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Antioxidants - lipid peroxidase and macroangiopathy in diabetic subjects

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Resistance to insulin is often observed in patients with chronic renal failure (CRF). It very rarely leads to a disturbance in glucose regulation but participates in the cardiovascular morbidity observed during CRF. Impaired insulin action at the muscular level and reduced plasma insulin clearance have already been reported. These disorders are improved either by dialysis or low-protein diets.

In 6 CRF patients (plasma creatinine level $453 \pm 41 \mu\text{mol/L}$ ($m \pm \text{SD}$), 5 men and 1 woman (50 ± 11 years of age)), we studied the effect of a very low-protein diet (0.3 g/kg/d), supplemented with essential amino acids, keto derivatives and hydroxy analogs (Cetolog-Cernep France) and balanced in lipid content (30% of total caloric content) upon the endogenous glucose production (EGP) before and 3 months after dietary prescription. The EGP was studied using dideuterated glucose and the sensitivity of EGP to insulin by means of its change during a hyperinsulinic euglycemic clamp at a low level of hyperinsulinism ($23.5 \pm 2.8 \mu\text{U/mL}$).

The basal EGP decreased from $2.62 \pm 0.31 \text{ mg/kg/min}$ to $2.30 \pm 0.33 \text{ mg/kg/min}$ after 3 months of protein restriction ($p < 0.05$) (paired test). During the euglycemic clamp, the EGP decreases from 1.45 ± 0.28 to $0.57 \pm 0.21 \text{ mg/kg/min}$ reflecting an improvement in the insulin sensitivity of the liver as the plasma insulin concentrations measured during the clamp were no different before and after the protein restriction.

These results show a moderately elevated basal EGP and a resistance to its reduction by insulin. These parameters are corrected by protein restriction, evidence of another favorable metabolic effect of a low-protein diet in CRF.

Antioxydants – lipid peroxidase and macroangiopathy in diabetic subjects.

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Our objectives were to determine the importance of lipid peroxidation in diabetic patients and, at the same time, their antioxidant vitamin status in order to assess whether they are associated with a risk of macroangiopathy.

The study included 129 diabetic subjects (type II) who were compared with 45 controls (same age and sex). The diagnosis of macrovascular complications was based on antecedents or clinical signs; an electrocardiography (ECG) after effort and arterial echodoppler of the lower limbs were systematically performed. The variable clinical factors were: body mass index (BMI); arterial hypertension (AHT); tabagism. The biological measurements consisted of blood lipid levels (serum vitamins (A, E, C) erythrocyte vitamin E determined by high-performance liquid chromatography (HPLC) methods), 2 direct markers of lipid peroxidation, serum thiobarbituric acid reactive substances (TBARS) determined according to Yagi (1976, *Biochem Med* 15, 212-216) and the oxidative resistance of the low density lipoproteins (LDL). The univariate statistic analysis used the Mann and Whitney test; the multivariate analysis used logistic regression.

The antioxidant vitamins concentrations were higher in the controls than in diabetic subjects. The results are given as mean values \pm standard deviations control/diabetic subjects: serum vitamin C (mg/l) $6.98 \pm 3.2 / 6.08 \pm 4.42$, $p < 0.05$; serum vitamin E (μmol) $32.7 \pm 8.5 / 28.3 \pm 9.01$, $p < 0.01$;

erythrocyte vitamin E (nmol/gHB) $18.8 \pm 3.5 / 15.6 \pm 6.5$, $p < 0.001$. The ratio of TBARS to LDL mmol was lower in the controls than in the diabetic patients ($0.78 \pm 0.18 / 0.88 \pm 0.22$, $p < 0.3$) and was negatively related to the serum vitamin E concentration ($r = -0.19$, $p < 0.04$). In addition to the other classical factors linked to the macroangiopathy, an analysis by logistic regression showed that high levels TBARS ($p < 0.04$) and low serum concentrations of vitamin C ($p < 0.01$) are significantly associated with this vascular disease, especially with lower limb attack.

This study provides a correlation between lipid peroxidation and macroangiopathy and insights into a role for antioxidant vitaminic deficiency in the aetiology of atheroma in diabetic patients. Larger clinical trials are warranted to investigate the efficacy of antioxidant vitamin therapies in the prevention of macrovascular complications.

Changes in lipid metabolism after cecectomy depend on diet composition and experimental model. R Sablé-Amplis, R Sicart (CNRS, universit  Paul-Sabatier, rue F-Magendie, 31400 Toulouse, France)

To date, there are conflicting results concerning the beneficial effects of products derived from the fermentation of carbohydrate residues in the gut on lipid metabolism. The main sites of bacterial activity are the cecum and the proximal colon. The effects of cecectomy have been described in hamsters (Sicart *et al* (1984) *IRCS Med Sci* 12, 490-491). Here, we examined the consequences of cecectomies in rats, which differ greatly from the hamster in terms of the morphology of their gastrointestinal tract and lipid metabolism. The animals (6 rats per group) were fed either a standard diet or the same diet enriched with fiber (10% apple pectin) associated or not with cholesterol (2%). The surgical treatment was performed

after 15 d of adaptation to the experimental diet.

In rats receiving the standard diet, the levels of cholesterol (Ch) and triglycerides (TG) in the plasma and liver were not changed 4 weeks after removal of the cecum, even when the diet was enriched with fiber. In intact rats fed the cholesterol-enriched diet, the plasma Ch (not TG) level increased from 79 ± 7 to 126 ± 16 mg/100 mL, while in the liver, the level of cholesterol rose from 253 ± 16 to $1\ 068 \pm 144$ and that of TG from $1\ 068 \pm 198$ to $4\ 214 \pm 909$ mg/100 g of fresh tissue. In rats fed this diet, cecectomy increased plasma and liver cholesterol up to 156 ± 15 mg/100 mL (not significant) and $1\ 765 \pm 81$ mg/100 g ($p < 0.002$), respectively. The ingestion of pectin along with the cholesterol did not change the effect of cholesterol given alone in either intact or cecum-deprived rats.

These results are in contrast with those previously reported in hamsters. In this animal model, the removal of the cecum causes the level of plasma cholesterol to be dramatically augmented (+200%) and especially in animals fed a fiber-enriched diet prior to the cecectomy (+300%).

In conclusion, the effects of a cecectomy, which suppress a large part of the end-products of bacterial fermentation, on lipid metabolism, appear to be dependent on the diet composition and on the animal species used as the experimental model.

Phenotype and genotype of cytochrome P450 2E1, a key enzyme in ethanol metabolism. D Lucas ¹, P Bodenez ², F Berthou ¹, JF Menez ¹ (¹ *Laboratoire de biochimie-nutrition*; ² *Service d'alcoologie, facult  de m decine de Brest, 29285 Brest cedex, France*)

Cytochrome P450 2E1 (CYP2E1) is a key enzyme in ethanol metabolism and is induced after chronic administration of