Original article

Relationship between soluble intercellular adhesion molecule 1 and clinically manifest cardiovascular disease in diabetic chronic hemodialysis patients

Relația între molecula de adeziune intercelulară 1 solubilă şi boala cardiovasculară clinic manifestă la pacienții diabetici hemodializați cronic

Raluca Moldovan[1*], Ina Kacsò[2], Mirela Gherman-Căprioară[2]

1. Nefromed Dialysis Centers Alba-Iulia
2. "Mihai Manasia" Nephrology and Dialysis Clinic Cluj-Napoca

Abstract

Background: The relationship between soluble intercellular adhesion molecule-1 (sICAM-1) and the presence of cardiovascular disease in diabetic chronic dialysis patients has been studied to a lesser extent. Aims: to evaluate the relationship between the serum level of sICAM-1 and clinically manifest cardiovascular disease in diabetic chronic hemodialysis patients. Methods: Twenty-six diabetic chronic hemodialysis patients treated in the Alba-Iulia Dialysis Center were included in a crossectional study. The serum sICAM-1 levels were measured, the routine laboratory evaluation was performed and the presence of clinically manifest cardiovascular disease (CVD), defined as coronary artery disease (CAD), peripheral arterial disease (PAD) or cerebrovascular disease(CRD) as well as the current treatment scheme were assessed. Results: sICAM-1 level was positively correlated with the glycated hemoglobin (r=0.59; IC95% 0.22-0.81; p=0.004). Nineteen of the 26 patients had clinically manifest CVD. The sICAM-1 level was significantly higher in CVD patients vs. non-CVD patients: 290 ng/ml (262.5-367) vs. 238 ng/ml (208-283); p=0.03. sICAM-1>260 ng/ml was significantly associated with CAD: OR=5.33; IC95% 1.02-29.4; p=0.04 and with overall clinically manifest CVD: OR=1.33; IC95% 1.25-78.3; p=0.007. sICAM-1 was significantly lower in angiotensin-converting enzyme inhibitor (ACEI)-treated patients: 258 ng/ml (220-289) vs 292 ng/ml (263-348) in the untreated group, p=0.03. The ACEI treatment was significantly associated with sICAM-1 below 260 ng/ml (p=0.002). Conclusion: Clinically apparent CVD in diabetic hemodialysis-treated patients was associated with high sICAM-1 levels. The ACEI treatment and better glycemic control were associated with lower levels of sICAM-1.

Keywords: *sICAM-1, hemodialysis, diabetes, ACEI, cardiovascular disease*

Rezumat

Introducere: Relația între molecula de adeziune intercelulară-1 solubilă (sICAM-1) şi prezența bolii cardiovasculare la pacienții diabetici hemodializați cronic a fost puțin studiată.. Obiectivul lucrării a fost eva-

[*]**Corresponding author:** Raluca Moldovan, Nefromed Dialysis Centers Alba-Iulia, Str. Turnatoriei nr. 12, Alba Iulia, Jud. Alba, cod 510185
Telefon/Fax: 0258 830 394, E-mail: mraluca78@yahoo.com

