ORIGINAL ARTICLE

Polymporphism of monocyte chemoattractant protein 1 (*MCP1* –2518 A/G) and responsiveness to hepatitis B vaccination in hemodialysis patients

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KEY WORDS

diabetes, hemodialysis, hepatitis B vaccination, *MCP1* –2518 A/G rs1024611, monocyte chemoattractant protein 1

ABSTRACT

INTRODUCTION Monocyte chemoattractant protein 1 (MCP-1) is involved in the pathogenesis of renal diseases, diabetes, and hepatitis B virus (HBV) clearance.

OBJECTIVES The aim of the study was to evaluate the distribution of *MCP1*–2518 A/G (rs1024611) polymorphic variants in patients on hemodialysis (HD) with respect to their responsiveness to hepatitis B vaccination.

PATIENTS AND METHODS Patients on HD, never infected with HBV, were enrolled into the study after receiving an appropriate hepatitis B vaccine. The HD group consisted of 601 individuals who responded to vaccination with anti-HBs titer exceeding 10 IU/l considered as protective and 153 nonresponders, in whom no adequate response was observed (anti-HBs, ≤10 IU/l). There were 175 diabetic patients among responders and 47 diabetic patients among nonresponders. Healthy subjects served as controls (n = 437). *MCP1* genotyping was determined by polymerase chain reaction–restriction fragment length polymorphism.

RESULTS The distribution of *MCP1* rs1024611 polymorphic variants in controls was as follows: AA, 51%; AG, 41%; GG, 8%. There were no significant differences ($P > 0.05$) in *MCP1* distribution between the study groups and controls, independently of the occurrence of diabetes and responsiveness to hepatitis B vaccination. HD groups that were identified based on diabetic status and responsiveness to hepatitis B vaccination did not differ in *MCP1* distribution.

CONCLUSIONS *MCP1*-2518 A/G polymorphism is not associated with responsiveness to hepatitis B vaccination in patients on HD, independently of whether they have diabetes or not.

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INTRODUCTION Monocyte chemoattractant protein 1 (MCP-1) is a multifunctional cytokine, which has been reported to participate in the pathogenesis of renal diseases associated with diabetes, but also not related to this disease.[1-3] Serum levels of MCP-1 increase in renal dysfunction and are higher in patients on hemodialysis (HD) than those in a healthy population.[4-8] MCP-1 is also involved in the outcome of hepatitis B virus (HBV) infection,[9,10] which is still frequent in patients on HD.[11]

–2518 A/G polymorphism in the promoter region of the *MCP1* gene (*MCP1* rs1024611), located in chromosome 17q12, may alter MCP-1 expression.[12,13] The *MCP1*–2518G allele is associated with upregulation of both MCP-1 transcript and protein levels.[7,12,13] HD subjects with AG+GG genotypes had higher MCP-1 levels than those with the AA variant.[7] In Japanese HD patients, homozygosity for G at *MCP1* (*MCP1–2518G>A*) was proposed as a candidate for the genetic marker

of carpal tunnel syndrome.[14] A significant difference in *MCP1*–2518 A>G genotype frequencies between the entire group of HD patients and controls was also demonstrated, because allele G carriers occurred in this study significantly more often in patients with cardiovascular diseases (CVD), who constituted 63% of the group. There was no statistically significant difference in the distribution of *MCP1* genotypes between HD patients without CVD and healthy controls.[7] In the study by Park et al.[15] on Korean subjects, the promoter polymorphism of *MCP1* (*MCP1–2518G>A*) was involved in HBV clearance, which is associated with the development of antibodies to surface antigen of HBV (anti-HBs): the frequency of homozygotes for the *MCP1*–2518A allele among chronic HBV carriers was significantly higher than that among spontaneously recovered subjects. However, a year later, Cheong et al.[16] did not demonstrate an association of *MCP1–2518G>A* with the outcome of HBV infection in Korean patients.

As shown in the Multicenter Polish Population Health Status Study (WOBASZ), the incidence of diabetes in Poland is 6.8%.[17] Diabetes is the most common cause of end-stage renal disease (ESRD) in many HD settings.[18] The association of the *MCP1* polymorphism with diabetes was demonstrated,[19-22] and diabetes was also recognized as a cause of hypo- or nonresponsiveness to hepatitis B vaccination in patients on renal replacement therapy (RRT).[23] However, in the available literature, we have not found associations between the *MCP1* polymorphism in diabetes and responsiveness to hepatitis B vaccination in HD patients.

Our aim was to evaluate distribution of *MCP1* –2518 A/G (rs1 024 611) polymorphic variants in HD patients with respect to their responsiveness to hepatitis B vaccination. The effect of *MCP1* –2518 A/G genotypes on response to hepatitis B vaccination was also investigated in type 2 diabetes as the cause of diabetic nephropathy and ESRD.

PATIENTS AND METHODS

Patients and controls Unrelated HD patients were enrolled into the study if they 1) were never infected with HBV as indicated by medical history and results of HBV seromarkers: both surface antigen of HBV (HBsAg) and antibodies to core antigen of HBV (anti-HBc) were negative; 2) underwent full vaccination series against HBV that is recommended for HD patients (4 doses of 40 μg each at 0, 1, 2, 6 months) and developed anti-HBs titer considered as protective (>10 IU/l) in response to this primary vaccination or additional vaccine doses; 3) received full vaccination series against HBV that is recommended for HD patients and at least 3 additional vaccine doses and did not develop protective anti-HBs titer.

Patients were hepatitis-B vaccinated with recombinant DNA yeast-derived vaccines, composed of the S protein of HBsAg (Engerix B, GlaxoSmithKline Biologicals, Belgium; Hepavax–Gene, BIOMED SA, Poland; Euvax B, LG Life Sciences Ltd., South Korea).

HD patients with carpal tunnel syndrome or active tuberculosis or both were excluded from the study. CVD was not the inclusion criterion because diastolic cardiac dysfunction occurs in 93% of HD patients and progresses in the course of HD therapy.[24,25] Therefore, near all HD patients have more or less pronounced cardiac damage.

The entire HD group consisted of 754 patients. Type 2 diabetes was diagnosed in 222 patients (29.4%), and diabetes was a cause of diabetic nephropathy and ESRD in all those patients. There were no patients with type 1 diabetes. There were 601 hepatitis-B-vaccine responders (79.7%) and 153 nonresponders (20.3%). In the nondiabetic group (n = 532), there were 426 responders (80.1%); in the diabetic group (n = 222), there were 106 responders (47.7%). A difference in the prevalence of responders in nondiabetic and diabetic groups was significant ($P < 0.0001$). Selected demographic and clinical data of the main groups of HD patients are shown in **TABLE 1**.

Unrelated blood donors and healthy volunteers from the same geographical area served as controls (n = 437). This control group was also used in the earlier study for comparison of *MCP1* –2518 A>G (rs1 024 611) polymorphic variants in patients suffering from primary glomerulonephritis and healthy individuals.[26]

All examined subjects were Caucasians.

