DISTRIBUTION OF MONOCYTE CHEMOATTRACTANT PROTEIN-1 (*MCP1*) -2518 A/G POLYMORPHISM IN HEMODIALYSIS (HD) PATIENTS COMPARED TO CONTROLS

Alicja E. Grzegorzewska 1, Dominik Pajzderski 1, Anna Sowińska 2 and Paweł P. Jagodziński 3

1, Department of Nephrology, Transplantology and Internal Diseases, University of Medical Sciences, Poznań, Poland, 2, Department of Computer Science, University of Medical Sciences, Poznań, Poland and 3, Department of Biochemistry and Molecular Biology, University of Medical Sciences, Poznań, Poland

Objectives:

MCP-1 is a multifunctional cytokine which is reported to play a role in the pathogenesis of renal diseases and diabetes mellitus (DM), but also in outcome of hepatitis B virus (HBV) infection, tuberculosis, and development of carpal tunnel syndrome. Our aim was to compare distribution of *MCP1* -2518 A/G (rs1024611) polymorphic variants in HD patients free from HBV infection and successfully vaccinated against HBV with respective genotype frequencies in healthy volunteers. Possible associations between *MCP1* -2518 A/G genotypes and type 2 DM as a cause of ESRD were also explored.

Methods:

Patients

Unrelated HD patients were enrolled into the study when they
a) 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,
b) developed antibodies to HBsAg (anti-HBs) considered as protective (>10 IU/L) in response to hepatitis B vaccination.

Controls

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 (rs1024611) polymorphic variants in patients suffering from primary glomerulonephritis and healthy individuals [3].
All examined subjects were Caucasian race.

Carpal tunnel syndrome was not present in any case. None of patients had a history of tuberculosis. Patients were not selected by an occurrence of CVD, because it was shown that diastolic cardiac dysfunction occurs in 93% of HD patients and progresses in the course of HD therapy [1, 2]. Therefore near all HD patients have more or less pronounced cardiac damage.

The HD group of hepatitis B vaccine responders was composed of 601 individuals and included 175 patients with type 2 DM.

Genotyping

MCP1 rs1024611 genotyping was determined by polymerase chain reaction-restriction fragment length polymorphism as previously described [3].

Ethical issues

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

Selected demographic and clinical data of diabetic and non-diabetic patients treated with hemodialysis

Responders to hepatitis B vaccine (n = 601)			
Parameter	Diabetics (n = 175)	Non-diabetics (n = 426)	P value
Men, n (% of all)	103 (58.9)	257 (60.3)	0.784[a]
Age, years	65.8 ± 12.8	60.0 ± 15.7	**<0.0001[b]**
RRT duration, years	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)	-

RRT – renal replacement therapy
a – Chi square test
b – Mann-Whitney test
c – the ERA-EDTA renal diagnosis codes [4]
Significant differences are indicated using bold font.

References

[1] Grzegorzewska AE, Ratajewska A, Wiesiołowska A: Adv Clin Exp Med 2011, 20:431-440.
[2] Ratajewska A, Grzegorzewska AE, Wiesiołowska A: Pol Merkur Lekarski 2012, 33:64-69.
[3] Mostowska M, Lianeri M, Oko A, Mostowska A, Jagodziński PP: Mol Biol Rep 2012, 39:5933–5941.
[4] Venkat-Raman G, Tomson CR, Gao Y, Cornet R, Stengel B, Gronhagen-Riska C, et al: 2012, 27:4414-4419.

Results:

The distribution of *MCP1* rs1024611 genotypes in groups of HD patients in respect to HWE

MCP1 rs1024611	All HD cases		HD cases without DM		HD cases with DM	
Genotype frequencies	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 for deviation from HWE	**0.005**		**0.001**		0.814	

The distribution of *MCP1* rs1024611 polymorphic variants in HD responders with or without DM; a - Adjusted for gender, age, and duration of renal replacement therapy

Genotype	HD cases with DM (frequency)	HD cases without DM (frequency)	Odds ratio (95%CI)	Two-tailed P	P_{trend}	$P_{genotyping}$	Power (%)
	n = 175	n = 426					
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

Comparison of the distribution of *MCP1* rs1024611 polymorphic variants in all hemodialysis (HD) responders and controls

Genotype	Responders (frequency)	Controls (frequency)	Odds ratio (95%CI)	Two-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 DM 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 DM 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

Conclusions:

HD patients, showing maintained immune responsiveness to hepatitis B vaccination, do not differ significantly in distribution of *MCP1* rs 1024611 polymorphic variants compared to healthy controls, independently whether they are diabetic or non-diabetic.