

Plasma Protein Polymorphism In HIV-Seropositive Patients: Gc- AND Tf*c-SUBTYPES AND PI-SYSTEM

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SUMMARY

The paper reports on the distribution of three plasma protein systems in serum samples from 99 HIV-seropositive patients: Gc-subtyping, Tfc-subtyping and Pi- (alpha₁-antitrypsin) system. In the Gc-system - as in further studies - we found evidence for non-association of Gc-subtypes - especially 1F - with HIV-infection. Also the distribution of Tfc-subtypes seems to be very similar to studies on healthy persons. In the Pi-system this pilot study led to the suspicion that the phenotype Pi*M2 is overrepresented. The distribution found in these patients is not comparable with the control group.

INTRODUCTION

In 1987 *Eales et al.* reported on a strong association between AIDS and the GC-system (D-binding protein). They suggested that individuals with the GC*1F subtype would be more at risk to develop AIDS. Also it was suggested that the homozygous type GC*2 may render a relative protection.

In the meantime in several reports this observation could not be confirmed.

However, *Eales's* report 'has created considerable concern'.

Such studies on fringe groups take the risk of 'small volume'. Therefore we decided to carry out an additional examination. Furthermore we included in this study the PI- (alpha₁-antitrypsin) and the TF- (transferrin) system.

MATERIALS & METHODS

Blood samples were taken from 99 patients of the Institute of Blood Coagulation and Transfusion Medicine at the *Heinrich-Heine-University*. For this pilot study we restricted us to only one marker: HIV-seropositive. Therefore the collective included individuals that were HIV-seropositive only, patients with ARC (AIDS related complex), with AIDS and with *Kaposi-sarcoma*.

Because not all patients lived in the Düsseldorf area we compared this group to other German studies on distribution. Our PI-control group includes 160 obviously healthy persons.

RESULTS AND DISCUSSION

GC-System Our examination also resulted in non-association between AIDS and GC. The distribution of GC-subtypes in our HIV-seropositive group is comparable to those found in obviously healthy individuals. We found the following gene frequencies: GC*1S .5808, GC*1F .1414 and GC*2 .2778. Adding these results to the data of the other authors we come to the conclusion that the suspicion of association between GC and AIDS can not be upheld. But in our opinion it has shurely not been disproved that with a normal risk of infection any one allele may give a relative protection of developing AIDS. In this study we restricted us to the one marker "HIV-seropositive. Other author's data - splitting HIV-seropositive only, ARC and AIDS - were taken on small groups. Therefore we plan extended examinations on further patients - sampling has already started - which includes splitting into subgroups of sufficient volumes.

TF-system Transferrin (D-binding protein) is an iron binding glycoprotein of the β -globulin fraction. Because of its binding capacity and transport function transferrin seems to play a part in immune reactions. The common six phenotypes are due to three codominant alleles TF*C1, TF*C2 and TF*C3. In this study we examined the distribution of TF*C subtypes of 99 HIV-seropositive individuals. We found only the common phenotypes. The observed values are similar to the expected values (calculated by gene counting). We found the following gene frequencies: TF*C1 .7374, TF*C2 .1616 and TF*C3 .1010. The results seem to be similar to those found in obviously healthy persons. The some what higher frequencies of the TF*C2 and TF*C3 alleles might be caused by the small volume of the collective. In our opinion the differences are not significant.

PI-system PI (α_1 -antitrypsin) is the most important protease inhibitor of the extracellular compartment. It is coded by chromosome 14. Being a glycoprotein (mol.weight 50.000) of the 'acute phase' in inflammatory processes it has its physiological function in inhibiting neutral proteases, especially in inactivating elastase. Since the first description of genetic variation development of specific methods led to the observation of more than 60 genetic variants. The common six PI*M phenotypes are due to the codominant alleles M1, M2 and M3. The PI*S and PI*Z alleles have lower frequencies (0.03 and 0.01 in whites).

The expression of specific alleles (S,Z I) can cause a decrease of the α_1 -antitrypsin serum concentration. This may have a significant effect on health, the development of hepato and pneumopathy is dependent on these serum concentration and tissue deposition of abnormal molecules. Also association between rarer alleles and rheumatism is discussed. *Erban* et al. found significant increased α_1 -antitrypsin levels in blood samples of psychiatric (schizophrenics) patients.

Table 1 PI-PHENOTYPES IN HIV-SEROPOSITIVE PATIENTS

Phenotype	observed		expected	
	n	%	n	%
M1	59	59.60	54.57	55.12
M2M1	15	15.15	25.99	26.25
M2	9	9.09	3.09	3.13
M3M2	2	2.02	2.30	2.32
M3	0	0	0.43	0.43
M3M1	11	11.11	9.66	9.76
M1-Var*	3	3.03	2.23	2.26
M2-Var	0	0	0.53	0.57
M3-Var	0	0	0.02	0.20
total**	99	100	99	100

*The following values contain variants including Pi S and Pi Z

** Values rounded up

Table 2 PI*M-PHENOTYPES IN THE CONTROL GROUP

Phenotype	observed		expected	
	n	%	n	%
M1	87	54.37	89.25	55.78
M2M1	39	24.38	35.85	22.40
M2	3	1.88	3.60	2.25
M3M2	3	1.88	4.35	2.72
M3	2	1.25	1.31	0.82
M3M1	22	13.75	21.65	13.53
M1Var*	4	2.50	2.99	1.87
M2Var	0	0	0.60	0.38
M3Var	0	0	0.36	0.27
Var	0	0	0.03	0.02
total**	160	100	160	100

*The following values contain variants including Pi S and Pi Z

**Values rounded up

Chi²: 1.611 (Chi²* 3.841; df=1; alpha=0.05)

To our knowledge association between AIDS and the PI-system has never been discussed. We included PI typing in this pilot study because of its function as an 'acute phase' protein. In 99 serum samples of HIV-seropositive patients we found 3 persons with the heterozygous phenotype Pi^*M1S , the others showed phenotypes due to the M allele only. The findings are shown in table 1. In our small collective we found insufficient correlations between the observed and expected values. Especially the homozygous PI^*M2 and the heterozygous PI^*M2M1 show a distribution which is not consistent with the *Hardy-Weinberg*-equilibrium. The homozygous PI^*M2 phenotype is overrepresented in this spot check. Comparison with the control group (tab.2) confirms these findings. Comparison with other studies on PI-polymorphism shows that the phenotype's distribution of the control group is similar to those found in other German regions.

In our opinion it is absurd trying to discuss hypothetical theories of possible association. First, one must think about the risk of 'small number'. On the other hand the deviation is statistically significant. Referring to the 'GC theory' there are no comparable differences between whites and blacks. At least all associations found between the PI-system and other specific diseases are due to deficiency alleles but not to the common PI^*M alleles.

Therefore we come to the conclusion that hasty attempts of explanation are not useful. However, the findings are statistically significant. Nevertheless the possibility of 'super chance' must be excluded by extended examinations on spot checks of sufficient number. One specific feature of our HIV-seropositive group - patients have been treated with 'autovaccination' couldn't - in our opinion - influence our results. Other characteristics like homosexuality etc. must be itemized in further extended studies.

REFERENCES

- See: Huckenbeck W, Bonte W, Kuntz BME, Brüster HTH (1989) *Plasmaprotein-Polymorphismen bei HIV-seropositiven Probanden: GC- und TF*C-Subtypen, PI-, C3- und BF-System*
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