SOLUBLE CELL ADHESION MOLECULES S-VCAM-1 AND S-ICAM-1 IN SUBJECTS WITH FAMILIAL COMBINED HYPERLIPIDEMIA

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Familial combined hyperlipidemia (FCH) is the most common familial hyperlipidemia with a high risk for early atherosclerosis. The aim of this study was to compare levels of soluble intercellular cell adhesion molecule 1 (s-ICAM-1) and soluble vascular cell adhesion molecule 1 (s-VCAM-1) in asymptomatic members of FCH families with healthy controls and to determine the relation between s-ICAM-1, s-VCAM-1 and risk factors accompanying FCH. We also investigated the association between adhesion molecules and the intima-media thickness (IMT) of the common carotid artery, a recognized morphological marker of early atherosclerosis. 82 members of 29 FCH families were divided into the 2 groups: HL (probands and hyperlipidemic first-degree relatives, n = 47) and NL (normolipidemic first-degree relatives, n = 35). The control groups – HL-C (n = 20) and NL-C (n = 20) – consisted of sex- and age–matched healthy individuals. Hyperlipidemic members had significantly higher concentration of s-ICAM-1 (633.7 ± 169.6 ng/ml versus 546.2 ± 155.9 ng/ml, $p < 0.05$). The elevation of s-VCAM-1 was not significant (880.8 ± 202.9 ng/ml versus 826.5 ± 174.6 ng/ml, N.S.). Levels of s-ICAM-1 and of s-VCAM-1 in normolipidemic relatives were not significantly different from the control group (530.8 ± 113.9 ng/ml versus 530.0 ± 101.0 ng/ml and 860.2 ± 265.7 ng/ml versus 822.1 ± 197.0 ng/ml respectively). There was a significant correlation between s-ICAM-1 and apoB ($r = 0.42$; $p < 0.01$) in hyperlipidemic subjects and between s-ICAM-1 and proinsulin ($r = 0.54$; $p < 0.01$) in normolipidemic subjects. S-ICAM-1 correlated with IMT ($r = 0.32$; $p < 0.05$) in all members of FCH families. The increase of s-ICAM-1 in asymptomatic hyperlipidemic members of FCH families reflects their high cardiovascular risk. The positive association between s-ICAM-1 and IMT could indicate s-ICAM-1 as a potential predictor of atherosclerosis manifestation.

Abbreviations: apoB, apolipoprotein B; BMI, body mass index; CCA, common carotid artery; CHD, coronary heart disease; DBP, diastolic blood pressure; FCH, familial combined hyperlipidemia; HDL, high density lipoprotein; HDL–C, HDL cholesterol; HL, hyperlipidemic members of FCH families; HOMA, homeostasis model assessment; hs-CRP, high sensitivity C reactive protein; IMT, intima-media thickness; IRMA, immunoradiometric assay; LDL, low density lipoprotein; LDL–C, LDL-cholesterol; NL, normolipidemic members of FCH families; non-HDL-C, non-HDL cholesterol; RIA, radioimmune assay; SBP, systolic blood pressure; s-ICAM-1, soluble intercellular cell adhesion molecule 1; s-VCAM-1, soluble vascular cell adhesion molecule 1; TC, total cholesterol; TG, triglycerides; VLDL, very low density lipoprotein.

INTRODUCTION

Familial combined hyperlipidemia (FCH) is the most common genetic hyperlipidemia, affecting 1.0 % to 2.0 % of the population, and it has a high risk of early atherosclerosis manifestation (10 % to 20 % of survivors of premature myocardial infarction exhibit FCH) (ref.[1, 2]). FCH is characterized by increased levels of apolipoprotein B (apoB) containing lipoproteins – very low density lipoproteins (VLDL) and low density lipoproteins (LDL), particularly small, dense LDL (ref.[3–5]). FCH is frequently associated with a decrease in high density lipoprotein cholesterol (HDL-C) concentration, altered metabolism of fatty acids, prolonged postprandial lipaemia and impaired activity of lipoprotein lipase. In addition, FCH is associated with arterial hypertension and insulin resistance[6, 7]. The lipids and lipoprotein levels in FCH are – in comparison with familial hypercholesterolemia – relatively moderately elevated and do not fully explain the highly increased risk of cardiovascular disease.