luarea relației dintre nivelul seric al sICAM-1 şi boala cardiovasculară clinic manifestă la pacienții diabetici hemodializați cronic. Material şi metodă: Douăzeci şi şase de pacienți diabetici hemodializați cronic, prevalenți în centrul de dializă Alba au fost incluşi într-un studiu crossecțional. Subiecților li s-a dozat nivelul sICAM-1, s-a efectuat evaluarea de laborator standard şi a fost evaluată boala cardiovasculară clinic manifestă (BCV) (definită ca boală cardiacă ischemică, arteriopatie cronică obliterantă a membrelor inferioare sau accident vascular cerebral) precum şi tratamentul urmat. Rezultate: sICAM-1 s-a corelat pozitiv cu hemoglobina glicată (r=0,59; IC95% 0,22-0,81; p=0,004). Nouăsprezece dintre pacienți au prezentat boală cardiovasculară clinic manifestă. sICAM-1 a fost semnificativ mai mare la pacienții cu BCV față de cei fără BCV: 290 ng/ml (262,5-367) vs 238 ng/ml (208-283); p=0,03. sICAM-1˛260 ng/ml s-a asociat semnificativ cu prezența bolii coronariene: OR=5,33; IC95% 1,02-29,4; p=0,04 şi cu boala cardiovasculară clinic manifestă per ansamblu: OR=1,33; IC95% 1,65-78,3; p=0,007. Nivelul sICAM-1 a fost semnificativ mai redus la pacienții tratați cu inhibitori ai enzimei de conversie a angiotensinei (IECA): 258 ng/ml (220-289) vs 292 ng/ml (263-348) în grupul netratat, p=0,03. Tratamentul cu IECA s-a asociat semnificativ cu sICAM-1 sub 260ng/ml (p=0,002). Concluzii: Boala cardiovasculară clinic manifestă la pacienții diabetici tratați cu hemodializă cronică se asociază cu nivele crescute ale sICAM-1. Tratamentul cu IECA se asociază cu nivele mai reduse ale sICAM-1.

Cuvinte cheie: *sICAM-1, hemodializă, diabet zaharat, IECA, boală cardiovasculară*

Received: *29th July 2012;* ***Accepted:*** *11th November 2012;* ***Published:*** *24th November 2012.*

Background

Cardiovascular disease is the main cause of death in chronic dialysis patients. This population presents an excess of cardiovascular disease (CVD) mortality and morbidity, unexplained by the traditional risk factors. The endothelial dysfunction is frequent in diabetes mellitus patients (1). High levels of endothelial adhesion molecules associate with atherosclerotic plaques (2). Serum level of the sICAM-1 is increased in chronic hemodialysis patients (3, 4) and correlates with atherosclerotic manifestations (5, 6). Still, the relationship between the sICAM-1 and CVD in diabetic chronic hemodialysis has been less studied. The majority of the studies on dialysis patients excluded diabetic individuals (3, 5, 6). In a systematic PubMed search, the study with the highest number of diabetic patients was that of Zoccali (7), which included 35 diabetic patients. However, the aim of the study was not to assess the relationship between the sICAM-1 and cardiovascular disease, as much as to evaluate the relationship between sICAM-1 and clinically manifest cardiovascular disease in diabetic chronic dialysis patients in Nefromed Dialysis Center Alba-Iulia. The relationship between sICAM-1 and clinical, laboratory and treatment characteristics of these patients was evaluated.

Methods

All stable diabetes hemodialysis patients, with a dialysis vintage of more than 3 months (n=26) in the center in March 2011, were included. Patients with acute infections and those treated with immunosuppressives or antibiotics were excluded (n=2). Demographic and clinical parameters were registered, namely: predialysis blood pressure, presence of a central venous catheter, abdominal circumference, body mass index, insulin, erythropoiesis-stimulating agents (ESA) and antihypertensive treatment. The biological parameters were: complete blood cell count, creatinine, dialysis dose, expressed using the Kt/V parameter (where K represents the dialyzer clearance coefficient, t represents the dialysis time and V represents the urea distribution volume), glycated hemoglobin (HbA1c), total cholesterol, high-density lipoprotein cholesterol (HDL), triglycerides, uric acid, albumin, C reactive protein (CRP). Measurements were performed in the Medcenter Laboratory in Cluj-Napoca, during the routine lab evaluation, from blood sampled simultaneously with that used to determine the sICAM-1 level. For the determination of sICAM-1, the blood was centrifuged for 15 minutes at 1500 g. Centrifugation was started