Genotyping *MCP1* rs1024611 genotyping was determined by polymerase chain reaction–restriction fragment length polymorphism as previously described.[26]

Statistical methods Descriptive statistics are presented as percentage for categorical variables, as mean with 1 standard deviation for normally distributed continuous variables, or as median with range for not normally distributed continuous variables. The χ^2 test or Mann–Whitney test was used for the comparison of data obtained in selected groups of HD patients, as appropriate.

The Hardy–Weinberg equilibrium (HWE) was tested to compare the observed genotype frequencies to the expected ones using the χ^2 test with 1 degree of freedom. In all HD responders as well as in nondiabeitc HD responders, there was a deviation from the HWE in the observed *MCP1* genotype frequencies compared with the expected ones (Supplementary material online, *Table S1*). The Fisher exact test or χ^2 test was used to evaluate differences in genotype and allele prevalence between the study groups. The odds ratio and 95% confidence interval (95% CI) were also calculated and adjusted for sex, age, duration of RRT, and chronic glomerulonephritis, as appropriate. Polymorphisms were tested for association using the χ^2 test for trend (P_{trend}). Power analysis was performed by the uncorrected χ^2 test available at an online internet service.[27]

TABLE 1 Selected demographic and clinical data of the main groups of patients on hemodialysis

All HD patients (n = 754)			
parameter	responders (n = 601)	nonresponders (n = 153)	*P* value
men, n (% of all)	360 (59.9)	79 (51.6)	0.064[a]
age, y	61.7 ±15.1	66.9 ±14.4	<0.001[b]
RRT duration, y	2.6 (0.003–26.1)	1.1 (0.03–11.6)	<0.001[b]
causes of end-stage renal disease, n (% of all)			
diabetic nephropathy	175 (29.1)	47 (30.7)	0.766[a]
hypertensive nephropathy	118 (19.6)	29 (19.0)	0.909[a]
chronic glomerulonephritis	93 (15.5)	9 (5.8)	0.002[a]
chronic tubulointerstitial nephritis	57 (9.5)	19 (12.4)	0.293[a]
polycystic kidney disease	43 (7.2)	5 (3.2)	0.094[a]
3461[c], 1752[c], 3691[c], 1884[c], or other	115 (19.1)	44 (28.8)	0.011[a]
responders to hepatitis B vaccination (n = 601)			
parameter	diabetics (n = 175)	nondiabetics (n = 426)	*P* value
men, n (% of all)	103 (58.9)	257 (60.3)	0.784[a]
age, y	65.8 ±12.8	60.0 ±15.7	<0.001[b]
RRT duration, y	2.6 (0.09–18.3)	2.6 (0.003–26.1)	0.064[b]
causes of end-stage renal disease, n (% of all)			
diabetic nephropathy	175 (100)	0 (0)	
chronic glomerulonephritis	–	93 (21.8)	–
hypertensive nephropathy	–	118 (27.7)	–
chronic tubulointerstitial nephritis	–	57 (13.4)	–
polycystic kidney disease	–	42 (9.9)	–
3461[c], 1752[c], 3691[c], 1884[c], or other	–	116 (27.2)	–
nonresponders to hepatitis B vaccination (n = 153)			
parameter	diabetics (n = 47)	nondiabetics (n = 106)	*P* value
men, n (% of all)	24 (51.1)	55 (51.9)	1.000[a]
age, y	68.2 ±13.5	66.3 ±14.8	0.442[b]
RRT duration, y	1.0 (0.09–8.2)	1.2 (0.03–11.6)	0.373[b]
causes of end-stage renal disease, n (% of all)			
diabetic nephropathy	47 (100)	0 (0)	
chronic glomerulonephritis	–	9 (8.5)	–
hypertensive nephropathy	–	29 (27.4)	–
chronic tubulointerstitial nephritis	–	19 (17.9)	–
polycystic kidney disease	–	5 (4.7)	–
1752[c], 2578[c], 1832[c], 1396[c], or other	–	44 (41.5)	–

a χ^2 test
b Mann–Whitney test
c renal diagnosis codes for the ERA-EDTA[28]

Abbreviations: HD – hemodialysis, RRT – renal replacement therapy

A *P* value of less than 0.05 was considered statistically significant. All probabilities were 2-tailed.

Statistical calculations were performed using GraphPad InStat 3.06, 32-bit for Windows, created September 5, 2003 (GraphPad Software, Inc., La Jolla, California, United States), CytelStudio Version 9.0, created March 17, 2010 (CytelStudio Software Corporation, Cambridge, United States), and Statistica Version 10, 2011 (Stat Soft, Inc., Tulsa, Oklahoma, United States).

Ethical issues Informed consent was obtained from all participants. The research design was approved by the Institutional Review Board of the Poznan University of Medical Sciences, Poznań, Poland.

RESULTS HD patients (n = 754), nondiabetic patients (n = 532), and diabetic patients (n = 222) did not differ in *MCP1* genotype frequencies from controls (Supplementary material online, *Table S2*). The frequency of distribution of *MCP1* polymorphic variants was also nonsignificant between all diabetic and all nondiabetic subjects (Supplementary material online, *Table S3*). The distribution of the main demographic and

TABLE 2 Distribution of *MCP1* rs1024611 polymorphic variants in hemodialysed responders and controls

Genotype	Responders (frequency)	Controls (frequency)	Odds ratio (95% CI)	2-tailed *P*	P_{trend}	$P_{genotyping}$	Power, %
all HD cases vs. controls							
	n = 601	n = 437					
AA	284 (0.47)	225 (0.51)	referent	–	0.513	0.138	–
AG	279 (0.46)	177 (0.41)	1.249 (0.958–1.629)	0.103	–	–	38.7
GG	38 (0.07)	35 (0.08)	0.860 (0.511–1.453)	0.633	–	–	8.4
AG+GG	317 (0.53)	212 (0.49)	1.185 (0.919–1.528)	0.199	–	–	25.4
MAF	355 (0.29)	247 (0.28)	1.064 (0.874–1.296)	0.561	–	–	9.2
HD cases without diabetes vs. controls							
	n = 426	n = 437					
AA	201 (0.47)	225 (0.51)	referent	–	0.727	0.051	–
AG	203 (0.48)	177 (0.41)	1.284 (0.964–1.710)	0.089	–	–	42.6
GG	22 (0.05)	35 (0.08)	0.704 (0.380–1.281)	0.280	–	–	21.0
AG+GG	225 (0.53)	212 (0.49)	1.188 (0.901–1.566)	0.231	–	–	23.8
MAF	247 (0.29)	247 (0.28)	1.036 (0.836–1.284)	0.778	–	–	6.0
HD cases with diabetes vs. controls							
	n = 175	n = 437					
AA	83 (0.47)	225 (0.51)	referent	–	0.365	0.650	–
AG	76 (0.43)	177 (0.41)	1.164 (0.791–1.710)	0.475	–	–	12.4
GG	16 (0.09)	35 (0.08)	1.239 (0.606–2.441)	0.618	–	–	9.1
AG+GG	92 (0.53)	212 (0.49)	1.176 (0.815–1.698)	0.413	–	–	14.6
MAF	108 (0.31)	247 (0.28)	1.133 (0.855–1.496)	0.403	–	–	14.2

Abbreviations: CI – confidence interval, MAF – minor allele frequency, others – see **TABLE 1**

clinical data in the entire group of HD patients (n = 754) selected according to the genotypes of *MCP1* rs1024611 did not show statistical differences (Supplementary material online, *Table S4*).