Intercellular cell adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1) are two members of the immunoglobulin gene superfamily that play important, but different roles in the adhesion of leukocytes to the vascular endothelium. VCAM-1, which is the endothelial ligand for very late antigen 4, has been postulated to play the more critical role in monocyte adherence to endothelial cells under flow conditions. ICAM-1 ligands include CD11a/CD18 (lymphocyte function associated antigen-1) and CD11b/CD18 (macrophage antigen-1), which are present on monocytes, lymphocytes, and neutrophils. Increased expression of ICAM-1 and VCAM-1 is observed in atherosclerotic lesions, and mice deficient in either ICAM-1 or VCAM-1 have reduced response to experimental atherosclerotic stimuli. Cytokine activation dramatically up-regulates their expression on the cell surface where they support the interaction of leukocytes and endothelial cells[8-10]. Recently, in addition to being expressed on the cell surface, soluble forms of adhesion molecules have been detected in circulating blood and have been shown to retain their functional ability. A number of clinical investigators have measured levels of soluble ICAM-1 (s-ICAM-1) and/or VCAM-1 (s-VCAM-1) as potential biomarkers for endothelial dysfunction and early atherosclerosis.

The intima-media thickness (IMT) of the common carotid artery is a recognized morphological marker of early atherosclerosis. IMT reflects integrally the effect of individual risk factors of atherosclerosis and some intervention measures performed to eliminate the effect of these risk factors[11-13]. Moreover, IMT represents the ultrasound parameter with a good predictive value on the generalized status of atherosclerosis of coronary[14-16], cerebral[17,18] and lower extremity arteries[19,20].

The aim of this study was to investigate whether asymptomatic members of FCH families (without clinical manifestation of atherosclerosis) have higher plasma levels of s-ICAM-1 and/or s-VCAM-1 than controls. Furthermore, we studied whether parameters of lipid metabolism and insulin resistance are related to s-ICAM-1 and/or s-VCAM-1 levels. We also investigated the correlation between the above mentioned adhesion molecules and IMT of the common carotid artery.

MATERIAL AND METHODS

The study was carried out with 82 members of 29 FCH families, who had been examined in the Lipid Center of the 3rd Department of Internal Medicine, University Hospital Olomouc. A family with FCH was defined in the study under the following criteria. The proband exhibiting a combined hyperlipidemia should have both plasma total cholesterol (TC) and triglycerides (TG) concentrations above the 90th percentile, adjusted for age and gender, as obtained from the MONICA study, based on data from the Czech population (Table 1) (ref.[21]). At least one first-degree relative of the proband should have plasma TC and/or TG above 90th percentile, adjusted for age and

Table 1. Values of 90th percentiles of Czech population for total cholesterol and triglycerides in men and women in individual age categories (Czech post-MONICA study, kindly provided by doc. MUDr. R. Cifkova, CSc., IKEM, Prague).

Age category (years)	Men		Women	
	TC (mmol/l)	TG (mmol/l)	TC (mmol/l)	TG (mmol/l)
< 35	6.75	3.11	5.97	1.65
35–44	7.28	3.64	6.64	2.05
45–55	7.32	3.83	7.31	2.75
> 55	7.43	3.64	8.04	3.13

TC = total cholesterol, TG = triglycerides

gender, or a level of apoB ≥ 1.25 g/l (ref.[22,23]). At the same time, secondary or another primary hyperlipoproteinemia was excluded in those subjects. All subjects were tested for an underlying cause of secondary hyperlipidemia: diabetes mellitus, hypothyroidism, hepatic or renal impairment and nephrotic syndrome. None of the probands in these families were homozygous for the apo-E2 allele and none of them or their first-degree relatives had tendon xanthomas. Other exclusion criteria were as follows: history of clinically manifest atherosclerosis (coronary artery disease, heart failure, cerebrovascular ischemic disease, peripheral vascular disease), smoking, hypolipidemic therapy in the previous 8 weeks, hormone therapy with estrogens and clinical presence of acute infectious disease or trauma.