Table 1. Study group characteristics

Parameter	Average±SD/ Median (25-75 percentiles) / Percent (n=26)
Age, years	61±10
Male gender, n(%)	21 (81)
Dialysis vintage, years	3±3.8
Smoking present/history, n(%)	7 (26.9)
Central venous catheter, n(%)	5 (19)
Body mass index, kg/m^2	28±5.65
Abdominal circumference, cm	103 (97-110)
Predialysis systolic BP, mm Hg	136±25
Predialysis diastolic BP, mm Hg	76±10.6
ESA-treated, n(%)	23 (88.4)
ESA dose, U/week	4692±3988
ESA/Hb, (U/week)/g	283 (181-578)
Insulin treatment, n(%)	20 (77)
Antihypertensive treatment, n(%)	22 (84.6)
ACEI, n(%) (%yes)	15 (56.8)
sICAM-1, ng/ml	275 (252-336)
Total cholesterol, mg/dl	167±28
Triglycerides, mg/dl	232±89
Albumin, g/dl	3.82±0.38
CRP, mg/l	3 (3-6)
Uric acid, mg/dl	6.09±1.03
HbA1c%	6.94±1.69
Creatinine, mg/dl	8±2.44
Kt/V	1.35±0.13
Hemoglobin, g/dl	11±1.75
Thrombocyte count x10^3/mmc	198±59.8
Leukocyte count/mmc	7050 (6400-8400)

Legend: Numeric variables are expressed as average ± standard deviations for normally distributed variables and median (25-75 percentiles) for the abnormally distributed ones.

30 minutes after the sampling, serum was separated and frozen at -80 degrees Celsius. The sICAM-1 level was determined using ELISA R&D Systems method, in the Synevo Laboratory, Cluj-Napoca.

Clinically manifest cardiovascular disease was defined as the presence of one or more of the following: coronary artery disease (CAD), chronic peripheral artery disease (PAD) or cerebrovascular disease (CRD). CAD was defined as: history of angina pectoris, history of ischemic ECG changes or necessity of cardiac percutaneous or surgical revascularization. PAD was defined as: ankle-brachial index below 0.9, presence of trophic ischemic lesions in the lower limbs or limb amputation. The ankle-brachial index was measured using the auscultatory method in the brachial artery at the non-arterio-venous fistula upper limb and in the posterior tibial arteries, 5 minutes after the end of dialysis. Auscultatoric evaluation of ankle-brachial index was validated for detection of PAD in dialysis patients (8). The lowest ankle blood pressure value was taken into account for the calculation of the ankle-brachial index. CRD was defined as history of ischemic or hemorrhagic stroke.

The relationships between sICAM-1 and the clinical, biological and therapeutic parameters as well as cardiovascular disease were evaluated. The vascular access (arterio-venous fistula or central venous catheter) was registered and its relationship with sICAM-1 was evaluated.

Statistics: quantitative variables were expressed as averages and standard deviations for normally distributed variables and as medians and 25-75 percentiles for the non-normally distributed variables; quantitative variables were expressed as proportions. Differences between the study groups' parameters were determined using t-test and ANOVA test for normally distributed variables and U Mann-Whitney test for non-normally distributed variables. The relationship between continuous variables was evaluated using Spearman regression. Logistic regression was used to study the relationship between sICAM-1 and other clinical and biological parameters on one hand and CVD on the other hand. The statistically significant threshold chosen was $p \leq 0.05$.

Table 2. Comparative characteristics of the cardiovascular disease group and those of the non-clinically manifest cardiovascular disease group

