SERUM PROTEIN MARKERS IN SCHIZOPHRENIA: HAPTOGLOBIN, TRANSFERRIN AND GROUP-SPECIFIC COMPONENT TYPES

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SYNOPSIS

One hundred and ten Chinese male patients of Schizophrenia were investigated for the phenotypic distribution of three polymorphic serum protein systems — haptoglobin, transferrin and group-specific component. The distribution of these polymorphic systems were compared with those in a healthy control group of 110 Chinese male blood donors. The relative incidence of $Hp^{1-1}/Hp^{2-1+2-2}$ was found to be 0.51 and the gene frequencies of Hp^1 in patient and control groups were 0.2818 and 0.3227 respectively. The distribution of transferrin types was identical in the two groups. The relative incidence of $Gc^{2-2}/Gc^{2-1+1-1}$ was 1.82 with a higher frequency of Gc^2 (0.3177) in Schizophrenia compared with that in the control group (0.2545). However, the difference in the distribution of haptoglobin and group-specific component fell short of the significance level due to the small size of the sample.

INTRODUCTION

Schizophrenia is the major mental disorder in Singapore representing aout 75% of all first admission to Woodbridge Hospital (1). It is common familial psychiatric disorder with a life time risk of one per cent (2-3). The extent of genetic contribution to the aetiology of schizophrenia estimated by maximum-likelihood pathanalysis (h^2) has been reported to be between 0.628 and 0.668 in various series (4). Twin-studies also conclusively established the genetic transmission of the disease with con

cordance rates varying between 35 and 58% in monozygotic twins and between 9 and 26% in dizygotic pairs (5). The above evidence of a genetic influence of the aetiology of schizophrenia is further supported by the findings of adoption studies (6-7). The pattern of inheritance does not seem to be of Mendelian pattern. The recent view of the genetic transmission of schizophrenia is that of a multifactorial threshold model.

It is not possible to estimate the extent of genetic risk in a patient if multifactorial transmission is in operation. In an attempt to understand the mode of genetic operation in Schizophrenia, many workers in the past have looked into the blood genetic markers associated with a higher or lower risk of developing the disease. Most of the studies have been limited to the distribution of ABO, MN blood groups and secretor status. The results have been summarised by Mourant and his colleagues in 1978 (8) and updated in our earlier publication (9). The estimated relative incidence of A/O and B/O blood groups in Schizophrenia varied widely from 0.6 to 1.5 for the former and 0.20 to 3.08 for the latter. There are inadequate data on the distribution of other blood groups. We have observed a new association with Le^a blood group with higher risk in Le^a positive individual (9) which is in agreement with the observation of an association with secretor status by Faludi (10). The results of the study of association of Schizophrenia with HLA antigens have been inconclusive and contradictory (11-18). Rudduck et al (13) had suggested that the variability of the results of HLA association may be due to the hetero-geneity of schizophrenia itself, which is not evident in the results of family or twin studies. The studies on the association of the properdin factor B (Bf), a marker on chromosome 6 in which HLA loci are also located, has also been inconclusive (18-19).

There have been some studies in the past on the association of other serum protein systems: haptoglobin, transferrin and group-specific components (21-28). The results of the above studies are conflicting. There has been no study on the association of these protein markers in Schizophrenia in populations other than Caucasians. In our earlier studies we have observed that there could be wide degree of variation of an association in differnt populations eg. the commonly accepted association of A blood groups in myocardial infarction is lacking in Chinese population (29). Further the association of blood groups in duodenal ulcer has been different in white and Negro-populations. We have suggested differential expressions of genetic association in different populations as a result of a differential response to variable ecological factors (30).

In view of the above conflicting association of different serum protein polymorphisms literature, we thought it worthwhile to examine all the three polymorphisms (haptoglobin, transferrin and group-specific component) in a Singapore population. Further, in most of the above studies, only one marker has been studied in any particular series. It is generally believed that the mongoloid population is less heterogeneous than Caucasian and Negro population (31).

Probably studies of genetic association in diseases in Mongoloid population might be more valid than other populations as the control series is likely to be more homogeneous. We report in this paper results of a study on the distribution of haptoglobin (Hp), transferrin (Tf) and group-specific component (Gc) in Schizophrenia and a comparable control group.

MATERIALS AND METHOD

Patients

One hundred and ten Chinese, male, Schizophrenic patients, undergoing in-patient treatment at the Woodbridge Hospital, Singapore, formed the sample of the study.