Members of FCH families were divided into two groups: HL (hyperlipidemic members of FCH families, i.e. probands and their hyperlipidemic first-degree relatives, having plasma TC and/or TG level > the 90th percentile adjusted for age and gender, or the level of apoB ≥ 1.25 g/l) and NL (normolipidemic first degree relatives, who did not meet the above – mentioned criteria.). The control groups (HL-C and NL-C) – were sex- and age-matched to groups HL and NL. Control groups consisted of healthy individuals with a negative family history of hyperlipidemia and early manifestation of atherosclerosis. The Ethics Committee of the Medical Faculty and University Hospital Olomouc approved the design of the study and informed consent was obtained from all participants.

All subjects filled out a questionnaire on their previous medical history, especially cardiovascular status, medication, and smoking habits. Body mass index (BMI), waist circumference, systolic and diastolic blood pressure (SBP, DBP) were determined in all subjects. Venous blood samples were drawn in the morning after a 12 h fast. Total cholesterol, triglycerides and HDL-C were determined enzymatically on a Hitachi 917 analyzer (Roche, Basel, Switzerland). Determination of HDL-C was made by a direct method without precipitation of apoB containing

lipoproteins. LDL-C levels were calculated according to the Friedewald formula (for TG < 4.5 mmol/l). Concentration of apoB was determined immunoturbidimetrically using specific antibodies – Tina-Quant apoB kit (Roche, Basel, Switzerland). C-reactive protein (hs-CRP) was assessed by means of an ultra sensitive immunoturbidimetric method using the kit Tina-Quant CRP (Roche, Basel, Switzerland). Glycemia was determined using the enzyme based kit Glucose GOD-PAP. Insulin was determined using the commercially available kits – Insuline (Immunotech, Marseille, France) using specific antibodies by IRMA method. The result obtained was then used for calculation of the parameter of insulin resistance HOMA (homeostasis model assessment, described by Matthews et al.: fasting glycemia × fasting insulin / 22.5) (ref.[24]). C-peptide and proinsulin were determined using the commercially available kits – C-peptide (Immunotech, Marseille, France) and Proinsulin (DRG Instruments GmbH, Marburg, Germany) using specific antibodies by IRMA method (for C-peptide) and RIA method (for proinsulin). Serum levels of the soluble adhesion molecules s-ICAM-1 and s-VCAM-1 were measured by immunoenzymatic assay using commercially available standard kits – s-ICAM-1 and s-VCAM-1 (Immunotech, Marseille, France). Ultrasound scanning of IMT was performed with a 10 MHz linear array transducer (Hewlett-Packard, Image Point, M2410A, 1997). All measurements were performed with the subjects in a supine position. The head was tilted to the one side at an angle of 45°. The longitudinal B-mode image of the common carotid artery (CCA) was displayed just before the widening of the bulb. When an optimal longitudinal image of the far wall of the CCA in the region of 1 cm proximally from the bulb was obtained, it was frozen on the R wave according to a simultaneous ECG and videotaped (Panasonic VCR, AG-MD 830, S-VHS videocassette). Three video records were made on both CCA. IMT measurements were processed off-line using the software Image-Pro Plus (Version 4.0, Media-Cybernetics, Silver Spring, USA). The region under evaluation was the CCA wall 1–2 cm distant proximally from the mentioned border. The average of all mean IMT of three frozen images of both sides was chosen as the outcome variable. Subjects with an atherosclerotic plaque in the evaluated region were not included in the study. IMT was registered and evaluated independently by two physicians and the inter- and intra-individual variability of ultrasound measurements was evaluated in 22 healthy subjects (12 women, 10 men, mean age of 35.2 ± 7.8 years), who were examined repeatedly at an interval of one month. Mean differences were for IMT CCA sinistra 0.030±0.027 mm, IMT CCA dextra 0.030 ± 0.021 mm and mean IMT 0.032 ± 0.021 mm. Variation coefficients were 2.18 % for IMT CCA sinistra, 2.05 % for IMT CCA dextra and 1.72 % for mean IMT. The measurement of IMT was made without knowledge of laboratory results.

