

Food Advanced Glycation Endproducts (AGE) Acutely Induce Postprandial Impairment of Microvascular Function in Patients with Type 2 Diabetes Mellitus (T2DM), an Effect Prevented by Benfotiamine

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Background and aims

Food AGE can increase after 2-6 weeks in vivo serum markers of endothelial dysfunction (e.g. TNF α , VCAM-1). Benfotiamine (BT), liposoluble vitamin B₁, blocks several pathways common to hyperglycemia- and AGE-induced endothelial dysfunction. Acute effects of food AGEs on functional parameters of microcirculation in T2DM and regulation of these effects by benfotiamine have not yet been studied.

Materials and methods

We investigated 16 inpatients with T2DM (age 57.9 \pm 2.0 years, HbA1c:9.5 \pm 2.1%, 11 noninsulin-/5 insulin-treated, 5 with retinopathy, 3 with nephropathy, without acute cardiovascular events within the previous 6 months) on a standard diabetic diet for the 9 day study period. On day 4 and 6 we assessed in a randomized, investigator-blinded, cross-over design the acute effects of a high-AGE (HAGE) or a low-AGE (LAGE) meal on microvascular reactive hyperemia (RH). The HAGE and LAGE meal had the same ingredients (580 kcal, 54 g protein, 17 g lipids, 48 g carbohydrates), differences in AGE amount (HAGE vs LAGE: 15.100 vs. 2.750 kU AGE) were obtained by varying only the cooking conditions (e.g. temperature and time). In a subgroup of 11 patients the HAGE meal was repeated on day 9 after a 3-day pre-treatment with BT (Milgamma®, Woerwag, Germany): 3x350mg/d on day 7 and 8, respectively 1.050 mg on day 9, 1h prior to the meal. RH was measured at the right hypothenar site by laser-doppler flowmetry (LEA Medizintechnik, Germany) after an overnight fast at baseline and 2, 4 and 6 hours after each meal. RH is expressed as the ratio of blood flow velocity (BFV) increase following a 4.5 min forearm ischemia (RH= post-ischemic BFV/basal BFV).

Results

RH transiently decreased after the HAGE meal from 1.4 \pm 0.1 at baseline to 1.2 \pm 0.1^{**d} 2 h postprandially and recovered after 4 and 6h to 1.3 \pm 0.1 \dagger and 1.6 \pm 0.2^{*} respectively (^{**}p<0.01, ^{*}p<0.5, \dagger p=NS vs. baseline, ^dp<0.05 vs. LAGE). RH did not decrease after the LAGE meal: 1.4 \pm 0.1 at baseline and 1.5 \pm 0.1 \dagger , 1.4 \pm 0.1 \dagger and 1.5 \pm 0.1 \dagger at 2, 4 and 6 h postprandially (\dagger =NS vs. baseline). Pre-treatment with benfotiamine abolished the effect of the HAGE meal on RH: 1.3 \pm 0.1, 1.3 \pm 0.1 \dagger^* , 1.3 \pm 0.1 \dagger and 1.6 \pm 0.2 \dagger at baseline and 2, 4 and 6 hours postprandially (^{*}p<0.001 vs. HAGE without benfotiamine, \dagger =NS vs. baseline).

Conclusions

A standardised real-life meal with a high AGE content induces a transient impairment in microvascular function. This effect can be prevented by pre-treatment with benfotiamine. Since repeated exposure to food AGE might result in persistent microvascular dysfunction, long-term effects of benfotiamine treatment in the prevention of AGE-induced vascular effects remain to be established.