PSEUDOCHOLINESTERASES

III. The Presence of Pseudocholinesterase Variants in a Turkish Population*

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We have investigated the prevalence and gene frequency of pseudocholinesterase variants in a group of 725 randomly selected hospital patients. The prevalence of certain variants in this group was no different from that reported for other populations.

Material and Methods

The test material consisted of sera samples from surgical patients who had had blood typing and crossmatching at the Hacettepe Medical Center Blood Bank for a period of five months. About two hundred plasma samples from normal blood bank donors and sera from a few newborns were also included. Although all ethnic groups were not represented to the same extent, age groups and sexes were represented equally.

The «screening test» was done on all the samples and only those that yielded results after 220 seconds were examined for variant characteristics.[1,2] Variants of pseudocholinesterase are characterized by their kinetic behavior with various cholinesters, especially benzoylcholine, and by a decreased susceptibility to certain cholinesterase inhibitors such as dibucaine. This decreased susceptibility is expressed as per cent inhibition to a standard dibucaine concentration (dibucaine number = D. N.).[3]

A different type of pseudocholinesterase variant is characterized by decreased sensitivity to electrolyte inhibition, notably fluoride, the degree of which is indicated by its fluoride number (F. N.).[3] The D. N. and F. N., together with the kinetic characteristics of the enzyme in the hydrolysis of butyrylthiocholine,[4] were estimated for those sera with longer than normal screening test times.

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Phenotypes were assigned according to Harris,[5] as follows: U denotes a normal enzyme; A denotes the dibucaine insensitive type; F denotes the fluoride resistant variant. Standard biostatistical methods were used in the evaluation of results.[6]

Results

The distribution, prevalence and gene frequency of pseudocholinesterase variants in 725 samples are given in Table 1. The prevalence of an abnormal silent gene was not determined because families of patients with low enzymia were not always available for investigation. The prevalence of pseudocholinesterase variants in our samples is compared to those already reported in Table 2.

TABLE 1
THE DISTRIBUTION OF PSEUDOCHOLINESTERASE VARIANTS

VARIANT	NUMBER	PREVALENCE
UU	675	93.1 %
UA	45	5.9 %
UF	3	0.45 %
AA	1	0.1 %
AF	3	0.45 %
FF	0	0.0
VARIANT	GENE FREQUENCY	
U	0.963	
A	0.033	
F	0.004	

A comparison of the Chi square analysis of our results with those reported for other populations showed no statistically significant difference in the distribution of variants in our group ($X^2 = 3.37$; degrees of freedom $= 4$; overlapping 30 to 50 per cent).

Discussion

The genetic characteristics of pseudocholinesterase variants have been extensively investigated.[3, 7] The prevalence of these variants among many of the populations studied is high, ranging from 1.0 to 8.5 per cent. According to Simpson, the differences in prevalence rates are not statistically significant.[7] In fact, the prevalence of pseudocholinesterase variants among a randomly selected hospital population shows no statistically significant difference from that of other nations in the frequency of dibucaine and fluoride resistant variants.

TABLE 2

COMPARISON OF THE PREVALENCE OF PSEUDOCHOLINESTERASE VARIANTS IN SELECTED POPULATIONS

Source	Type						
	UU	UF	UA	FF	AF	AA	Number investigated
Harris group[5]	94 %	0.5-1.0 %	4.0 %	very rare	rare	0.04 %	—
Present group	93.1 %	0.45 %	5.9 %	0	0.45 %	0.1 %	725
Kalow[7]							
Canada	—	—	3.8 %	—	—	—	1556
England	—	—	3.8 %	—	—	—	703
Germany	—	—	3.4 %	—	—	—	—
Czechoslovakia	—	—	8.5 %	—	—	—	—
Greece	—	—	3.6 %	—	—	—	360
Portugal	—	—	3.4 %	—	—	—	179
Moroccan jew	—	—	2.0 %	—	—	—	51
Berber	—	—	2.0 %	—	—	—	55
Mexican Indian	—	—	2.6 %	—	—	—	—
Australian aborigine	—	—	1.0 %	—	—	—	—
Israeli jew	—	—	6.3 %	—	—	—	433
Brazil	—	—	2.8 %	—	—	—	More than 6000

The presence of a variant in an individual does not lead to any disease, unless the variant gene is homozygous. In that case the individual will suffer prolonged apnea when given succinyldicholine. The high frequency of this gene in many populations is puzzling since it leads to no inherent protection from any environmental factor. Another bizarre observation in connection with pseudocholinesterase is that this enzyme definitely has no known physiological function because cholinesters are not present in the circulation unless administered for a therapeutic purpose.[1] Furthermore, erythrocytes themselves contain a potent cholinesterase capable of hydrolizing the physiological cholinester, acetylcholine, and this enzyme is able to cope with any amount of acetylcholine that could leak into the circulation from nerve tissues. Why pseudocholinesterase is synthesized in the liver remains to be elucidated, and until its rôle in body physiology is established, the reason for the high frequency of variants will remain a mystery.

In the meantime, the variants can be put to good use as genetic markers, and in conjunction with prevalence rates of other mutant genes, may be descriptive of the genetic character of various ethnic groups. We plan to survey different ethnic groups in Turkey for pseudocholinesterase variants, and to compare the gene frequency in these groups with already known values. It has been found that, in Turkey, gene frequencies for other mutant biochemical characteristics vary among the different ethnic groups. A well-documented example is the prevalence of glucose — 6 — phosphate dehydrogenase deficiency in certain of these groups.[8] It would be interesting to establish the gene frequencies of pseudocholinesterase variants in these same groups. Such studies may help in deciding whether the frequent glucose — 6 —phosphate dehydrogenase deficiency and abnormal hemoglobin mutations encountered in these groups represent a protective mechanism in an extremely malarial environment, or are the result of consanguinous marriages that constantly occur in these closed groups. Until such studies have been completed, we connot say definitely that pseudocholinesterase variants give no protection to their carriers.

Summary

A study of the prevalence and gene frequency of pseudochlinesterase variants among a randomly selected hospital population of 725 indicates that the distribution of variants for this population is not significantly different from that of other populations.

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