

# 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 $\alpha$ , VCAM-1). Benfotiamine (BT), liposoluble vitamin B<sub>1</sub>, 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<sup>\*\*d</sup> 2 h postprandially and recovered after 4 and 6h to 1.3 $\pm$ 0.1 $\dagger$  and 1.6 $\pm$ 0.2<sup>\*</sup> respectively (\*\*p<0.01,\*p<0.5,  $\dagger$ p=NS vs. baseline, <sup>d</sup>p<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.