The effect of ascorbic acid on protein glycation in streptozotocin-diabetic rats

Dear Sir,

Protein glycation is assumed to be one of the main reasons for a generation of diabetic complications [1]. This process has been reported to be affected by ascorbic acid [2]. Examinations on healthy volunteers have shown the inhibiting effect of oral ascorbic on protein glycation [3]. We decided to investigate the effect of oral ascorbic acid supplementation on fructosamine and HbA_{1c} levels in Wistar rats with streptozotocin diabetes.

Diabetic and non-diabetic rats were divided into control and untreated groups, and groups treated with ascorbic acid added to drinking water (1 g/litre) for 3 months. Blood was sampled from the tail vein of non-fasted animals at the start of the study and 1, 2, and 3 months after the initial administration of ascorbic acid. Blood was assayed for glucose, fructosamine and HbA_{1c}. Supplementation with ascorbic acid did not cause any significant changes in blood glucose levels throughout the study in the diabetic or the non-diabetic rats. Figure 1 shows that there were no significant changes in either fructosamine or HbA_{1c} levels in non-diabetic rats treated with ascorbic acid. The initial values were 129.5 ± 13.7 µmol/l and 1.91 ± 0.12 %, respectively, and remained at this level during supplementation. They did not differ from those observed in untreated non-diabetic rats. In contrast, ascorbic acid supplementation affected the HbA_{1c} concentration in diabetic rats. The initial HbA_{1c} concentrations of diabetic rats were 2.06 ± 0.09 % and 2.21 ± 0.07 % in the treated and untreated group, respectively. HbA_{1c} levels in diabetic rats rose significantly in both groups but they remained higher in the untreated group [2.74 ± 0.06 vs 2.36 ± 0.08 % ($p < 0.01$), 2.96 ± 0.07 vs 2.40 ± 0.08 % ($p < 0.001$) and 3.51 ± 0.06 vs 2.66 ± 0.06 % ($p < 0.001$) at 1, 2, and 3 months, respectively]. Ascorbic acid administration had a small effect on plasma fructosamine concentration. The statistically significant difference between groups was found at 3 months; 227.4 ± 19.5 µmol/l (treated diabetic) vs 316.3 ± 20.5 µmol/l (untreated diabetic) ($p < 0.01$). It has been suggested that the fructosamine assay is a measurement of many serum glycated proteins which may be susceptible in different ways to ascorbic acid influence [3]. Similarly, Sinclair et al. [4] did not find significant differences in plasma fructosamine levels in diabetic patients treated with ascorbate for 6 weeks.

Our results indicate that ascorbic acid administration decreases the rate of protein glycation, which may be important in prevention of secondary diabetic complications.

Yours sincerely,

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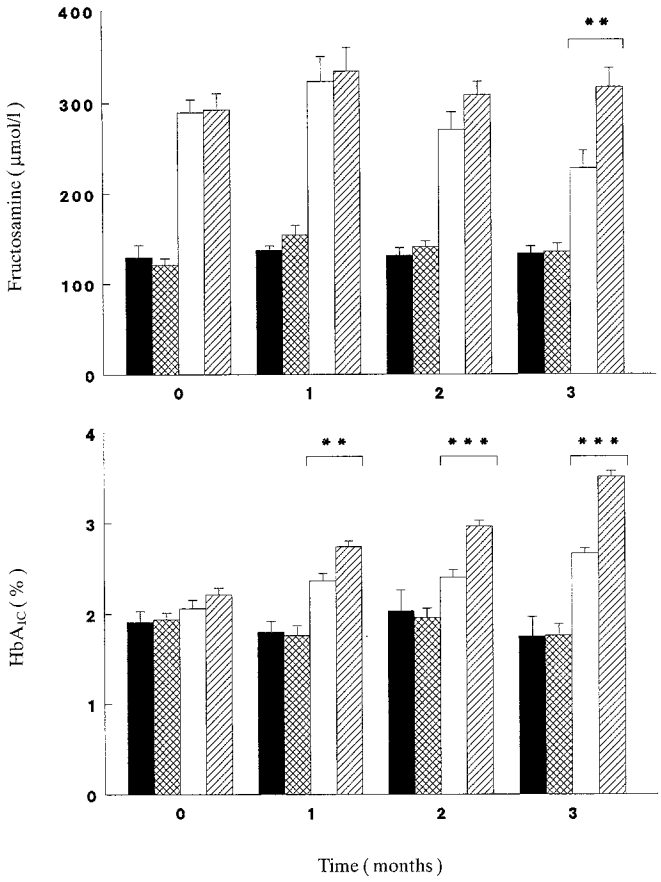

Fig. 1. Effect of ascorbic acid supplementation on fructosamine (upper panel) and HbA_{1c} (lower panel) levels in the four examined groups of rats: ■ non-diabetic rats treated with ascorbic acid; ▩ non-diabetic control; □ diabetic rats treated with ascorbic acid; ▨ diabetic control.
For all groups $n = 8$. The results are expressed as means ± SEM. ** $p < 0.01$ (unpaired Student's t-test; treated vs untreated rats); *** $p < 0.001$ (unpaired Student's t-test; treated vs untreated rats)

References

1. Cerami A, Vlassara H, Brownlee M (1988) Role of advanced glycosylation products in complications of diabetes. Diabetes Care 11 [Suppl 1]: 73–79
2. Svoboda P, Štolba P, Hegenbartová M, Strašková J, Adam M (1992) The mechanism of lowering of nonenzymatic glycation by vitamin C. Diabetologia 35 [Suppl 1]: A55 (Abstract)
3. Davie SJ, Gould BJ, Yudkin JS (1992) Effect of vitamin C on glycosylation of proteins. Diabetes 41: 167–173
4. Sinclair AJ, Girling AJ, Gray L, Le Guen C, Lunec J, Barnett AH (1991) Disturbed handling of ascorbic acid in diabetic patients with and without microangiopathy during high dose ascorbate supplementation. Diabetologia 34: 171–175