Smoking is associated with increased levels of osteopontin in type 2 diabetic patients: preliminary results

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A strong relationship between cigarette smoking and atherosclerosis is documented in non diabetic and diabetic subjects. Smoking has been associated with dyslipidaemia, increase of inflammation markers, hypercoagulability, insulin resistance, oxidative stress as well as impaired endothelial dysfunction [1-4]. Osteopontin, a proinflammatory cytokine, is an adhesive protein, implicated in the development of atherosclerosis [5-7]. Interestingly, in mice, it was shown that levels of osteopontin increased when exposed to a combination of toxicants including nitrosamines derived from tobacco alkaloids [8]. Therefore, we evaluated the possible relationship between smoking and circulating osteopontin in a cohort of 29 type 2 diabetic patients.

Subjects were classified on the basis of self-reported smoking history as follows: non smokers (group 1; n=10), former smokers who quit smoking 18 years ago (1.5 to 38) (median; range) (group 2; n=10), and current smokers (20 cigarettes/day) (5-50) (group 3; n=9). They were matched for age, sex ratio, duration of diabetes and body mass index. Peripheral artery disease was present in 2, 3 and 4 patients of group 1, 2 and 3 respectively. Treatment of diabetes as well as concomitant medications, in particular angiotensin-converting enzyme inhibitors and angiotensin-II-receptor antagonists, were also comparable among groups. Glycated haemoglobin (HbA1c) was measured by HPLC (TOSOH, Bioscience, Japan). Plasma osteopontin was determined by a solid phase sandwich ELISA using two specific antibodies (Immuno-biological Laboratories, Hamburg). The normal values ranged from 124 to 394 ng/ml in our laboratory. We also measured plasma adiponectin by a quantitative sandwich enzyme immunoassay technique (R & D Systems, INC, Minneapolis, USA) (normal values: 6.500±3.700 ng/ml [mean±SD]).

Results were expressed as median (range). Comparison between the 3 groups was performed by the non parametric Kruskal Wallis test. Association between variables was assessed by the Spearman's Rho rank correlation. Between groups differences of categorical variables were evaluated by Chi Square test.

HbA1c levels were comparable in the three groups. As shown in the figure 1, plasma osteopontin concentrations were three fold higher in active smokers than in non smokers and former smokers: 989 (273-1904), 284 (135-993) and 341 (134-751) ng/ml respectively (P=0.006). In contrast, plasma adiponectin concentrations were not different between groups: 2897 (1910-5407), 3467 (1364-5815) and 3815 (1571-6711) ng/ml in groups 1, 2 and 3 respectively (P=0.736). Osteopontin was not correlated with HbA1c (r=0.14; P=0.47), nor with adiponectin (r=0.217; P=0.9).

We conclude from these results that in a subgroup of type 2 diabetic patients, active smoking is associated with increased levels of circulating osteopontin. These observations are in line with the experimental data reporting that, in mice, tobacco alkaloids are able to stimulate osteopontin [7]. Previous in vitro studies have shown that high glucose could upregulate osteopontin levels [9]. In our study, however, no correlation was found between osteopontin and HbA1c. It is known that osteopontin levels are affected by several medications [10]. This is not the cause in the present...
study since current treatments were comparable in the three groups.

Osteopontin has recently emerged as a key factor in the development of atheromatosis [5-7]. However, in such studies, the possible confounding factor of tobacco exposure was not overtly taken into consideration. Given the proinflammatory action of osteopontin on vessels, it could be hypothesized that macroangiopathy related to tobacco is partially mediated by osteopontin stimulation. Other studies would be required to elucidate the relationship between osteopontin and vascular disease in larger cohorts of individuals.

References