

Relationship of endothelial cell selective adhesion molecule to markers of oxidative stress in type 2 diabetes

Ina Maria Kacso¹, Alina Ramona Lenghel¹, Diana Moldovan¹, Crina Claudia Rusu¹, Anca Rusu¹, Rodica Rahaian², Cosmina Ioana Bondor¹

¹ – University of Medicine and Pharmacy Iuliu Hatieganu Cluj ²- Emergency County Hospital Cluj

OBJECTIVES

Accumulating evidence suggests that in type 2 diabetes (T2D) endothelial dysfunction is reflected by increased oxidative stress. The recently described endothelial cell selective adhesion molecule (ESAM) is responsible for stabilizing the tight interendothelial junction, but it also influences other functions of endothelial cells. The aim of our study was to assess, for the first time to our knowledge, the relationship between soluble ESAM and markers of oxidative stress in T2D patients.

METHODS

We conducted a cross sectional study in T2D patients. Patients with T2D for at least 6 months were included and those with glomerular filtration rate < 30 ml/min, nephrotic syndrome, presence of urinary abnormalities apart from albuminuria, other cause of kidney disease, acute clinical conditions were excluded. Patients were compared to non-diabetic controls. Clinical and routine laboratory data were collected. Catalase activity was determined in erythrocyte lysate by spectrophotometric method. Plasma malondialdehyde (MDA) was measured by fluorimetric method using the thiobarbituric acid test. ESAM was determined in serum using an ELISA assay (Uscn Life Science Inc) Statistical analysis was performed using SPSS 13.0 and Statistica 8.0.

RESULTS

General characteristics of patients and comparison to controls are presented below. We found significant inverse **correlation** between catalase and serum soluble ESAM ($r=-0.27$, $p=0.046$). MDA was significantly related only to HbA1 C ($r=0.35$, $p=0.02$); relationship of MDA to ESAM was direct but not significant ($r=0.16$, $p=0.24$). MDA was inversely related to catalase ($r=-0.28$, $p=0.04$). In **multiple regression** with catalase as dependent variable, ESAM was the only parameter significantly correlated to catalase ($p=0.027$). When studying MDA as a dependent variable, relationship of the latter to HbA1 C was statistically significant ($p=0.013$) but there was a trend towards a positive correlation with ESAM ($p=0.085$). Comparison of patients according to level of oxidative stress: patients with catalase<3.38 mg/g (lowest tertile of catalase) and MDA>2.98 nmol/ml (highest tertile of MDA) versus patients with catalase> 3.38 mg/g or MDA<2.98 nmol/ml revealed higher ESAM in the first patients, with higher oxidative stress (table below).

Parameter	Diabetes (n=54)	Control (n=43)	p
Age (years)	64.83±11.81	61.41±11.20	0.14
Male n(%)	34 (62.96)	20(46.51)	0.19
BMI (kg/m ²)	31.45± 6.09	25.33±6.38	<0.0001
SBP (mmHg)	130(120-140)	120(110-135)	<0.0001
DBP (mmHg)	80(70-80)	80(70-80)	<0.0001
Catalase (mg/g)	3.07(2.63-3.44)	8.72(4.55-10.46)	<0.0001
MDA (nmol/ml)	3.88±1.50	1.58±0.72	<0.0001
ESAM (ng/ml)	16.07±5.77	8.57±5.28	<0.0001
Hb A1C (%)	7.47±1.74	5.13±0.94	<0.0001
LDL chol. (mg/dl)	104.60(79.35-135.45)	133.80(98.25-163.55)	0.006
HDL chol(mg/dl)	44.15±12.30	48.50(36.00-57.25)	0.15
Triglycerides (mg/dl)	138.50(103.50-199.25)	139.50(89.00-207.50)	0.03
CRP (mg/dl)	0.25(0.12-0.47)	0.28(0.15-0.41)	0.74
UACR (mg/g)	16.19(4.49-55.78)	10.011(5.25-12.90)	0.032
GFR (ml/min)	92.52±33.38	90.43±40.69	0.91

General characteristics of patients and comparison to controls

Parameter	Group A (n=26)	Group B (n=28)	p
Age (years)	63.23±11.71	66.32±11.92	0.34
Male n(%)	17(65.40%)	17(60.70%)	0.72
BMI (kg/m ²)	31.89±6.24	30.99±6.03	0.60
SBP (mmHg)	130(120-140)	130(120-140)	0.64
DBP (mmHg)	80(70-80)	80(70-80)	0.27
Catalase	2.71(2.27-3.04)	3.44(3.07-3.59)	<0.0001
MDA (nmol/ml)	4.81±1.25	3.01±1.17	<0.0001
ESAM (ng/ml)	17.99±5.02	14.29±5.94	0.017
Hb A1C (%)	7.82±1.65	7.17±1.79	0.21
LDL chol.(mg/dl)	91.4(72.4-136.7)	104.60(89.85-134.9)	0.36
HDL chol. (mg/dl)	46.65±12.30	43.68±12.50	0.77
Triglycerides (mg/dl)	143(104.75-232.25)	135.5(95.25-198.25)	0.27
CRP (mg/dl)	0.25(0.13-0.55)	0.29(0.11-0.37)	0.44
UACR (mg/g)	20.55(5.23-53.19)	12.65(3.74-70.74)	0.57
GFR (ml/min)	86.97±32.12	97.80±34.26	0.23

Comparison of patients according to level of oxidative stress: group A= patients with catalase <3.38 mg/g (lowest tertile of calalase) and MDA>2.98 nmol/ml (highest tertile of MDA), group B = patients with > catalase 3.38 mg/g or MDA<2.98 nmol/ml

CONCLUSIONS

Both oxidative stress and ESAM are increased in diabetic patients when compared to controls. ESAM correlates to oxidative stress in type 2 diabetic patients. The nature of our findings is observational; the fact that soluble ESAM parallels oxidative stress might be only a consequence of a process influencing both ESAM and redox state, or there might be a direct pathogenic link between the two processes.