Parameter	CVD group Average±SD/ Median (25-75 percentiles) / Percent (n=17)	NCVD group Average±SD/ Median (25-75 percentiles) / Percent (n=9)	p
Age, years	60±11	63±6 6	0.25
Male gender, n(%)	13 (76)	8 (89)	0.4
Dialysis vintage, years	3.94±4.13	2.33±2.92	0.15
Smoking (present/antecedent), n(%)	6 (35)	1 (11)	0.15
Central venous catheter, n(%)	5 (29)	0	0.15
Body mass index, kg/m^2	28.37±6.76	27.4±2.8	0.3
Abdominal circumference, cm	104 (89-111)	100 (97.8-109)	0.9
Predialysis systolic BP, mm Hg	135.8±27.85	136.6±21.2	0.4
Predialysis diastolic BP, mm Hg	76.5±11.69	75.6±8.8	0.4
ESA treated, n(%)	15 (88.2)	8 (88.8)	0.9
ESA dose, U/week	4400±3906	5500±4250	0.5
ESA/Hb, (U/week)/g	384 (142-797)	219 (157-400)	0.34
Insulin treated, n(%)	14 (82)	6 (67)	0.7
Antihypertensive treatment, n(%)	15 (88)	7 (78)	0.9
ACEI, n(%) (%yes)	11 (66.7)	4 (41.2)	0.4
sICAM-1, ng/ml	290 (262.5-367)	238 (208-283)	**0.03**
Total cholesterol, mg/dl	169±25.5	163±33.5	0.3
Triglycerides, mg/dl	256.4±80	190.4±94.3	**0.03**
Albumin, g/dl	3.84±0.24	3.76±0.56	0.35
CRP, mg/l	3 (3-6)	6 (3-7.5)	0.4
Uric acid, mg/dl	5.93±1.09	6.32±0.95	0.2
HbA1c%	7.28±2.07	6.42±0.71	0.1
Creatinine, mg/dl	8.36±2.37	7.16±2.5	0.1
Kt/V	1.35±0.13	1.34±0.13	0.4
Hemoglobin, g/dl	11.4±1.9	10.9±1.4	0.1
Thrombocyte count x10^3/mmc	201.3±70	191.6±36	0.25
Leukocyte count/mmc	7200 (6475-8525)	6900 (6250-8125)	0.2

Legend: Numeric variables are expressed as average ± standard deviations for normally distributed variables and median (25-75 percentiles) for the abnormally distributed ones.

Results

The study group characteristics are shown in *Table 1*.

Correlations between sICAM-1 and different clinical and biological parameters were studied. The sICAM-1 was weakly positively correlated with the weekly ESA dose (r=0.38; IC95% 0.0002-0.67; p=0.04), the ESA/hemoglobin ratio (r=0.4; IC95% 0.02-0.68; p=0.04), glycated hemoglobin (r=0.59; IC95% 0.22-0.81; p=0.004) and leukocyte count/mmc (r=0.49; IC95% 0.13-0.74; p=0.01). In multiple regression with sICAM-1 as a dependent variable and glycated hemoglobin, leukocyte count, weekly ESA dose, ESA/Hemoglobin ratio, sICAM-1 weakly correlated with glycated hemoglobin (R^2=0.28, p=0.01). In logistic regression, after introduction of the same variables and ACEI treatment in the model, sICAM-1<260 ng/ml

Table 3. Comparative characteristics of patients treated with ACEI *vs* non- treated ones

Parameter	ACEI group Average±SD/ Median (25-75 percentiles) / Percent (n=15)	NonACEI group Average±SD/ Median (25-75 percentiles) / Percent (n=11)	p
Age, years	60±9.2	61.5±10.8	0.57
Male gender, n(%)	13 (86.7)	8 (72.7)	0.34
Dialysis vintage, years	2 (1-3)	2 (2-3.75)	0.34
Smoking (present/antecedent), n(%)	5 (33)	2 (18)	0.68
Central venous catheter, n(%)	4 (26.6)	1 (9.1)	0.5
Body mass index, kg/m^2	27.9 (25.3-31.2)	27.8 (23.9-29.8)	0.7
Abdominal circumference, cm	102 (98.2-112.3)	104 (87.8-109.5)	0.45
Predialysis systolic BP, mm Hg	133±30.5	136.4±20.6	0.75
Predialysis diastolic BP, mm Hg	76.7±9.8	75.5±12.1	0.78
ESA treated, n(%)	14 (93)	9 (81)	0.81
ESA dose, U/week	3000 (200-5500)	6000 (1000-11500)	0.71
ESA/Hb, (U/week)/g	280.4 (181-390)	594 (77-998)	0.65
Insulin treated, n(%)	11 (73.3)	9 (81.8)	0.98
sICAM-1, ng/ml	258 (220-289)	292 (269-348)	**0.03**
Total cholesterol, mg/dl	170 (150-184)	173 (150-222)	0.6
Triglycerides, mg/dl	188 (58-339)	184 (122-233)	0.7
Albumin, g/dl	3.56±0.39	3.68±0.58	0.53
CRP, mg/l	4.5 (3-6)	3 (3-5.25)	0.36
Uric acid, mg/dl	6.4 (5.6-7.8)	6.2 (5.3-6.4)	0.19
HbA1c%	6.6 (5.6-7.4)	6.8 (6.4-7.4)	0.8
Creatinine, mg/dl	8.04±1.6	7.8±3.35	0.8
Kt/V	1.37±0.09	1.33±0.17	0.44
Hemoglobin, g/dl	11.9 (11.4-13.3)	11 (10.5-11.6)	0.17
Thrombocyte count x10^3/mmc	180±41.2	222±73.8	0.08
Leukocyte count/mmc	6900±1187	8845±3269	**0.04**