Classification of HD patients (all subjects, diabetic, nondiabetic) into responders and nonresponders to hepatitis B vaccine did not reveal differences in the distribution of the respective genotypes and allele frequencies of *MCP1* rs1024611 between all HD groups and controls (**TABLES 2** and **3**) as well as between all HD groups (**TABLES 4–6**). However, a borderline significance was demonstrated between all HD nonresponders and controls as well as nondiabetic HD nonresponders and controls (**TABLE 3**). To clarify this trend, the genotype analysis was repeated with the exclusion of 20 patients in whom causes or accelerators of ESRD included severe immunocompromise diseases (multiple myeloma, 7 cases; amyloidosis, 4 cases; antineutrophil cytoplasmic antibodies-related vasculitis, 4 cases; lupus nephritis, 3 cases; renal/urinary tract cancer, 2 cases). To treat those diseases, appropriate medications including corticosteroids and immunosuppressants were used. HD patients who entered the final analysis (n = 133) did not show any differences in the distribution of *MCP1* rs1024611 genotypes, while a small group of severely immunocompromised HD patients (n = 20) demonstrated a borderline difference in *MCP1* polymorphism compared with controls (Supplementary material online, *Table S5*).

DISCUSSION In the past decade, the association of immune response to hepatitis B vaccination with genotypes of cytokines, their receptors, and toll-like receptors (*IL1A*, *IL1RA*, *IL1B*, *IL2*, *IL4*, *IL4R*, *IL6*, *IL10*, *IL10RA*, *IL12A*, *IL12B*, *IL13*, *IL18*, *MAPK (JNK1)*, *TLR3, TNF-a*) was intensively studied with different results.[29-40] In this study, we focused on the polymorphic variants of *MCP1*.

Distribution of *MCP1* –2518 G>A polymorphism varies significantly in published reports, even among healthy subjects[7,19-21,26,41-46] (Supplementary material online, *Table S6*). In uremic milieu, the immune system is compromised, but severity of its deterioration may differ between HD patients. An example of this variability is responsiveness to hepatitis B vaccination. Up to 20% of HD patients are nonresponders despite advanced vaccination strategy.[47] A similar percentage of nonresponders was shown in our study.

Inflammatory monocytes, recruited by production of MCP-1, are necessary for effective immunity after vaccination, but these monocytes may also generate potent counter-regulatory immune responses.[48] The *MCP1* –2518 G allele upregulates MCP-1 levels[7,12,13]; therefore, nonresponders could show higher prevalence of the GG genotype. Vaccinated HD patients, who are able to produce anti-HBs, usually have a satisfactory clinical

TABLE 3 Distribution of *MCP1* rs1024611 polymorphic variants in hemodialysed nonresponders and controls

Genotype	Nonresponders (frequency)	Controls (frequency)	Odds ratio (95% CI)	2-tailed *P*	P_{trend}	$P_{genotyping}$	Power, %
all HD cases vs. controls							
	n = 153	n = 437					
AA	65 (0.42)	225 (0.51)	referent	–	0.073	0.158	–
AG	73 (0.48)	177 (0.41)	1.428 (0.951–2.145)	0.089	–		43.0
GG	15 (0.10)	35 (0.08)	1.484 (0.706–2.992)	0.323	–		19.9
AG+GG	88 (0.57)	212 (0.49)	1.437 (0.975–2.122)	0.068	–		47.7
MAF	103 (0.34)	247 (0.28)	1.288 (0.963–1.717)	0.089	–		41.5
HD cases without diabetes vs. controls							
	n = 106	n = 437					
AA	44 (0.42)	225 (0.51)	referent	–	0.099	0.182	–
AG	52 (0.49)	177 (0.41)	1.502 (0.937–2.412)	0.093	–	–	39.7
GG	10 (0.09)	35 (0.08)	1.461 (0.599–3.294)	0.444	–	–	15.1
AG+GG	62 (0.58)	212 (0.49)	1.495 (0.953–2.358)	0.082	–	–	41.6
MAF	72 (0.34)	247 (0.28)	1.305 (0.933–1.816)	0.123	–	–	35.6
HD cases with diabetes vs. controls							
	n = 47	n = 437					
AA	21 (0.45)	225 (0.51)	referent	–	0.337	0.630	–
AG	21 (0.45)	177 (0.41)	1.271 (0.638–2.531)	0.562	–	–	10.1
GG	5 (0.11)	35 (0.08)	1.531 (0.423–4.538)	0.579	–	–	11.7
AG+GG	26 (0.55)	212 (0.49)	1.314 (0.687–2.536)	0.463	–	–	13.4
MAF	31 (0.33)	247 (0.28)	1.249 (0.765–2.004)	0.398	–	–	15.0

Abbreviations: see **TABLES 1** and **2**

status, and also their genetic pattern associated with protective antibody generation may be typical of the majority of healthy subjects. Not surprisingly, HD patients with maintained responsiveness to hepatitis B vaccination did not differ significantly from controls with respect to the distribution of *MCP1* –2518 G>A polymorphic variants, independently of the cause of ESRD (diabetic or nondiabetic). However, nonresponders had a similar distribution of *MCP1* polymorphic variants to healthy subjects, which indicates that *MCP1* polymorphism does not contribute significantly to the responsiveness to hepatitis B vaccination in HD patients, at least in those having primary renal diseases or type 2 diabetes as a cause of ESRD.

In the largest groups (all HD responders and nondiabetic HD responders), there was a deviation from the HWE in the observed *MCP1* genotype frequencies compared with the expected ones. Such a lack of consistency with the HWE was also shown in the group of HD patients in the study by Buraczyńska et al.[7] We can explain the deviation from the HWE by variability in the causes of ESRD and existence of comorbidities in both these groups. Associations of *MCP1* polymorphic variants with many pathological conditions have been demonstrated, which are frequently present also in HD patients: CVD[7] (including coronary artery disease,[49] myocardial infarction,[50] and ischemic stroke[7]) carpal tunnel syndrome,[14] HBV clearance,[15] progression of renal disease in immunoglobulin A nephropathy,[51] metabolic syndrome,[52] and diabetes.[19-22] On the other hand, there have also been studies that failed to show associations between *MCP1* –2518 A/G and coronary artery disease[53] or myocardial infarction.[54] Recently, it has been suggested that the -2518 A/G polymorphism in *MCP1* would be a risk factor for tuberculosis.[41,42,45,55] HD patients in our study had no acute tuberculosis during the study period, but 4 responders had tuberculosis in the past. There have also been reports on associations of *MCP1* polymorphism with lupus nephritis,[56] psoriasis,[57] and hypertension.[58] Despite efforts to obtain a relatively homogenous HD group, patients differed in the causes of ESRD, which may result in a deviation of their genotypes from the HWE, especially that a consistency with the HWE was shown for *MCP1* polymorphic variants in healthy controls and diabetic HD group.