All values given in the present paper are expressed as means ± SD. Comparison of individual groups (FCH subjects respectively normolipidemic subjects and controls) was made using a Mann-Whitney U test, because this test assumes eventual non normal data distribution. It is based on simple ranking of data. For statistical evaluation of the dependence of s-ICAM-1 and of s-VCAM-1 on risk factors for atherosclerosis and their relation to IMT we used a univariate correlation analysis. A Kolmogorov-Smirnov test was used to test for normal distribution and a Pearson correlation test was subsequently used in the case of normal distribution of constants. In the case of abnormal distribution of constants (TG, proinsulin, insulin, C-peptide, HOMA, SBP, DBP) we used Spearman correlation test. Statistical analysis was using SPSS for Windows version 12.0 (Chicago, Illinois, USA). Probability values of $p < 0.05$ were considered as statistically significant.

RESULTS

Basic characteristics

Table 2 shows the anthropometric and biochemical characteristics and IMT in subjects with FCH (HL) and their normolipidemic relatives (NL) compared to controls (HL-C and NL-C respectively). In comparison to sex- and age- matched controls, hyperlipidemic subjects had significantly higher DBP, BMI and exhibited insulin resistance – significantly elevated levels of C-peptide and proinsulin compared to controls. They also had higher hs-CRP. By definition the FCH subjects had higher plasma TC and TG concentrations compared to controls and normolipidemic relatives. In addition, they had a more atherogenic lipid and lipoprotein profile as reflected by increased LDL-C and apoB concentrations. Hyperlipidemic subjects had also significantly higher IMT compared to healthy controls. Normolipidemic relatives had significantly higher diastolic blood pressure, TG and proinsulin concentrations compared to their sex- and age- matched controls. There was no difference in IMT and other measured anthropometric and biochemical parameters.

Levels of s-ICAM-1 and s-VCAM-1

The first aim of this study was to investigate whether subjects with FCH or their normolipidemic relatives had higher plasma levels of soluble cell adhesion molecules (s-VCAM-1 and s-ICAM-1) than controls (graph 1, 2). In comparison to healthy sex- and age- matched controls, the hyperlipidemic individuals had significantly higher levels of s-ICAM-1 (633.7 ± 169.6 ng/ml versus 546.2 ± 155.9 ng/ml, p<0.05). No significant difference was found in the levels of s-VCAM-1 (880.8 ± 202.9 ng/ml versus 826.5 ± 174.6 ng/ml) in these groups. The levels of s-VCAM-1, respectively of s-ICAM-1 in normolipidemic relatives were not significantly different from sex- and age-matched controls (860.2 ± 265.7 versus 822.1 ± 197.0, respectively 530.8 ± 113.9 versus 530.0 ± 101.0).

Relation to metabolic parameters, anthropometric parameters, and IMT

In hyperlipidemic subjects a significant correlation was found between s-ICAM-1 and apoB (r = 0.42, p < 0.01). In the group of normolipidemic subjects a significant correla-

Table 2. Basic characteristics in individual groups

	HL	HL-C	NL	NL-C
women/men	20/27	8/12	24/11	14/6
age (years)	44.7 ± 1.5	44.2 ± 13.5	31.5 ± 11.0	31.8 ± 7.6
TC (mmol/l)	6.96 ± 1.16***	4.88 ± 0.92	4.88 ± 0.72	4.82 ± 0.58
TG (mmol/l)	3.01 ± 2.20***	1.15 ± 0.54	1.25 ± 0.43**	0.92 ± 0.34
HDL-C (mmol/l)	1.43 ± 0.41	1.49 ± 0.32	1.53 ± 0.42	1.61 ± 0.41
LDL-C (mmol/l)	4.25 ± 1.27***	2.87 ± 0.76	2.76 ± 0.62	2.75 ± 0.45
non-HDL-C (mmol/l)	5.53 ± 1.03***	3.4 ± 0.88	3.35 ± 0.71	3.21 ± 0.49
apoB (g/l)	1.39 ± 0.23***	0.92 ± 0.21	0.93 ± 0.24	0.90 ± 0.11
SBP (mm Hg)	127 ± 12	123 ± 12	119 ± 15	120 ± 9
DBP (mm Hg)	82 ± 6***	75 ± 9	77 ± 8*	71 ± 9
BMI (kg/m^2)	26.5 ± 3.0*	24.7 ± 2.4	22.4 ± 3.0	23.0 ± 2.6
waist circumference (cm)	88 ± 11	84 ± 11	75 ± 10	76 ± 8
fasting glycemia (mmol/l)	5.16 ± 0.78*	4.76 ± 0.49	4.98 ± 0.92	4.62 ± 0.32
C-peptide (mg/l)	2.68 ± 1.69*	1.99 ± 1.20	1.95 ± 0.69	1.66 ± 0.66
proinsulin (mIU/l)	17.57 ± 13.02*	11.25 ± 8.41	11.27 ± 3.82*	8.26 ± 1.57
insulin (mIU/l)	9.52 ± 6.25	7.38 ± 4.33	7.13 ± 2.48	6.97 ± 2.69
HOMA (mIU*mmol/l^2)	2.29 ± 1.80	1.62 ± 1.19	1.61 ± 0.73	1.45 ± 0.61
hs-CRP (mg/l)	2.13 ± 1.71*	1.10 ± 1.23	2.17 ± 2.50	1.50 ± 1.83
IMT (mm)	0.68 ± 0.11***	0.60 ± 0.07	0.55 ± 0.05	0.55 ± 0.04