Legend: Numeric variables are expressed as averages ± standard deviations for normally distributed variables and median (25-75 percentils) for the abnormally distributed ones.

significantly associated only with the ACEI treatment (OR 0.06; IC95% 0.0006-0.7; p=0.02).

Nineteen of the patients had manifest CVD: 13 of them had CAD, 12 had PAD and 5 had CRD. Comparative characteristics of the cardiovascular disease group and those of the non-clinically manifest cardiovascular disease group are shown in *Table 2*.

The CVD and NCVD groups did not show statistically significant differences from the point of view of the demographic, clinical and ESA, insulin or antihypertensive treatment, including the ACEI use or of the dialysis dose (Kt/V). Of the biological variables, sICAM-1 and triglyceridemia were significantly higher in the CVD group. All the central venous catheter patients were in the CVD group. The sICAM-1>260 ng/ml was significantly associated with CAD: OR=5.33; IC 95% 1.02-29.4; p=0.04 and with overall clinically manifest CVD: OR=1.33; IC 95% 1.25-78.3; p=0.007.

In logistic regression, sICAM-1 was the main predictor of the clinically manifest cardiovascular disease. The association between sICAM-1>260 ng/ml and CVD remained significant after the following parameters were intro-

Table 4. Comparative characteristics of central venous catheter (CVC) and non-CVC groups

Parameter	CVC group Average±SD/ Median(25-75 percentiles) / Percent (n=5)	Non CVC group Average±SD/ Median(25-75 percentiles) / Percent (n=21)	p
Age, years	51 (47.8-63.8)	62 (55.5-63.8)	0.12
Male gender, n(%)	2 (40)	19 (90)	0.06
Dialysis vintage, years	3 (1.75-3.25)	2 (1-3.25)	0.6
Smoking (present/antecedent), n(%)	2 (40)	5 (23.8)	0.86
Body mass index, kg/m^2	28.4 (22.2-35.2)	27.9 (25-30.2)	0.87
Abdominal circumference, cm	105 (86-112)	102 (98-110.8)	0.9
Predialysis systolic BP, mm Hg	140 (115-143)	140 (120-150)	0.62
Predialysis diastolic BP, mm Hg	80 (67.5-90)	80 (70-80)	0.64
ESA treated, n(%)	4 (80)	19 (90)	0.88
ESA dose, U/week	6000 (750-9000)	3000 (2000-6000)	0.81
ESA/Hb, (U/week)/g	392 (68-935)	280 (176-595)	0.76
Insulin treated, n(%)	4 (80)	16 (76)	0.69
Antihypertensive treatment, n(%)	5 (100)	17 (81)	0.71
ACEI, n(%) (%yes)	4 (80)	11 (52)	0.52
sICAM-1, ng/ml	294 (271-430)	264 (236-312)	0.1
Total cholesterol, mg/dl	177.5 (165-205)	155 (149-177)	0.12
Triglycerides, mg/dl	253 (199-297)	215 (140-312)	0.6
Albumin, g/dl	3.9 (3.75-3.9)	3.8 (3.6-4.1)	0.62
CRP, mg/l	3 (3-4.5)	3 (3-7.5)	0.43
Uric acid, mg/dl	5.3 (5.08-7.2)	6 (5.3-6.7)	0.59
HbA1c%	6.4 (5.7-9.7)	6.4 (6.1-7.1)	0.87
Creatinine, mg/dl	8.2 (6.25-9)	8.1 (6-9.3)	0.82
Kt/V	1.3 (1.25-1.43)	1.4 (1.3-1.43)	0.6
Hemoglobin, g/dl	11.1 (10-13.7)	11 (10.3-12)	0.63
Thrombocyte countx10^3/mmc	198 (192-216)	190 (144-238)	0.6
Leukocyte count/mmc	7900 (6975-8525)	6900 (6375-8125)	0.5

Legend: Numeric variables are expressed as averages ± standard deviations for normally distributed variables and median (25-75 percentiles) for the abnormally distributed ones.

duced in the model, namely: age, dialysis vintage, central venous catheterism, ACEI and insulin treatment and HbA1c.