Diabetes is the main cause of ESRD requiring RRT. In the Hemodialysis (HEMO) Study, the group of HD patients comprised approximately 45% of diabetic subjects.[18] In our previous study, among HD nonresponders to hepatitis B vaccination, the number of diabetic subjects was higher by over 12% compared with the group of responders.[28] The current study showed that responsiveness to hepatitis B vaccination in the diabetic group was lower by 32.4% than that in

TABLE 4 Distribution of *MCP1* rs1024611 polymorphic variants in hemodialyed nonresponders and responders

Genotype	Nonresponders (frequency)	Responders (frequency)	Odds ratio (95% CI)	2-tailed *P*	P_{trend}	$P_{genotyping}$	Power, %
all HD cases							
	n = 153	n = 601					
AA	65 (0.42)	284 (0.47)	referent	–	0.139	0.253	–
AG	73 (0.48)	279 (0.46)	1.143 (0.774–1.690) 1.167 (0.791–1.722)	0.543 0.435[a]	–	–	10.8
GG	15 (0.10)	38 (0.07)	1.725 (0.828–3.437) 1.289 (0.903–1.838)	0.151 0.160[a]	–	–	57.7
AG+GG	88 (0.57)	317 (0.53)	1.213 (0.835–1.767) 1.223 (0.842–1.777)	0.334 0.290[a]	–	–	17.4
MAF	103 (0.34)	355 (0.29)	1.211 (0.916–1.593)	0.184	–	–	27.9
HD cases without diabetes							
	n = 106	n = 426					
AA	44 (0.42)	201 (0.47)	referent	–	0.127	0.202	
AG	52 (0.49)	203 (0.48)	1.170 (0.731–1.878) 1.238 (0.775–1.977)	0.564 0.370[a]	–	–	9.0
GG	10 (0.09)	22 (0.05)	2.076 (0.815–4.953) 1.475 (0.943–2.306)	0.131 0.087[a]	–	–	39.0
AG+GG	62 (0.58)	225 (0.53)	1.259 (0.801–1.988) 1.321 (0.842–2.071)	0.347 0.224[a]	–	–	16.8
MAF	72 (0.34)	247 (0.29)	1.260 (0.900–1.753)	0.185	–	–	28.2
HD cases with diabetes							
	n = 47	n = 175					
AA	21 (0.45)	83 (0.47)	referent	–	0.691	0.923	
AG	21 (0.45)	76 (0.43)	1.092 (0.522–2.285) 1.001 (0.492–2.057)	0.935 0.986[a]	–	–	4.3
GG	5 (0.11)	16 (0.09)	1.235 (0.317–4.073) 1.154 (0.614–2.172)	0.907 0.652[a]	–	–	5.8
AG+GG	26 (0.55)	92 (0.53)	1.117 (0.557–2.258) 1.002 (0.525–1.913)	0.866 0.995[a]	–	–	5.7
MAF	31 (0.33)	108 (0.31)	1.103 (0.653–1.834)	0.782	–	–	6.3

a adjusted for sex, age, duration of renal replacement therapy, and chronic glomerulonephritis

Abbreviations: see **TABLE 2**

TABLE 5 Distribution of *MCP1* rs1024611 polymorphic variants in hemodialysis responders with or without diabetes

Genotype	HD cases with diabetes (frequency), n = 175	HD cases without diabetes (frequency), n = 426	Odds ratio (95% CI)	2-tailed *P*	P_{trend}	$P_{genotyping}$	Power, %
AA	83 (0.47)	201 (0.47)	referent	–	0.493	0.167	
AG	76 (0.43)	203 (0.48)	0.907 (0.617–1.331) 0.893 (0.611–1.307)	0.668 0.561[a]	–	–	7.9
GG	16 (0.09)	22 (0.05)	1.761 (0.819–3.707) 1.358 (0.947–1.947)	0.157 0.095[a]	–	–	33.3
AG+GG	92 (0.53)	225 (0.53)	0.990 (0.685–1.431) 0.977 (0.680–1.404)	1.000 0.900[a]	–	–	4.8
MAF	108 (0.31)	247 (0.29)	1.093 (0.825–1.444)	0.564	–	–	9.4

a adjusted for sex, age, and duration of renal replacement therapy

Abbreviations: see **TABLE 2**

TABLE 6 Distribution of *MCP1* rs1024611 polymorphic variants in hemodialysed nonresponders with or without diabetes

Genotype	HD cases with diabetes (frequency), n = 47	HD cases without diabetes (frequency), n = 106	Odds ratio (95% CI)	2-tailed *P*[a]	P_{trend}	$P_{genotyping}$	Power, %
AA	21 (0.45)	44 (0.42)	referent	–	0.862	0.880	
AG	21 (0.45)	52 (0.49)	0.874 (0.414–1.844)	0.722[a]	–	–	6.3
GG	5 (0.11)	10 (0.09)	1.203 (0.631–2.294)	0.568[a]	–	–	3.6
AG+GG	26 (0.55)	62 (0.58)	0.902 (0.442–1.838)	0.775[a]	–	–	5.1
MAF	31 (0.33)	72 (0.34)	0.957 (0.550–1.647)	0.975	–	–	4.6

a adjusted for sex, age, and duration of renal replacement therapy

Abbreviations: see **TABLE 2**

the nondiabetic group. However, the observed difference in responsiveness was not related to the *MCP1* –2518 G>A polymorphism.

We conclude that *MCP1* –2518 A/G (rs1024611) polymorphism is not associated with responsiveness to hepatitis B vaccination in HD patients, independently of whether they have diabetic nephropathy or primary renal disease as a cause of ESRD. Therefore, determination of the *MCP1* –2518 G>A polymorphism to explain nonresponsiveness to hepatitis B vaccination in HD patients seems not to be useful in clinical practice. Lack of significance of the *MCP1* –2518 G>A polymorphism in response to hepatitis B vaccination does not preclude its association with the development of anti-HBs in response to HBV infection. The involvement of the *MCP1* –2518 G>A polymorphism in the outcome of HBV infection still remains controversial,[15,16] and the issue requires further studies.

Supplementary material online Supplementary material is available at the journal's website at www.pamw.pl.

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REFERENCES

1 Murea M, Register TC, Divers J, et al. Relationships between serum MCP-1 and subclinical kidney disease: African American-Diabetes Heart Study. BMC Nephrol. 2012; 3: 148.

2 Suzuki E, Karam E, Williams S, et al. Fli-1 transcription factor affects glomerulonephritis development by regulating expression of monocyte chemoattractant protein-1 in endothelial cells in the kidney. Clin Immunol. 2012; 145: 201-208.

3 Ellina O, Chatzigeorgiou A, Kouyanou S, et al. Extracellular matrix-associated (GAGs, CTGF), angiogenic (VEGF) and inflammatory factors (MCP-1, CD40, IFN-γ) in type 1 diabetes mellitus nephropathy. Clin Chem Lab Med. 2012; 50: 167-174.

