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Genetic Markers in Alcoholism: No Association with HLA

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Summary. We carried out a study on 63 patients suffering from alcoholism in order to determine the frequency of 27 HLA antigens. In comparison to healthy blood donors no significant deviation of HLA distributions in alcoholics was found. The data on alcoholic patients with physical consequences such as cerebral seizures, liver cirrhosis and polyneuropathy failed to identify an assocation with HLA.

Key words: Alcoholism – Genetic marker – HLA

Zusammenfassung. In einer Populationsuntersuchung mit 63 Alkoholikern wurden 27 HLA Antigene hinsichtlich ihres Auftretens bestimmt. Im Vergleich zu gesunden Blutspendern ergaben sich keine signifikanten Differenzen der Antigenfrequenzen. Es konnten keine Assoziationen zwischen HLA und Alkoholkrankheit aufgedeckt werden. Im Verlauf von Alkoholismus auftretende Komplikationen wie Krampfanfälle, Leberzirrhose und Polyneuropathie waren nicht mit HLA assoziiert.

Schlüsselwörter: Alkoholismus – genetische Marker – HLA

1. Introduction

An approach to separating genetic factors from environmental factors is to study alcoholics with characteristics known to be inherited. The purpose of our investigation was to study the distribution of the human leucocyte antigens (HLA), as a genetic marker in alcoholics and to search for an association between HLA and susceptibility to alcoholism or its physical consequences. The HLA gene complex is located on the short arm of chromosome 6 and is frequently called the major histocompatibility complex of man. In addition to the importance in organ

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Table 1. Comparison of HLA distributions in alcoholics, patients with alcoholic first degree relatives and with controls

HLA	Controls $n=447$	Alcoholics $n=63$	Pat. with alc. relatives $n=20$	Corrected P
A1	27.1%	33.3%	40%	NS
A2	51.9%	42.9%	35%	
A3	26.6%	31.7%	30%	
A9	17.7%	19.0%	25%	
A10	11.2%	9.5%	10%	
A11	10.1%	1.6%	0%	
A28	6.7%	12.7%	10%	
A29	7.6%	1.6%	5%	
B5	12.3%	12.7%	4%	NS
B7	23.0%	17.5%	10%	
B8	15.9%	20.6%	10%	
B12	25.0%	27.0%	25%	
B13	6.7%	4.8%	5%	
B14	4.0%	4.8%	10%	
B15	12.3%	19.0%	25%	
B16	6.0%	3.2%	5%	
B17	9.6%	6.3%	10%	
B18	10.5%	6.3%	0%	
B21	6.5%	1.6%	0%	
B22	5.6%	1.6%	0%	
B27	4.7%	6.3%	5%	
B35	11.6%	9.5%	10%	
B37	3.6%	1.6%	5%	
B40	8.5%	9.5%	10%	
Cw2	9.6%	11.1%	10%	NS
Cw3	12.3%	19.0%	10%	
Cw4	19.0%	28.6%	40%	

transplantation, HLA is known to be associated with various diseases (review: Svejgaard et al. 1975). An extraordinary correlation of clinical value exists between HLA B27 and spondylitis deformans (Bechterew's disease).

In earlier studies we found evidence of an association between HLA B27 and a subgroup of schizophrenics with a family history of endogenous psychosis. Preliminary data of a schizoaffective sample suggest a positive association with HLA B7, while patients with endogenous major depressive disorders failed to identify an association with HLA (Giannitsis et al. 1982; Rösler et al. 1982; Rösler et al. 1983).

2. Subjects and Methods

The sample consisted of 63 patients, 43 men and 20 women, meeting criteria for a diagnosis of alcoholism (DSM III 1980). Ages ranged between 24 and 61 years (average: 40.7). All were inpatients participating in a treatment program and were tested after withdrawal symptoms subsided and medication was discontinued.

The patients were examined with regard to the signs of cerebral seizures, liver cirrhosis, polyneuropathy and alcoholism in first degree relatives. Results showed partly overlapping samples of 20 patients with alcoholism in first degree relatives, 21 patients with cerebral seizures, 14 patients with liver cirrhosis and 11 patients with polyneuropathy.

Histocompatibility antigen-typing of 27 HLA antigens of the loci A, B and C was performed using the method of Terasaki and McClelland (1964).

The HLA distributions were compared with a control group of 447 healthy blood donors. Only German individuals of our region were included in both samples. Differences were tested with Fisher's Exact Test or χ^2 test with and without correction for continuity in dependence of the sample size using SPSS 8 program CROSSTABS. The P values were multiplied by 27 (number of antigens tested) to correct for type-1-errors.

3. Results

In Table 1 alcoholics and patients with alcoholic first degree relatives were compared with the control sample. No finding approached statistical significance after P correction.

We found no correlation between HLA and the subgroups of patients with cerebral seizures, cirrhosis and polyneuropathy (Table 2).

No differences in HLA distributions existed between male and female alcoholics in comparison to controls.

Between HLA and alcoholism and its physical consequences we were unable to detect any correlation.