TC = total cholesterol, TG = triglycerides, HDL–C = HDL cholesterol, LDL–C = LDL-cholesterol, non-HDL-C = non-HDL cholesterol (TC – HDL-C), apoB = apolipoprotein B, SBP = systolic blood pressure, DBP = diastolic blood pressure, BMI = body mass index, HOMA = homeostasis model assessment [fasting glycemia × fasting insulin / 22.5], hs-CRP = high sensitivity C reactive protein, IMT = intima-media thickness of the common carotid artery
HL = hyperlipidemic members of FCH families, HL-C = control group of HL
NL = normolipidemic members of FCH families, NL-C = control group of NL
* ~ p < 0.05, ** ~ p < 0.01, *** ~ p < 0.001 ...statistical significance level (Mann Whitney – U test)

tion was found between s-ICAM-1 and proinsulin (r = 0.54, p < 0.01). There was no significant correlation between s-VCAM-1 and measured anthropometric and biochemical parameters either in these groups. IMT of all members of FCH families (NL+HL) significantly correlated with s-ICAM-1 (graph 3), but not with s-VCAM-1.

DISCUSSION

FCH is associated with early atherosclerosis, despite a relatively late manifestation of hyperlipidemia. The lipids and lipoprotein levels in FCH are relatively moderately elevated and do not fully explain the total increased risk of cardiovascular disease. Thus surrogate markers of vascular damage are investigated to better identify subject with higher cardiovascular risk[25]. Soluble adhesion molecules – s-ICAM-1 and s-VCAM-1 – are accepted as potential biomarkers for endothelial dysfunction and atherosclerosis. The primary aim of this study was to investigate whether asymptomatic members of FCH families have higher plasma levels of s-ICAM-1 and/or s-VCAM-1 than controls. This study shows that asymptomatic subjects with FCH have increased levels of s-ICAM-1 – in contrast to levels of s-VCAM-1 – compared to sex- and age- matched controls. Their normolipidemic relatives exhibit no significant differences either of s-VCAM-1 or of s-ICAM-1 concentrations.

Four large prospective studies of healthy individuals have shown a relationship between s-ICAM-1 and inci-

s-ICAM-1 (ng/ml)
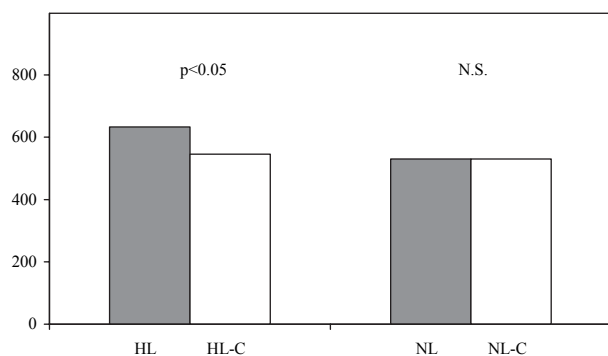
**Graph 1.** Levels of s-ICAM-1 in individual groups