4 Uchida E, Anan F, Masaki T, et al. Monocyte chemoattractant protein-1 is associated with silent cerebral infarction in patients on haemodialysis. Intern Med J. 2012; 42: 29-34.

5 Morena M, Jaussent I, Chalabi L, et al. Biocompatibility of heparin-grafted hemodialysis membranes: impact on monocyte chemoattractant protein-1 circulating level and oxidative status. Hemodial Int. 2010; 14: 403-410.

6 Olsson J, Paulsson J, Dadfar E, et al. Monocyte and neutrophil chemotactic activity at the site of interstitial inflammation in patients on high-flux hemodialysis or hemodiafiltration. Blood Purif. 2009; 28: 47-52.

7 Buraczyńska M, Bednarek-Skublewska A, Buraczyńska K, et al. Monocyte chemoattractant protein-1 (MCP-1) gene polymorphism as a potential risk factor for cardiovascular disease in hemodialyzed patients. Cytokine. 2008; 44: 361-365.

8 Papayianni A, Alexopoulos E, Giamalis P, et al. Circulating levels of ICAM-1, VCAM-1, and MCP-1 are increased in haemodialysis patients: association with inflammation, dyslipidaemia, and vascular events. Nephrol Dial Transplant. 2002; 17: 435-441.

9 Meng ZF, Wang HJ, Yao X, et al. Immunization with HBsAg-Fc fusion protein induces a predominant production of Th1 cytokines and reduces HBsAg level in transgenic mice. Chin Med J (Engl). 2012; 125: 3266-3272.

10 Fierro NA, Roman S, Realpe M, et al. Multiple cytokine expression profiles reveal immune-based differences in occult hepatitis B genotype H-infected Mexican Nahua patients. Mem Inst Oswaldo Cruz. 2011; 106: 1007-1013.

11 Grzegorzewska AE, Kaczmarek-Leki V, Młot-Michalska M, Niepolski L. Seroconversion rate to positivity for antibodies against core antigen of hepatitis B virus and duration of renal replacement therapy. Nephrol Dial Transplant. 2011; 26: 970-976.

12 Rovin BH, Lu L, Saxena R. A novel polymorphism in the MCP-1 gene regulatory region that influences MCP-1 expression. Biochem Biophys Res Commun. 1999; 259: 344-348.

13 Fenoglio C, Galimberti D, Lovati C, et al. MCP-1 in Alzheimer's disease patients: A -2518G polymorphism and serum levels. Neurobiol Aging. 2004; 25: 1169-1173.

14 Omori K, Kazama JJ, Song J, et al. Association of the MCP-1 gene polymorphism A-2518G with carpal-tunnel syndrome in hemodialysis patients. Amyloid. 2002; 9: 175-182.

15 Park BL, Kim YJ, Cheong HS, et al. Association of common promoter polymorphisms of MCP1 with hepatitis B virus clearance. Exp Mol Med. 2006; 38: 694-702.

16 Cheong JY, Cho SW, Choi JY, et al. RANTES, MCP-1, CCR2, CCR5, CXCR1 and CXCR4 gene polymorphisms are not associated with the outcome of hepatitis B virus infection: results from a large scale single ethnic population. J Korean Med Sci. 2007; 22: 529-535.

17 Polakowska M, Piotrowski W. Incidence of diabetes in the Polish population: results of the Multicenter Polish Population Health Status Study – WOBASZ. Pol Arch Med Wewn. 2011; 121:156-163.

18 Sattar A, Argyropoulos C, Weissfeld L, et al. All-cause and cause-specific mortality associated with diabetes in prevalent hemodialysis patients. BMC Nephrol. 2012; 13: 130.

19 Karadeniz M, Erdogan M, Cetinkalp S, et al. Monocyte chemoattractant protein-1 (MCP-1) 2518G/A gene polymorphism in Turkish type 2 diabetes patients with nephropathy. Endocrine. 2010; 37: 513-517.

20 Simeoni E, Hoffmann MM, Winkelmann BR, et al. Association between the A-2518G polymorphism in the monocyte chemoattractant protein-1 gene and insulin resistance and Type 2 diabetes mellitus. Diabetologia. 2004; 47: 1574-1580.

21 Yang B, Houlberg K, Millward A, Demaine A. Polymorphisms of chemokine and chemokine receptor genes in Type 1 diabetes mellitus and its complications. Cytokine. 2004, 26: 114-121.

22 Zhang Y, Zhang J, Tian C, et al. The -2518A/G polymorphism in the monocyte chemoattractant protein-1 (MCP-1) gene and diabetes risk: a meta-analysis. Diabetes Res Clin Pract. 2011; 94: e89-92.

23 Alavian SM, Tabatabaei SV. The effect of diabetes mellitus on immunological response to hepatitis B virus vaccine in individuals with chronic kidney disease: A meta-analysis of current literature. Vaccine. 2010; 28: 3773-3777.

24 Grzegorzewska AE, Ratajewska A, Wiesiołowska A. Echocardiographic indices in hemodialysis patients in a six-month observation. Adv Clin Exp Med. 2011; 20: 431-440.

25 Ratajewska A, Grzegorzewska AE, Wiesiołowska A. [Dilatation of the left atrium as one of the indicators of worse prognosis in patients treated with intermittent hemodialysis]. Pol Merkur Lekarski. 2012; 33: 64-69. Polish.

26 Mostowska M, Lianeri M, Oko A, et al. No association of monocyte chemoattractant protein-1 22518 A/G polymorphism with the risk of primary glomerulonephritis in the Polish population. Mol Biol Rep. 2012; 39: 5933-5941.

27 PS: Power and Sample Size Calculation http://biostat.mc.vanderbilt.edu/twiki/bin/view/main/powersamplesize. Accessed August, 2013.

28 Venkat-Raman G, Tomson CR, Gao Y, et al. New primary renal diagnosis codes for the ERA-EDTA. Nephrol Dial Transplant. 2012; 27: 4414-4419.

29 Grzegorzewska AE, Wobszal P, Mostowska A, et al. Antibodies to hepatitis B virus surface antigen and interleukin 12 and interleukin 18 gene polymorphisms in hemodialysis patients. BMC Nephrol. 2012; 13: 75.

30 Grzegorzewska AE, Wobszal P, Jagodzinski PP. Interleukin-18 promoter polymorphism and development of antibodies to surface antigen of hepatitis B virus in hemodialysis patients. Kidney Blood Press Res. 2012; 35: 1-8.

31 Grzegorzewska AE, Pajzderski D, Sowińska A, et al. IL4R and IL13 polymorphic variants and development of antibodies to surface antigen of hepatitis B virus in hemodialysis patients in response to HBV vaccination or infection. Vaccine. 2013; 31: 1766-1770.

32 Lin YJ, Lan YC, Huang YC, et al. Effects of cytokine and cytokine receptor gene variation on high anti-HB titers: following up on Taiwan's neonatal hepatitis B immunization program. Clin Chim Acta. 2012; 413: 1194-1198.

