<td>Male cases Female cases</td>
</tr>
<tr>
<td></td>
<td>46</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>1,333±308 (979–2,019)</td>
<td>1,533±201 (970–2,702)</td>
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<td></td>
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<td>47±18 (51–160)</td>
<td>49±18 (40–124)</td>
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<tr>
<td></td>
<td>108±39 (86.1–127.5)</td>
<td>109±45 (109–129.5)</td>
</tr>
<tr>
<td></td>
<td>1.0±0.33 (0.5–1.7)</td>
<td>1.1±0.4 (0.5–0.7)</td>
</tr>
</tbody>
</table>

M±SD, the parentheses show the ranges of nutrient intakes.

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Erythrocyte transketolase activity was 441.2 ± 140.3 µg/ml/h in diabetics over 65 years, and 557.5 ± 112 µg/ml/h in those under 65 years. Between these two groups, a significant difference was found at $p < 0.005$.

FBS value was 170.8 ± 45.3 mg/dl for diabetics over 65 years, and 101.6 ± 39.6 mg/dl in diabetics under this age. There was no significant correlation between blood thiamine level and aging in diabetics given thiamine treatment. There was no significant difference in dietary records between diabetic outpatients not given thiamine treatment and those given thiamine treatment (Table 1). Blood thiamine level and erythrocyte transketolase activity were significantly higher in diabetics given thiamine treatment than in diabetics not given it ($p < 0.005$, $p < 0.025$, respectively). Erythrocyte TPP effect was significantly lower in diabetics given thiamine treatment than in those not given thiamine treatment ($p < 0.005$).

Relationship between blood thiamine level and patellar tendon reflex (PTR) in diabetic outpatients

The PTR response was decreased severely in 10 cases (31%), moderately in 4 cases (12%), and was normal in 19 cases (57.6%) of the 33 diabetics not given thiamine treatment, who were examined neurologically. The PTR response was decreased severely in 6 cases (33.3%), moderately in 2 cases (11.1%) and was normal in 10 cases (55.6%) of the 18 diabetics given thiamine treatment, who were examined neurologically. In diabetics not given thiamine treatment, no significant differences were found in blood thiamine level, erythrocyte transketolase activity, or the erythrocyte TPP effect, with respect to the PTR responses (data not shown).

DISCUSSION

For assessing the nutritional status of thiamine, erythrocyte transketolase activity and the TPP effect are suitable parameters in addition to blood thiamine concentration (6, 7). The blood thiamine level was below the normal lower limit in most diabetic outpatients (75%) not given thiamine treatment, who were prescribed 1,300 to 1,800 kcal a day from food. The status of marginal thiamine deficiency was also confirmed by low erythrocyte transketolase activity and high erythrocyte TPP effect (6, 7).

On the contrary, the blood thiamine level was above the normal lower limit in most diabetic outpatients (83%) given thiamine treatment. It has been reported that oral administration of 100 mg thiamine for 14 days elevated erythrocyte transketolase activity (8), and that oral administration of thiamine propyl disulfide or thiamine tetrahydrofurfuryl disulfide elevated the blood thiamine level (9). Oral administration of 75 mg or 25 mg thiamine tetrahydrofurfuryl disulfide per day for one month elevated the blood thiamine level in students (10). Many diabetic outpatients may suffer from subclinical thiamine malnutrition if they do not receive thiamine drugs.

Vitamin deficiency has been found in a large proportion of hospital inpatients.
25% of whom were biochemically deficient in vitamin status (11). Moreover, vitamin deficiency was more frequent in noninsulin-dependent diabetes mellitus than in insulin-dependent diabetes mellitus (12).

The main causes of marginal thiamine deficiency in diabetics may be due to the restricted intake of foodstuffs under dietary treatment as shown in Table 1. In addition to the reduced intake, reduced absorption, reduced storage capacity, malutilization, the antithiamine factor, increased metabolism or the increased excretion of thiamine can induce thiamine deficiency, especially in alcoholic consumers. Thiamine deficiency status results in the alterations of pyruvate and α-ketoglutarate decarboxylation which influence transketolase formation (12).

In diabetic outpatients, we found no significant correlation between blood thiamine level and FBS, although Hobara et al. reported that FBS correlated positively with blood thiamine concentration in diabetics (13). The lowered response of patellar tendon reflex in diabetic outpatients was observed in about 30% of all cases irrespective of the administration of thiamine drugs. There was no direct relationship between the lowered response of patellar tendon reflex and the nutritional-biochemical status of thiamine in this investigation. Therefore, the decreased response of patellar tendon reflex might be due to diabetic neuropathy or aging.

The relationship between aging and blood thiamine level was not usually observed despite the trends of reduced energy or reduced thiamine in the elderly subjects. However, thiamine intake per 1,000 kcal was not different between young and old individuals (9), being rather large in the latter (9, 14). There was a positive correlation between blood thiamine level and aging in 24 healthy subjects (14). It was found that diabetic outpatients tended to have a low blood thiamine level under the restricted diet, although Rieder et al. reported a normal blood thiamine level in diabetics (15), and oral administration of thiamine drugs is probably effective for improving thiamine status.

REFERENCES


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