s-ICAM-1 = soluble intercellular adhesion molecule – 1
HL = hyperlipidemic members of FCH families,
HL-C = control group of HL
NL = normolipidemic members of FCH families,
NL-C = control group of NL
p ~ statistical significance level (Mann Whitney – U test),
N.S. = non significant

s-VCAM-1 (ng/ml)
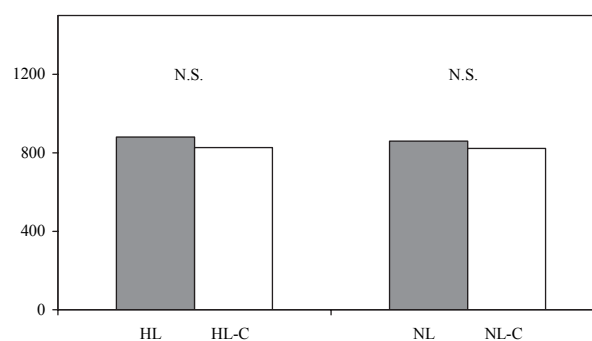
Graph 2. Levels of s-VCAM-1 in individual groups

s-VCAM–1 = soluble vascular cell adhesion molecule – 1
HL = hyperlipidemic members of FCH families,
HL-C = control group of HL
NL = normolipidemic members of FCH families,
NL-C = control group of NL
p ~ statistical significance level (Mann Whitney – U test),
N.S. = non significant

IMT (mm)
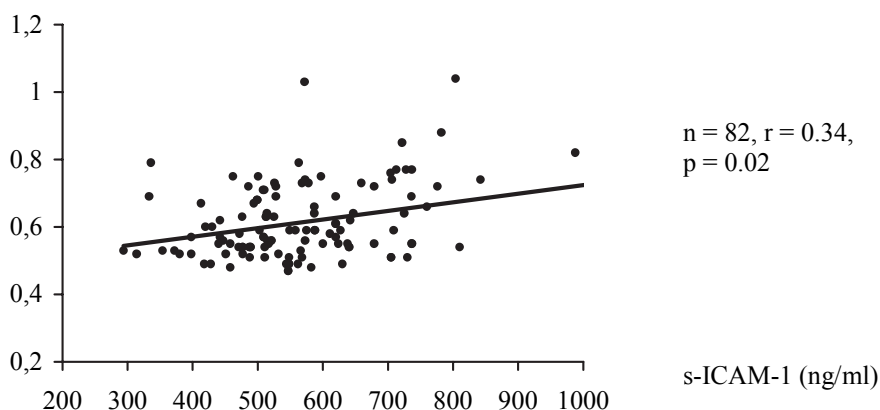
Graph 3. Correlation between IMT and ICAM-1 in all members of FCH families

IMT = intima-media thickness of the common carotid; artery,
s-ICAM-1 = soluble intercellular adhesion molecule-1,
n = number of FCH families members,
r = Pearson correlation coefficient,
p = statistical significance level

dent coronary heart disease (CHD) (ref.[26-29]). Another trial has shown that in stable patients with CHD, levels of s-ICAM-1 were associated with increased risk for future CHD events[30]. In contrast, no relationship has been found between s-VCAM-1 and incident CHD in several of these studies[26,29,31]. Levels of s-ICAM–1 – but not of s-VCAM-1 – were also found significantly higher in healthy individuals, in whom subsequent development of symptomatic peripheral arterial disease was documented[32]. In contrast

is the finding of Blankenberg et al. who determined in patients with the documented CHD, the level of s-VCAM-1 as the best predictor of mortality due to CHD, after adjustment for other clinical risk factors[33]. Another study proved that levels of s-VCAM-1, in contrast to levels of s-ICAM-1, correlated with severity of clinically manifest atherosclerosis of lower extremity arteries[34]. On the basis of the above-mentioned studies, many researchers consider the levels of s-ICAM-1 as a potential predictor of

cardiovascular risk in healthy persons, while the levels of s-VCAM-1 may be related to the extent of the existing atherosclerotic involvement and prediction of subsequent cardiovascular progression in subjects with diagnosed CHD (ref.[9, 10]). This is supported by our findings. FCH subjects without clinical manifestation of atherosclerosis had elevated levels of s-ICAM-1, but not of s-VCAM-1.