33 Lin YJ, Lan YC, Wan L, et al. Serological surveillance and IL-10 genetic variants on anti-HBs titers: hepatitis B vaccination 20 years after neonatal immunization in Taiwan. Clin Chim Acta. 2011; 412: 766-773.

34 Wang C, Tang J, Song W, et al. HLA and cytokine gene polymorphisms are independently associated with responses to hepatitis B vaccination. Hepatology. 2004; 39: 978-988.

35 Girndt M, Sester U, Sester M, et al. The interleukin-10 promoter genotype determines clinical immune function in hemodialysis patients. Kidney Int. 2001; 60: 2385-2391.

36 Höhler T, Reuss E, Freitag CM, Schneider PM. A functional polymorphism in the IL-10 promoter influences the response after vaccination with HBsAg and hepatitis A. Hepatology. 2005; 42: 72-76.

37 Yucesoy B, Sleijffers A, Kashon M, et al. IL-1beta gene polymorphisms influence hepatitis B vaccination. Vaccine. 2002; 20: 3193-3196.

38 Chen J, Liang Z, Lu F, et al. Toll-like receptors and cytokines/cytokine receptors polymorphisms associate with non-response to hepatitis B vaccine. Vaccine. 2011; 29: 706-711.

39 Sleijffers A, Yucesoy B, Kashon M, et al. Cytokine polymorphisms play a role in susceptibility to ultraviolet B-induced modulation of immune responses after hepatitis B vaccination. J Immunol. 2003; 170: 3423-3428.

40 Hennig BJ, Fielding K, Broxholme J, et al. Host genetic factors and vaccine-induced immunity to hepatitis B virus infection. PLoS One. 2008; 3: e1898.

41 Flex A, Gaetani E, Papaleo P, et al. Proinflammatory genetic profiles in subjects with history of ischemic stroke. Stroke. 2004; 35: 2270-2275.

42 Ben-Selma W, Harizi H, Boukadida J. MCP-1 -2518 A/G functional polymorphism is associated with increased susceptibility to active pulmonary tuberculosis in Tunisian patients. Mol Biol Rep. 2011; 38: 5413-5419.

43 Flores-Villanueva PO, Ruiz-Morales JA, Song CH, et al. A functional promoter polymorphism in monocyte chemoattractant protein-1 is associated with increased susceptibility to pulmonary tuberculosis. J Exp Med. 2005; 202: 1649-1658.

44 Möller M, Nebel A, Valentonyte R, et al. Investigation of chromosome 17 candidate genes in susceptibility to TB in a South African population. Tuberculosis (Edinb). 2009; 89: 189-194.

45 Szalai C, Duba J, Prohászka Z, et al. Involvement of polymorphisms in the chemokine system in the susceptibility for coronary artery disease (CAD). Coincidence of elevated Lp(a) and MCP-1 -2518 G/G genotype in CAD patients. Atherosclerosis. 2001; 158: 233-239.

46 Xu ZE, Xie YY, Chen JH, et al. [Monocyte chemotactic protein-1 gene polymorphism and monocyte chemotactic protein-1 expression in Chongqing Han children with tuberculosis]. Zhonghua Er Ke Za Zhi. 2009; 47: 200-203. Chinese.

47 Nahar K, Jahan M, Nessa A, Tabassum S. Antibody responses after hepatitis B vaccination among maintenance haemodialysis patients. Bangladesh Med Res Counc Bull. 2011; 37: 88-91.

48 Mitchell LA, Henderson AJ, Dow SW. Suppression of vaccine immunity by inflammatory monocytes. J Immunol. 2012; 189: 5612-5621.

49 Lin HL, Ueng KC, Hsieh YS, et al. Impact of MCP-1 and CCR-2 gene polymorphisms on coronary artery disease susceptibility. Mol Biol Rep. 2012; 39: 9023-9030.

50 El Mahgoub IR, Afify RA, Aal AA, Beda DG. Association between the monocyte chemoattractant protein-1 -2518G/A gene polymorphism and acute myocardial infarction patients among Egyptian population. Blood Coagul Fibrinolysis. 2011; 22: 7-13.

51 Mori H, Kaneko Y, Narita I, et al. Monocyte chemoattractant protein-1 A-2518G gene polymorphism and renal survival of Japanese patients with immunoglobulin A nephropathy. Clin Exp Nephrol. 2005; 9: 297-303.

52 Kaur S, Panicker SR, James T, et al. Association of monocyte chemoattractant protein-1 -2518 polymorphism with metabolic syndrome in a South Indian cohort. Metab Syndr Relat Disord. 2009; 7: 193-198.

53 Zhong C, Luzhan Z, Genshan M, et al. Monocyte chemoattractant protein-1-2518 G/A polymorphism, plasma levels, and premature stable coronary artery disease. Mol Biol Rep. 2010; 37: 7-12.

54 Cermakova Z, Petrkova J, Arakelyan A, et al. The MCP-1 -2518 (A to G) single nucleotide polymorphism is not associated with myocardial infarction in the Czech population. Int J Immunogenet. 2005; 32: 315-318.

55 Zhang Y, Zhang J, Zeng L, et al. The -2518A/G polymorphism in the MCP-1 gene and tuberculosis risk: a meta-analysis. PLoS One. 2012; 7: e38918.

56 Tucci M, Barnes EV, Sobel ES, et al. Strong association of a functional polymorphism in the monocyte chemoattractant protein 1 promoter gene with lupus nephritis. Arthritis Rheum. 2004; 50: 1842-1849.

57 Wang L, Yang L, Gao L, et al. A functional promoter polymorphism in monocyte chemoattractant protein-1 is associated with psoriasis. Int J Immunogenet. 2008; 35: 45-49.

58 Jemaa R, Ben Ali S, Kallel A, et al. Association between the -2518G/A polymorphism in the monocyte chemoattractant protein-1 (MCP-1) gene and hypertension in Tunisian patients. Clin Biochem. 2009; 42: 34-37.

SUPPLEMENTARY DATA

TABLE S1 Distribution of *MCP1* rs1024611 genotypes in hemodialysis patients depending on the Hardy–Weinberg equilibrium

MCP1 rs1024611 genotype frequencies	All HD cases		HD cases without diabetes		HD cases with diabetes	
	observed	expected	observed	expected	observed	expected
responders to hepatitis B vaccine (n = 601)						
AA	284 (0.47)	298 (0.50)	201 (0.47)	215 (0.50)	83 (0.47)	84 (0.48)
AG	279 (0.46)	250 (0.41)	203 (0.48)	175 (0.41)	76 (0.43)	75 (0.43)
GG	38 (0.07)	52(0.09)	22 (0.05)	36 (0.09)	16 (0.09)	17 (0.09)
P value[a]	0.005		0.001		0.814	
nonresponders to hepatitis B vaccine (n = 153)						
AA	65 (0.42)	67 (0.44)	44 (0.42)	46 (0.44)	21 (0.45)	21 (0.45)
AG	73 (0.48)	68 (0.45)	52 (0.49)	48 (0.45)	21 (0.45)	21 (0.44)
GG	15 (0.10)	17 (0.11)	10 (0.09)	12 (0.11)	5 (0.11)	5 (0.11)
P value[a]	0.398		0.335		0.941	

a for deviation from the Hardy–Weinberg equilibrium

Abbreviations: HD – hemodialysis

TABLE S2 Distribution of *MCP1* rs1024611 polymorphic variants in hemodialysis patients, diabetic hemodialysis patients, and nondiabetic hemodialysis patients compared with respective genotype frequencies in controls