The analysis of ACEI treated and non-treated patient subgroups is shown in *Table 3*.

The ACEI group had a lower sICAM-1 and a higher leukocyte count (*Table 3*). The subgroups were not significantly different in the other biological parameters, or in the clinical and treatment characteristics, including the dialysis dose. In the logistic regression, the ACEI use was significantly associated with the sICAM-1 below 260ng/ml (OR 20, CI 95% 1.97-203, p=0.002).

In central venous catheter (CVC) patients there was a tendency, although not statistically significant, for a higher sICAM-1 (*Table 4*): all central venous catheter patients had serum SICAM-1 levels higher than 250 ng/ml. There were no statistically significant differences between the two groups (CVC vs. non CVC group) in the CRP levels and in the leukocyte count.

Discussion

The serum sICAM-1 levels found in the current study are close to those reported by previous studies (7, 9, 10).

In our group, sICAM-1 levels were significantly associated with clinically manifest cardiovascular disease. Several studies have addressed the role of the sICAM-1 in the pathogenesis and progression of atherosclerosis. Cell adhesion molecules regulate attachment of leukocytes to the endothelium, an important step in the migration of leukocytes to the sites of inflammation. Macrophages and endothelial cells produce sICAM-1 as a response to the proinflammatory cytokine action. Stimulated endothelial cells secrete cytokines, amplifying the inflammatory cascade and being the first step in the atheroma plaque formation. Though the exact action mechanism of these molecules is not completely clear, cell adhesion molecules are useful as endothelial activation and vascular inflammation markers (11, 12).

ICAM-1 has been studied as a cardiovascular morbidity predictor in apparently healthy patients, or in other words as a marker of incipient atherosclerosis (13). The interest in its role as a cardiovascular risk marker in dialysis patients is more recent. Papagianni et al found a significant association of the sICAM-1 with subclinical atherosclerosis as well as with clinically manifest cardiovascular diseases, but diabetic patients were excluded from the study. It is well known that sICAM-1 levels are increased in diabetic and hypertensive patients compared to the healthy ones. The utility of sICAM-1 in assessing the cardiovascular risk in diabetic hemodialysis patients has been less studied. In a search conducted on PubMed using as a key word sICAM-1, diabetes and dialysis, no study with this aim was identified.

The positive correlation between the ESA dose and sICAM-1 found in our study was weak and larger studies are needed to clarify the association between ESA and sICAM-1 in diabetic dialysis patients. A positive correlation would, apparently, be in contradiction with *in vivo* (14) and *in vitro* (15) studies, showing that erythropoietin reduces the expression and level of the sICAM-1. Nevertheless, the sICAM-1 weakly positively correlated with the ESA/hemoglobin ratio, that expresses the erythropoietin resistance and it is probably linked to the ESA resistance induced by inflammation. Sezer 2004 (16) described a significant association between the sICAM-1 and the erythropoietin dose in dialyzed patients with an inflammatory syndrome.

The positive correlation between glycated hemoglobin and sICAM-1 is consistent with data described in diabetic patients without renal failure, showing that diabetes mellitus decompensation induces an increase in cell adhesion molecules synthesis (17), but no data has yet been published about the relationship between sICAM-1 and glycated hemoglobin in diabetic dialysis patients.

ACEI treated patients had lower levels of sICAM-1. The ACEI treatment was shown to be associated with a reduction in the sICAM-1 in coronary artery disease patients (18, 19) and with a reduction in other inflammation markers in cerebrovascular disease patients (20), but the association has not yet been described in dialysis patients.