Furthermore, the plasma level of s-ICAM-1 is associated with apoB in hyperlipidemic and with proinsulin in normolipidemic members of FCH families. The association between lipids and levels of adhesive molecules had been investigated in several studies. Hackman et al. observed elevated levels of s-ICAM-1 in hypercholesterolemic subjects in a relatively small group of patients. Patients with hypertriglyceridemia even exhibited elevated levels of both s-ICAM-1 and s-VCAM-1 (ref.[35]). However, larger studies have not confirmed elevated levels of s-ICAM-1 and s-VCAM-1 in hypercholesterolemic subjects[36, 37]. Kowalski et al. recorded elevated levels of s-ICAM-1 but not of s-VCAM-1 in persons with hyperlipidemia II b (according to Frederickson) (ref.[38]). Kvasnička et al. reported elevated levels of s-ICAM-1 in obese subjects with combined hyperlipidemia[39]. In our group under study, hyperlipidemic individuals showed a significant correlation between s-ICAM-1 and apoB, which corresponds to the findings of other authors confirming an evident and independent correlation between apoB and CHD (ref.[22]). Correlation between s-ICAM-1 and proinsulin in normolipidemic relatives indicates an association of s-ICAM-1 with insulin resistance. Marfella et al. found elevated levels of both s-VCAM-1 and s-ICAM-1 in type 2 diabetics and confirmed that acute hyperglycemia increased levels of s-ICAM-1 (but not of s-VCAM-1) in healthy controls too. In contrast, euglycemia normalized elevated levels of s-ICAM-1 but not those of s-VCAM-1 (ref.[40]). An association was shown between s-ICAM-1 (not of s-VCAM-1) and insulin resistance in non-diabetic patients and subjects with hypertension[41]. The presence of insulin resistance in FCH patients is well known and may be related to the concrete lipid profile of individual family members. Vakkilainen et al. showed the more frequent disorder of glucose tolerance in subjects with isolated hypertriglyceridemia or combined hyperlipidemia compared to persons with isolated hypercholesterolemia or healthy controls[42]. Pihlajamaki et al. also reported on a reduced insulin-stimulated uptake of glucose only in subjects with hypertriglyceridemia or combined hyperlipidemia. However, elevated levels of free fatty acids were found in all FCH family members, including those without hyperlipidemia. This finding indicates that even normolipidemic FCH relatives had a certain form of insulin resistance[43]. Increased proinsulin levels, together with higher triglyceride levels and diastolic blood pressure values recorded in our normolipidemic FCH family members could also indicate the presence of insulin resistance. However, with regard to late manifestation of hyperlipidemia in FCH and the low mean age of this group, it is probable that the NL group also comprises persons in whom FCH is still latent and insulin resistance is manifested first.

Controversial are results of studies comparing the levels of adhesion molecules and the early morphological markers of atherosclerosis. The Rotterdam study reported on the association between s-ICAM-1 and only carotid plaques, not IMT, nor ankle occlusion index. The levels of s-VCAM-1 did not correlate with any of those parameters[44]. Hwang et al. found a significant correlation between the levels of s-ICAM-1 and IMT but no significant association between IMT and s-VCAM-1 (ref.[45]). Rohde et al. showed a statistically significant correlation between IMT and both s-ICAM-1 and s-VCAM-1 (ref.[46]) and a similar finding was described by De Caterina et al. (ref.[47]). Our group showed only a correlation between IMT and s-ICAM-1, not s-VCAM-1. This may be explained by the fact that s-VCAM-1 is associated with the extent of existing atherosclerotic involvement and our subjects had no clinically diagnosed manifestation of atherosclerosis.

CONCLUSION

It is concluded that significantly increased levels of s-ICAM-1 in FCH patients without atherosclerotic manifestation indicate a high cardiovascular risk induced by dyslipidemia, insulin resistance, visceral obesity and arterial hypertension. The levels of s-ICAM-1 may reflect the presence of low grade systemic inflammation and endothelial dysfunction leading to the advancement and progression of atherosclerosis. Correlation between s-ICAM-1 and IMT, respected morphological marker of early atherosclerosis, suggests that assessment of s-ICAM-1 may be useful in prediction of cardiovascular risk for members of FCH families.

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