Genotype	HD patients (frequency)	Controls (frequency)	Odds ratio (95% CI)	2-tailed *P*	P_{trend}	$P_{genotyping}$	Power, %
all HD cases vs. controls							
	n = 754	n = 437					
AA	349 (0.46)	225 (0.51)	referent	–	0.260	0.117	–
AG	352 (0.47)	177 (0.41)	1.282 (0.995–1.653)	0.055	–	–	52.9
GG	53 (0.07)	35 (0.08)	0.976 (0.603–1.595)	1.000	–	–	4.8
AG+GG	405 (0.54)	212 (0.49)	1.232 (0.96 561.570)	0.096	–	–	40.0
MAF	458 (0.30)	247 (0.28)	1.107 (0.918–1.337)	0.298	–	–	18.4
HD cases without diabetes vs. controls							
	n = 532	n = 437					
AA	245 (0.46)	225 (0.51)	referent	–	0.388	0.055	–
AG	255 (0.48)	177 (0.41)	1.323 (1.008–1.738)	0.043	–	–	56.3
GG	32 (0.06)	35 (0.08)	0.840 (0.486–1.448)	0.590	–	–	13.8
AG+GG	287 (0.54)	212 (0.49)	1.243 (0.957–1.615)	0.105	–	–	37.5
MAF	319 (0.30)	247 (0.28)	1.087 (0.888–1.331)	0.436	–	–	12.6
HD cases with diabetes vs. controls							
	n = 222	n = 437					
AA	104 (0.47)	225 (0.51)	referent	–	0.250	0.507	–
AG	97 (0.44)	177 (0.41)	1.186 (0.832–1.689)	0.370	–	–	16.8
GG	21 (0.09)	35 (0.08)	1.298 (0.682–2.421)	0.470	–	–	19.7
AG+GG	118 (0.53)	212 (0.49)	1.204 (0.860–1.687)	0.297	–	–	19.8
MAF	139 (0.31)	247 (0.28)	1.157 (0.894–1.494)	0.278	–	–	20.9

Abbreviations: CI – confidence interval, MAF – minor allele frequency, others – see TABLE S1

TABLE S3 Distribution of *MCP1* rs1024611 polymorphic variants in hemodialysis patients with or without diabetes

Genotype	HD cases with diabetes (frequency), n = 222	HD cases without diabetes (frequency), n = 532	Odds ratio (95% CI)	2-tailed *P*	P_{trend}	$P_{genotyping}$	Power, %
AA	104 (0.47)	245 (0.46)	referent	–	0.290	0.195	–
AG	97 (0.44)	255 (0.48)	0.896 (0.637–1.260) 0.903 (0.646–1.263)	0.567 0.552[a]	–	–	8.6
GG	21 (0.09)	32 (0.06)	1.546 (0.806–2.911) 1.269 (0.933–1.727)	0.203 0.127[a]	–	–	12.1
AG+GG	118 (0.53)	287 (0.54)	0.968 (0.699–1.343) 0.973 (0.707–1.339)	0.904 0.865[a]	–	–	4.8
MAF	139 (0.31)	319 (0.30)	1.064 (0.830–1.361)	0.652	–	–	7.6

a adjusted for sex, age, and duration of renal replacement therapy

Abbreviations: see TABLES S1 and S2

TABLE S4 Demographic and clinical data in hemodialysis patients (n = 754) divided according to the genotypes of *MCP1* rs1024611

Parameter	AA, n = 349	AG, n = 352	GG, n = 53	*P* value between all groups
male sex, n (%)	217 (62.2)	197 (56.0)	25 (47.2)	0.059[a]
age, y	64 (17.4–93.1)	64.8 (17–91.7)	61.7 (17.9–87)	0.911[b]
diabetic nephropathy, n (%)	104 (29.9)	97 (27.6)	21 (39.6)	0.200[a]
chronic glomerulonephritis, n (%)	49 (14.1)	45 (12.8)	8 (15.1)	0.839[a]
hypertensive nephropathy, n (%)	67 (19.2)	69 (19.7)	11 (20.7)	0.965[a]
chronic tubulointerstitial nephritis, n (%)	37 (10.6)	31 (8.8)	8 (15.1)	0.330[a]
polycystic kidney disease, n (%)	23 (6.6)	22 (6.2)	3 (5.7)	0.960[a]
RRT vintage, y	2.1 (0.05–19.1)	2.3 (0.003–26.1)	1.8 (0.04–22.7)	0.776[b]

a χ^2 test
b Kruskal–Wallis test

Abbreviations: RRT – renal replacement therapy

TABLE S5 Distribution of *MCP1* rs1024611 polymorphic variants in hemodialysis nonresponders without or with severe immunocompromise diseases compared with controls

Genotype	Nonresponders (frequency)	Controls (frequency)	Odds ratio (95% CI)	2-tailed *P*	P_{trend}	$P_{genotyping}$	Power, %
HD nonresponders without severe immunocompromise diseases vs. controls							
	n = 133	n = 437					
AA	59 (0.44)	225 (0.51)	referent	–	0.130	0.315	–
AG	60 (0.45)	177 (0.41)	1.293 (0.840–1.989)	0.261	–	–	24.5
GG	14 (0.11)	35 (0.08)	1.525 (0.709–3.134)	0.303	–	–	34.3
AG+GG	74 (0.56)	212 (0.49)	1.331 (0.885–2.007)	0.180	–	–	29.4
MAF	88 (0.33)	247 (0.28)	1.255 (0.922–1.700)	0.153	–	–	31.4
HD nonresponders with severe immunocompromise diseases vs. controls							
	n = 20	n = 437					
AA	6 (0.30)	225 (0.51)	referent	–	0.203	0.094	–
AG	13 (0.65)	177 (0.41)	2.754 (0.951–8.999)	0.064	–	–	53.6
GG	1 (0.05)	35 (0.08)	1.071 (0.023–9.246)	1.000	–	–	3.63
AG+GG	14 (0.70)	212 (0.49)	2.476 (0.873–7.997)	0.097	–	–	43.4
MAF	15 (0.38)	247 (0.28)	1.523 (0.733–3.061)	0.279	–	–	22.5

Abbreviations: see TABLES 1 and 2

TABLE S6 Comparison of *MCP1* –2518 A>G polymorphism between the healthy population of different countries and ethnicity and our controls

