Evaluating thiamine deficiency in patients with diabetes

The pivotal role of hyperglycaemia as part of the disease mechanism of the late specific complications of diabetes mellitus has been documented in several clinical studies. Recently, a new molecular mechanism has been implicated in the pathobiology of the microvascular and macrovascular complications of diabetes.\(^1\) In experimental settings, increased polyol pathway flux, increased hexosamine pathway flux, increased advanced glycation endproduct (AGE) formation and activation of protein kinase-C (PKC) isoforms have been observed. All these mechanisms reflect a hyperglycaemia-induced process of overproduction of superoxide by the mitochondrial electron transport chain, resulting in a partial inhibition of the glycolytic enzyme glyceraldehyde phosphate dehydrogenase. Supplementation with benfotiamine – a lipid-soluble thiamine derivative – can increase transketolase activity, providing a diverse metabolic pathway for increased fructose-6-phosphates and glyceraldehyde-3-phosphate concentrations to pentose-5-phosphates and erythrose-4-phosphate.

Although hyperglycaemia has been shown to result in a decrease of transketolase activity in experimental diabetes, it is not known whether systemic thiamine deficiency leads to the same phenomenon. There are limited data regarding thiamine status in clinical settings, especially in patients with diabetes. Higher erythrocyte transketolase activity (εETK), indicating subnormal thiamine status, has been documented in chronic alcoholic patients,\(^3\) among hospitalised elderly patients\(^4\) and in subjects with congestive heart failure receiving long-term furosemide therapy.\(^5\) As for εETK in diabetes, a marginal thiamine deficiency in diabetic outpatients was documented in a study from Japan.\(^6\)

We investigated εETK in a non-selected diabetic population of Caucasian origin.

Seventy-five consecutive patients with diabetes (37 women and 38 men; 13 with type 1 diabetes and 62 with type 2 diabetes; aged 55.4±1.3 years; duration of diabetes 9.7±0.9 years; serum creatinine 85±1 µmol/L; HbA1C 9.6±0.2%) from our outpatient department were investigated. (Measurements are given as mean±SEM.) Exclusion criteria were elevated serum creatinine level (>150 µmol/L), clinical signs of congestive heart failure, chronic alcoholism, ketoadidosis and a vegetarian diet. Fasting blood samples were taken for measuring εETK using a standard laboratory method.\(^7\) This method tests transketolase activity in red blood cells before and after saturation with exogenous thiamine. Thus, the higher the εETK, the higher the risk for thiamine deficiency. The normal value of εETK was established by measuring blood samples of 60 healthy subjects without diabetes (28 women and 32 men; aged 54.1±2.5 years), resulting in a reference range (mean±2 x standard deviation) of 1.00–1.26. According to one widely accepted evaluation,\(^7\) risk for thiamine deficiency may be indicated by the level of εETK: a level < 1.16 denoting low risk, 1.16–1.25 moderate risk, and a level ≥ 1.26 denoting high risk.

The εETK of patients with diabetes was significantly higher than that of control subjects (1.14±0.01 vs. 1.08±0.02; p<0.01). Abnormal (≥ 1.26) εETK was found in only six subjects (8.0%). The εETK was < 1.16 in 45 patients, and εETK levels between 1.16 and 1.25 were found in 24 patients. In order to evaluate the effect of benfotiamine, five patients with diabetes were treated with benfotiamine 320 mg daily for seven days. A significant decrease of εETK was found in these patients (1.10±0.03 vs. 1.02±0.02).

Suboptimal εETK, that is, a marginal thiamine deficiency, was observed in some patients with diabetes but εETK levels could be improved by using benfotiamine. Benfotiamine treatment has been shown to prevent experimental diabetic retinopathy,\(^1\) nephropathy\(^7\) and neuropathy.\(^8\) Although the results of a small pilot study with benfotiamine were encouraging in patients with diabetic polyneuropathy,\(^9\) its potential clinical usefulness for preventing late diabetic complications should be tested in large randomised, controlled clinical trials.

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Conflict of interest
None declared.

References
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So, what are HDLs? Where are they formed? How are they regulated? What is their function? How do they protect against atherosclerosis? Why is the plasma level of HDL-C low in some people and how can it be raised? These, and many other questions, are addressed in this book.

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