Control

One hundred and ten Chinese male blood donors formed the control series.

Experimental

Haptoglobin and transferrin phenotypes were determined by Polyacrylamide Gel electrophoresis. The group specific component was phenotyped by PAG electrophoresis. Both the transferrin and group-specific component systems were counterchecked by Isoelectric Focusing using carrier ampholine of pH 3.5-9.5 (LKB) and pH 4.0-6.5 (Pharmacia) respectively.

The relative incidence of serum protein types in the patient and control populations was tested by Wolf's method (32).

RESULTS AND DISCUSSION

The results of the investigation are presented in Table I-III. Table I shows the distribution of the haptoglobin phenotypes in schizophrenic and healthy

TABLE 1
DISTRIBUTION OF THE HAPTOGLOBIN TYPES IN SCHIZOPHRENIA

PHENOTYPES	CONTROL		PATIENT	
	Nc	%	Nc	%
1 — 1	13	11.82	7	6.36
2 — 1	45	40.91	48	43.64
2 — 2	52	47.27	55	50.00
ALL	110	100.00	100	100.00
Gene frequencies	Hp^1	0.3227		0.2818
	Hp^2	0.6773		0.7182
Relative Risk:	$Hp^{1-1}/Hp^{2-1} + Hp^{2-2} = 0.51$			
Lack of Hp^{1-1}: ($x_1^2 = 2.77$)				

Chinese males. There is a lack of the Hp 1-1 phenotype (6.36%) compared with that in the control series (11.82%). The gene frequencies of Hp^1 and Hp^2 are found to be 0.2818 and 0.7182 in the patient group; and 0.3227 and 0.6773 in the control series. The estimted relative risk of $Hp^{1-1}/Hp^{2-1+2-2}$ is 0.51. However, the difference is not statistically significant ($X_1^2 = 2.77$) due to the small size of the sample. Göhler and Göhler 1963 (20), Lange (1980, 1982) (27-28) have also reported an excess of Hp^{2-2} in schizophrenic sub-groups while Lovegrove and Nicholls, 1965 (21) and Sorokina (1976)(23) did not observe any association of haptoglobin polymorphism in schizophrenia. The results of the present series is suggestive of an association of the haptoglobin allele in Schizophrenia — Hp^1 offering protection. Further studies are in progress, with a larger sample to examine this association of the Hp^1 allele in Schizophrenia.

Distribution of transferrin types in the Schizophrenic and control series is presented in table II. The frequency of rare transferrin types in both the groups was identical. There is only one report on the association of transferrin B variant in schizophrenia (27). However, we failed to confirm this association in the present investigation. Table III shows the distribution of the Gc types in Schizophrenia compared with that in control series. There was an excess of Gc^2 (0.3177) in the schizophrenic compared to that in a healthy control (0.2545). The relative incidence of $Gc^{2-2}/Gc^{2-1+1-1}$ is 1.82, however, the difference was not statistically significant ($X_1^2 = 3.62$). A similar tendency of the excess of Gc^2 in schizophrenia has been reported (15, 28). However, Lange (26, 27) had reported as excess of Gc^{1-1} in schizophrenia. Lack of any association of the Gc allele in Schizophrenia has been reported by Beckman et al (24). In view of the above conflicting results a larger series needs to be tested for the distribution of Gc types for a valid interpretation.

It may be concluded that the marginal association of Gc and Hp alleles detected in the present schizophrenic series needs to be tested on a larger series.

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TABLE II
DISTRIBUTION OF TRANSFERRIN TYPES IN SCHIZOPHRENIA

PHENOTYPE	CONTROL		PATIENTS	
	No	%	No	%
CC	106	96.36	106	96.36
OTHERS (CD & CB)	4	3.64	4	3.64
ALL	110	100.00	110	100.00

TABLE III
DISTRIBUTION OF GROUP-SPECIFIC COMPONENT IN SCHIZOPHRENIA

PHENOTYPES	CONTROL		PATIENTS	
	No	%	No	%
1 — 1	62	56.36	47	48.96
2 — 1	40	36.36	37	38.54
2 — 2	8	7.27	12	12.50
ALL	110	99.99	96	100.00
Gene frequencies				
Gc^1		0.7455		0.6823
Gc^2		0.2545		0.3177
Relative Risk	$Gc^{2-2}/Gc^{2-1+1-1} = 1.82$			
Excess of	Gc^{2-2}: ($X_1^2 = 3.62$)			

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