Studies in controls	Country	Ethnicity	*MCP1* –2518 A>G rs1024611			P_{trend}
			AA	AG	GG	
Mostowska et al.[1]	Poland (Wielkopolska)	Caucasian	225 (0.51)	177 (0.41)	35 (0.08)	referent
Ben-Selma et al.[2]	Tunisia	African	93 (0.62)	49 (0.33)	8 (0.05)	0.029
Buraczyńska et al.[3]	Poland (Lubelskie)	Caucasian	209 (0.64)	101 (0.31)	15 (0.05)	0.0004
Flex et al.[4]	Italy	Caucasian	124 (0.56)	87 (0.39)	12 (0.05)	0.211
Flores-Villanueva et al.[5]	Korea	Asian	66 (0.41)	74 (0.46)	22 (0.13)	0.007
Karadeniz et al.[6]	Turkey	Caucasian	49 (0.47)	44 (0.42)	12 (0.11)	0.274
Möller et al.[7]	South Africa	South African colored	270 (0.56)	173 (0.36)	38 (0.08)	0.277
Simeoni et al.[8]	Germany	Caucasian	1335 (0.52)	1043 (0.41)	190 (0.07)	0.742
Szalai et al.[9]	Hungary	Caucasian	186 (0.58)	115 (0.36)	19 (0.06)	0.060
Xu et al.[10]	China	Asian	41 (0.41)	45 (0.45)	14 (0.14)	0.026
Yang et al.[11]	United Kingdom	Caucasian	36 (0.35)	60 (0.58)	8 (0.07)	0.019

REFERENCES

1 Mostowska M, Lianeri M, Oko A, et al. No association of monocyte chemoattractant protein-1 22518 A/G polymorphism with the risk of primary glomerulonephritis in the Polish population. Mol Biol Rep. 2012; 39: 5933-5941.

2 Ben-Selma W, Harizi H, Boukadida J. MCP-1 -2518 A/G functional polymorphism is associated with increased susceptibility to active pulmonary tuberculosis in Tunisian patients. Mol Biol Rep. 2011; 38: 5413-5419.

3 Buraczyńska M, Bednarek-Skublewska A, Buraczyńska K, Książek A. Monocyte chemoattractant protein-1 (MCP-1) gene polymorphism as a potential risk factor for cardiovascular disease in hemodialyzed patients. Cytokine. 2008; 44: 361-365.

4 Flex A, Gaetani E, Papaleo P, et al. Proinflammatory genetic profiles in subjects with history of ischemic stroke. Stroke. 2004; 35: 2270-2275.

5 Flores-Villanueva PO, Ruiz-Morales JA, Song CH, et al. A functional promoter polymorphism in monocyte chemoattractant protein-1 is associated with increased susceptibility to pulmonary tuberculosis. J Exp Med. 2005; 202: 1649-1658.

6 Karadeniz M, Erdogan M, Cetinkalp S, et al. Monocyte chemoattractant protein-1 (MCP-1) 2518G/A gene polymorphism in Turkish type 2 diabetes patients with nephropathy. Endocrine. 2010; 37: 513-517.

7 Möller M, Nebel A, Valentonyte R, et al. Investigation of chromosome 17 candidate genes in susceptibility to TB in a South African population. Tuberculosis (Edinb). 2009; 89: 189-194.

8 Simeoni E, Hoffmann MM, Winkelmann BR, et al. Association between the A-2518G polymorphism in the monocyte chemoattractant protein-1 gene and insulin resistance and Type 2 diabetes mellitus. Diabetologia. 2004; 47: 1574-1580.

9 Szalai C, Duba J, Prohászka Z, et al. Involvement of polymorphisms in the chemokine system in the susceptibility for coronary artery disease (CAD). Coincidence of elevated Lp(a) and MCP-1 -2518 G/G genotype in CAD patients. Atherosclerosis. 2001; 158: 233-239.

10 Xu ZE, Xie YY, Chen JH, et al. [Monocyte chemotactic protein-1 gene polymorphism and monocyte chemotactic protein-1 expression in Chongqing Han children with tuberculosis]. Zhonghua Er Ke Za Zhi. 2009; 47: 200-203. Chinese.

11 Yang B, Houlberg K, Millward A, Demaine A. Polymorphisms of chemokine and chemokine receptor genes in Type 1 diabetes mellitus and its complications. Cytokine. 2004, 26: 114-121.

ARTYKUŁ ORYGINALNY

Polimorfizm białka chemotaktycznego dla monocytów typu 1 (*MCP1* –2518 A/G) a odpowiedź na szczepienie przeciwko wirusowemu zapaleniu wątroby typu B u chorych hemodializowanych

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SŁOWA KLUCZOWE

białko chemotaktyczne dla monocytów 1, cukrzyca, hemodializa, *MCP1* –2518 A/G rs1024611, szczepienie przeciwko wirusowemu zapaleniu wątroby typu B

STRESZCZENIE

WPROWADZENIE Białko chemotaktyczne dla monocytów 1 (MCP-1) uczestniczy w patogenezie chorób nerek, cukrzycy, a także zakażenia wirusem zapalenia wątroby typu B (*hepatitis B virus* – HBV).

CELE Celem badania była ocena dystrybucji wariantów polimorficznych *MCP1* –2518 A/G (rs1024611) u chorych poddawanych hemodializie (HD) w odniesieniu do stwierdzonej u nich odpowiedzi na szczepienie przeciwko wirusowemu zapaleniu wątroby typu B.

PACJENCI I METODY Chorzy leczeni HD, nigdy niezakażeni HBV, zostali zakwalifikowani do badania po przeprowadzeniu odpowiedniego szczepienia przeciwko wirusowemu zapaleniu wątroby typu B. Grupa leczonych HD składała się z 601 osób, które odpowiedziały na szczepienie wytworzeniem miana anty-HBs >10 IU/l uważanego za ochronne, i 153 osób, u których nie wystąpiła adekwatna odpowiedź poszczepienna (anti-HBs ≤10 IU/l). Wśród chorych, którzy odpowiedzieli na szczepienie, było 175 chorych na cukrzycę, a wśród chorych z brakiem adekwatnej odpowiedzi poszczepiennej – 47 chorych na cukrzycę. Osoby zdrowe stanowiły grupę kontrolną (n = 437). Genotypowanie *MCP1* wykonano przy użyciu łańcuchowej reakcji polimerazy–polimorfizmu długości fragmentów restrykcyjnych.

WYNIKI Częstości występowania wariantów polimorficznych *MCP1* rs1024611 w grupie kontrolnej były następujące: 51% AA, 41% AG, 8% GG. Nie wykazano istotnych różnic (p >0,05) w dystrybucji genotypów *MCP1* między żadną z badanych grup leczonych HD a kontrolną, niezależnie od występowania cukrzycy i odpowiedzi na szczepienie. Grupy leczone HD wyodrębnione na podstawie występowania cukrzycy lub rodzaju odpowiedzi na szczepienie nie różniły się pod względem dystrybucji genotypów *MCP1*.

WNIOSKI U chorych leczonych HD polimorfizm *MCP1* –2518 A/G nie jest powiązany z odpowiedzią na szczepienie przeciwko zakażeniu HBV, niezależnie od występowania cukrzycy lub nie.

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