All patients with central venous catheters had levels of sICAM-1 higher than 250 ng/ml. This was unlikely to be caused by catheter infection, since the CRP and leukocyte counts were similar in catheter and fistula patients and one of the exclusion criteria was active infection. The status of central venous catheter bearer might in fact be a marker of prothrombotic state (in patients with multiple antecedents of thrombosed arterio-venous fistulas) and, indirectly, a marker of endothelial dysfunction. There are very few studies (2 search results on PubMed: Zohny 2008 (21) and Chang 2009 (22)) regarding the relationship between the ICAM-1 (sICAM-1 and ICAM-1 expression respectively) and the arterio-venous fistula thrombosis. These papers identified

ICAM-1 as a predictor of arterio-venous fistula thrombosis. This is to be confirmed by future research. The extent to each an increase in adhesion molecules levels as a predictor of fistula thrombosis should prompt interventions, as a Doppler ultrasound, fistulography, anticoagulant treatment or interventional treatment on the fistula is yet to be shown.

A limitation of the current research is the relatively low number of patients included. Still, this is the first study addressing sICAM-1 in diabetic hemodialysis patients as a clinically manifest cardiovascular disease marker. Our results draw attention to possible therapeutic implications of interactions between an endothelial dysfunction marker and clinically apparent cardiovascular disease.

Conclusions

Clinically manifest cardiovascular disease in diabetic hemodialysis patients is associated with increased levels of sICAM-1. ACEI treatment is associated with lower levels of sICAM-1.

Acknowledgements: The sICAM-1 levels were determined using kits from the grant number CNCSIS Idei 1168/2008, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca.

Abbreviations

ACEI=angiotensin converting enzyme inhibitor
BP=blood pressure
CAD=coronary artery disease
CRD=cerebrovascular disease
CRP=C reactive protein CVC=central venous catheter
CVD= clinically manifest cardiovascular disease
ESA/Hb=ratio between the weekly ESA dose and hemoglobin (english language version)
ESA=erythropoesis-stimulating agents
HbA1c=glycated hemoglobin
HDL=high-density lipoprotein cholesterol
ICAM-1=intercellular adhesion molecule 1
Kt/V= parameter used to quantify the dialysis dose, where K=dialyzer clearance coefficient, t=dialysis time and V=urea distribution volume
PAD=peripheral arterial disease
sICAM-1=soluble intercellular adhesion molecule 1

References

1. Rubio-Guerra AF, Vargas-Robles H, Medina-Santillán R, Escalante-Acosta BA. Levels of soluble adhesion molecules among normal and hypertensive type 2 diabetic patients. Gac Med Mex. 2008;144(1):11-4.
2. Rizzoni D, Muiesan ML, Porteri E, Castellano M, Salvetti M, Monteduro C, et al. Circulating adhesion molecules and catorid artery structural changes in patients with non-insulin dependent diabetes mellitus. J Hum Hypertens. 2003;17:453–470.
3. Bolton CH, Downs LG, Victory JG, Dwight JF, Tomson CR, Mackness MI et al. Endothelial dysfunction in chronic renal failure: roles of lipoprotein oxidation and pro-inflammatory cytokines. Nephrol Dial Transplant. 2001;16(6):1189-97.
4. Rabb H, Calderon E, Bittle PA, Ramirez G. Alterations in soluble intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 in hemodialysis patients. Am J Kidney Dis. 1996;27(2):239-43.
5. Papagianni A, Alexopoulos E, Giamalis P, Ginanlis L, Belechri AM, Koukoudis P et al. Circulating levels of ICAM-1, VCAM-1 and CP-1 are increased in haemodialysis patients. Association with inflammation, dyslipidaemia and vascular events. Nephrol Dial Transplant. 2002;17:435–41.
6. Papagianni A, Dovas S, Bantis C, Belechri AM, Kalovoulos M, Dimitriadis C, et al. Carotid atherosclerosis and endothelial cell adhesion molecules as predictors of long-term outcome in chronic hemodialysis patients. Am J Nephrol. 2008;28(2):265-74.
7. Zoccali C, Tripepi G, Cutrupi S, Pizzini P, Mallamaci F. Low triiodothyronine: a new facet of inflammation in end-stage renal disease. J Am Soc Nephrol. 2005;16(9):2789-95.
8. Fiegleson HS, Criqui MH, Fronek A, Langer RD, Molgaard CA. Screening for peripheral arterial disesase: The sensitivity, specificity, and predictive value of noninvasive tests in a defined popoulation. Am J Epidemiol. 1994;140:526–34.
9. Mrowka C, Heintz B, Sieberth H-C. Is dialysis membrane responsible for increased circulating adhesion molecules during chronic haemodialysis? Clin Nephrol. 1999;52: 312–321.
10. Tylen P, Fernvik E, Lundahl J, Lins LE, Jacobson SH. Monocyte and granulocyte CD11b/CD18, CD62L expression and sICAM-1 concentration in the interdialytic period. Nephron 1996; 74: 275–282.
11. Blake GJ, Ridker PM. Novel clinical markers of vas-