4. Discussion

Genetic marker studies in alcoholism have shown no consistent findings (Goodwin and Guze 1974). Cruz-Coke (1964) and Cruz-Coke and Varela (1966) found that alcoholism, cirrhosis of the liver and color vision defects were associated and suggested that a locus on the X chromosome could play a role in alcoholism. Later studies of Fialkow et al. (1966), Gorrel (1967) and Thuline (1967) failed to confirm the relation between color vision defects and alcoholism. No deviation in the frequencies of the blood group substances ABO was found in alcoholics. A significant increase in nonsecretors of salivary ABH blood group substances in alcoholics was found. The excess of nonsecretion was predominantly in subjects with blood group A (Camps and Dodd 1967; Camps et al. 1969; Swinson and Madden 1973).

Hill et al. (1975) found a significant difference between the prevalence of the S antigen in alcoholics and their nonalcoholic relatives.

In the present population study we found no evidence of an association between 27 HLA antigens of the loci A, B and C and alcoholism and its physical consequences. Our hypothesis of an association must be rejected.

Table 2. HLA distributions in patients with physical consequences of alcoholism

HLA	Controls $n=447$	Alc. with seizures $n=21$	Alc. with cirrhosis $n=14$	Alc. with polyneurop. $n=11$	Corrected P
A1	27.1%	38.1%	57.1%	36.4%	NS
A2	51.9%	42.9%	42.9%	54.5%	
A3	26.6%	33.3%	35.7%	45.5%	
A9	17.7%	23.8%	21.4%	18.2%	
A10	11.2%	9.5%	0.0%	0.0%	
A11	10.1%	0.0%	0.0%	0.0%	
A28	6.7%	14.3%	14.3%	9.1%	
A29	7.6%	0.0%	0.0%	0.0%	
B5	12.3%	4.8%	21.4%	18.2%	NS
B7	23.0%	4.8%	28.6%	9.1%	
B8	15.9%	28.6%	28.6%	36.4%	
B12	25.0%	33.3%	35.7%	9.1%	
B13	6.7%	9.5%	0.0%	0.0%	
B14	4.0%	0.0%	0.0%	0.0%	
B15	12.3%	19.0%	14.3%	9.1%	
B16	6.0%	4.8%	0.0%	0.0%	
B17	9.6%	4.8%	7.1%	0.0%	
B18	10.5%	9.5%	0.0%	9.1%	
B21	6.5%	4.8%	0.0%	0.0%	
B22	5.6%	0.0%	0.0%	0.0%	
B27	4.7%	0.0%	7.1%	0.0%	
B35	11.6%	19.0%	21.4%	9.1%	
B37	3.6%	4.8%	7.1%	0.0%	
B40	8.5%	19.0%	0.0%	18.2%	
Cw2	9.6%	4.8%	7.1%	9.1%	NS
Cw3	12.3%	23.8%	0.0%	9.1%	
Cw4	19.0%	19.0%	35.7%	27.3%	

The studies with genetic markers in alcoholism have produced ambiguous results but further work with biological variables should be done since Goodwin (1982) pointed out that: „there is now sufficient evidence for a genetic factor to encourage investigators to look for mechanisms of transmission."

References

Camps F, Dodd B (1967) Increase in the incidence of nonsecretors of ABH blood group substances among alcoholic patients. Br Med J 1:30-31

Camps F, Dodd B, Lincoln P (1969) Frequencies of secretors and nonsecretors of ABH group substances among 1,000 alcoholic patients. Br Med J 4 : 457–459
Cruz-Coke R (1964) Color-blindness and cirrhosis of the liver. Lancet: 1064–1065
Cruz-Coke R, Varela A (1966) Inheritance of alcoholism. Lancet: 1282
Diagnostic and Statistical Manual of Mental Disorders, 3rd edn, American Psychiatric Association 1980
Fialkow P, Thuline H, Fenster LF (1966) Lack of association between cirrhosis and the common types of color blindness. N Engl Med 275 : 584–587
Giannitsis D, Rösler M, Bellaire W, Jarovici A, Braun S (1982) HLA-antigens and schizophrenia. Blut 45 : 68
Goodwin DW (1982) Familial alcoholism. In: Perris C, Struwe G, Jansen B (eds) Biological psychiatry 1981. Elsevier/North Holland Biomedical Press, Amsterdam New York Oxford, pp 936–940
Goodwin DW, Guze SB (1974) Heredity and alcoholism. In: Kissin B, Begleiter H (eds) The biology of alcoholism. Plenum Press, New York London
Gorrell GJ (1967) Inheritance of alcoholism. Lancet: 274
Hill SY, Goodwin W, Cadoret R, Osterland CK, Doners SM (1975) Association and linkage between alcoholism and eleven serological markers. J Stud Alcohol 36 : 981–992
Rösler M, Bellaire W, Giannitsis D, Jarovici A, Greß H (1982) Zusammenhang zwischen HLA-Antigenen und schizophrenen Syndromen. Psycho Supplement 1 : 70–71
Rösler M, Bellaire W, Gressnich N, Giannitsis D, Jarovici A (1983) HLA-Antigens in schizophrenia, major depressive disorder and schizoaffective disorder. Med Microbiol Immunol 172 : 57–65
Svejgaard A, Platz P, Ryder LP, Nielsen LS, Thomsen N (1975) HL-A and disease associations —A survey. Transplant Rev 22 : 3–43
Swinson RP, Madden JS (1973) ABO blood groups and ABH substance secretion in alcoholics. J Stud Alcohol 34 : 64–70
Terasaki P, McClelland J (1964) Microdroplet assay of human serum cytotoxins. Nature 204 : 998–1000
Thuline HC (1967) Inheritance of alcoholism. Lancet: 274–275

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