cular wall inflammation. Circ Res. 2001; 26;89(9):763-71.
12. Kooshki A, Taleban FA, Tabibi H, Hedayati M. Effects of marine omega-3 fatty acids on serum systemic and vascular inflammation markers and oxidative stress in hemodialysis patients. Ann Nutr Metab. 2011;58(3):197-202.
13. Pradhan AD, Shrivastava S, Cook NR, Rifai N, Creager MA, Ridker PM. Symptomatic peripheral arterial disease in women: nontraditional biomarkers of elevated risk. Circulation. 2008;117(6):823-31.
14. Makis AC, Chaliasos N, Hatzimichael EC, Bourantas KL. Recombinant human erythropoietin therapy in a transfusion-dependent beta-thalassemia major patient. Ann Hematol. 2001;80(8):492-5.
15. Szczepański M, Kamianowska M, Wnuczko K, Pietruczuk M, Wołczyński S. The influence of erythropoietin (Epo) on intercellular adhesion molecule-1 (ICAM-1, CD54) and platelet-endothelial cell adhesion molecule-1 (PECAM-1, CD31) expression on human umbilical vein endothelial cells (HUVEC) induced by tumor necrosis factor-alpha (TNF-alpha). Wiad Lek. 2007;60(1-2):22-7.
16. Sezer S, Külah E, Ozdemir FN, Tutal E, Arat Z, Haberal M. Clinical consequences of intermittent elevation of C-reactive protein levels in hemodialysis patients. Transplant Proc. 2004;36(1):38-40.
17. El Amine M, Sohawon S, Lagneau L, Gaham N, Noordally S. Plasma levels of ICAM-1 and circulating endothelial cells are elevated in unstable types 1 and 2 diabetes. Endocr Regul. 2010;44(1):17-24.
18. Schieffer B, Bunte C, Witte J, Hoeper K, Boger RH, Schwedhelm E, et al. Comparative effects of AT1-antagonism and angiotensin-converting enzyme inhibition on markers of inflammation and platelet aggregation in patients with coronary artery disease. J Am Coll Cardiol. 2004;44: 362–368.
19. Berg AH, Scherer PE. Adipose tissue, inflammation, and cardiovascular disease. Circ Res. 2005;96(9):939-49.
20. Di Napoli M, Papa F. Angiotensin-converting enzyme inhibitor use is associated with reduced plasma concentration of C-reactive protein in patients with first-ever ischemic stroke. Stroke. 2003;34: 2922–2929.
21. Zohny SF, Abd el-Fattah M. Evaluation of circulating vascular endothelial growth factor and soluble adhesion molecules as reliable predictors of native arteriovenous fistula thrombosis in chronic hemodialysis patients. Clin Biochem. 2008;41(14-15):1175-80. Epub 2008 Jul 28.
22. Chang CJ, Ko YS, Ko PJ, Hsu LA, Chen CF, Yang CW, et al. Thrombosed arteriovenous fistula for hemodialysis access is characterized by a marked inflammatory activity. Kidney Int. 2005;68(3):1312-9.