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RESEARCH REGARDING THE ROLE OF INHERITANCE IN ALCOHOLISM

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***Key words**: alcoholism, multifactorial inheritance, metabolic monitoring*

INTRODUCTION

In the past, drinking alcohol in high amounts and alcoholism were regarded as a moral decline or a vice. At the beginning of the 19th century the "drinking problem" was identified, from the medical point of view, with a disease.

Complete recognition of alcohol addiction was achieved only in the 20th century, but there were still voices that described it as a "behavioral deviation" or "bad habit". Nowadays pathologists are fighting against such conceptions with the following evidence: the concept "illness" as applied to alcoholism is in perfect accordance with the most recent model of disease: the bio-psycho-social concept. One may also state that alcoholism involves medical therapy as any other disease does, but such theories can induce some "taboo" misconceptions in ordinary people.

Two main research directions can be identified in what concerns the inheritance of alcoholism (Tudose et al, 2000):

- identification of candidate genes which predispose to alcoholism for humans and comparison with various animal models;
- the study of variability regarding alcohol induced behavior in human populations and families.

Humans are very different in what concerns the drinking motivations and the inherited predisposition to alcoholism. The genetic factors of this variability are certainly different in comparison to the genetic factors which generate the variability of species (Quian, 2005).

There are many studies that prove the existence of a strong correlation between inheritance and alcoholism. There are, also, many studies that identified candidate genes for alcoholism, but it is obvious that classical mendelian rules cannot be applied to this complex, multifactorial trait (Dick et al., 2006; Kim et al., 2005).

MATERIAL AND METHOD

To study the correlation between inheritance and alcoholism we have gathered two groups of humans:

- the group of study was composed of 72 probands diagnosed with alcohol induced addiction selected from the patients assisted by various psychiatric services in Iaşi; the structure of the group was: 38 males and 34 females.
- the control group consisted of 89 normal persons in what concerns the behavior of drinking alcohol; the structure of the group was: 60 males and 29 females.

All the probands respected the following selection rules:

- all the probands confirm their primary state of alcoholism,
- the medical documents confirm the diagnose of chronically alcoholism,
- the probands originate from big families, with good interpersonal relationship and good evidence of their family history,
- the free consent of the proband and relatives.

The general patterns of alcohol consumption were those generally accepted and proved by statistics: no alcohol consumption, occasional consumption and abusive consumption of alcohol. The structure of the studied groups from this point of view is depicted in figure 1.

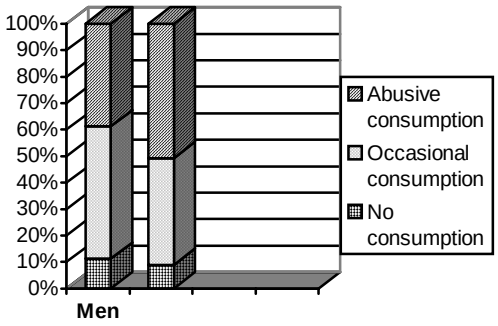

Fig. 1. The general structure of the studied groups

The average age of the studied groups was: 42.3 (±13.4) years for males and 39.9 (±11.1) years for females. For each proband with a positive history of familial alcoholism was performed family inquiries (first degree relatives were directly questioned frequently), pedigrees were drawn and eventually were analyzed the patterns of transmission (Cîmpeanu et. al, 2002).

The specific features of alcohol metabolism were analyzed for all probands in comparison to

controls focusing especially on the blood levels of acetaldehyde and alcohol (after provoked ingestion).

RESULTS AND DISCUSSIONS

Our study regarding the transmission of the genetic predisposition to alcoholism proved a higher family concentration for proband males in comparison to the proband females. Considering also the affected relatives of first and second degree, alcoholism prevailed in males (sex ratio 163 males : 104 females or 61,1% : 38,9 %). 64% of the male probands belonged to families with male alcoholics, but only 28% of the female probands belonged to families with alcoholics of same sex).

For the male probands the main alcoholic relative was the father (in 27.1% of cases), the mother (in 11.8% of cases), a brother (in 31.2% of cases) or a sister (in 15% of cases). For the female probands the main alcoholic relative was the father (in 32.2% of cases), the mother (in 13.6% of cases), a brother (in 28.9% of cases) or a sister (in 18.8% of cases).

The pedigrees showed more often unilinear transmission (in 72% of cases) than bilinear transmission (in 38% of cases).

Two clear examples of bilinear transmission are depicted in figure 1.

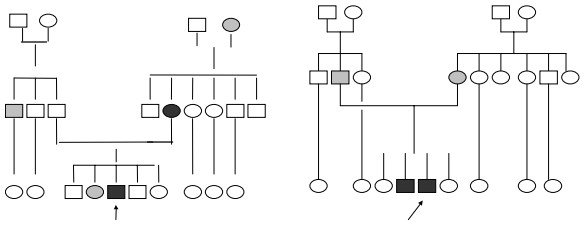

Fig. 1. Pedigrees depicting genetic predisposition to alcoholism for two male probands

The principal causes for alcohol ingestion, as affirmed by probands, were mainly social factors, compulsive motivation and subjective reasons.

Probands form rural regions considered as main causes of alcohol ingestion: tiredness after physical efforts (46% of males and 32% of females), mood for alcohol consumption (58% of males and 27% of females) and stimulating effect (33% of males and 37% of females). Probands form urban regions considered as main causes of alcohol ingestion: influence/pressure of friends (76% of males and 27% of females), social motivation (59% of males and 37% of females) and anxiolytic effect (28% of males and 33% of females).

The second part of our study consisted in biochemical investigations of the metabolic profile for probands, based on the fact that alcoholism has a biological substrate. We focused especially on the blood levels of acetaldehyde and alcohol (after provoked ingestion).

More relevant was the dynamic of acetaldehyde (the main alcohol metabolite) in peripheral blood after provoked alcohol ingestion. The average acetaldehyde concentrations were significantly lower in probands blood in comparison to controls during the entire time of monitoring (60, 120 and 240 minutes after ingestion) (fig.2).

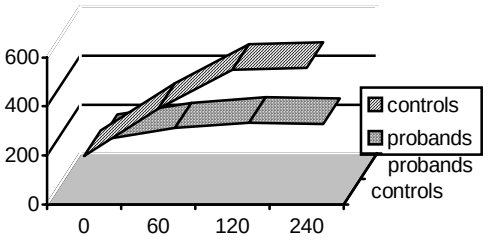

Fig. 2. The dynamic of the average acetaldehyde concentrations in peripheral blood (μmol x 10^{-2}/ml) at 60, 120 and 240 minutes after provoked ingestion.

This fact may explain the lack of unpleasant secondary effects of alcohol ingestion in alcoholism and the predisposition to ingestion. These metabolic patterns have probably a polygenic determinism supporting the theory of inheritance for the genetic predisposition in alcoholism (Patraş and Tudose, 2003).

CONCLUSIONS

1. The high incidence of familial cases of alcoholism found in our study supports both the theory of a genetic predisposition in alcoholism and the heterogeneity of their familial distribution.
2. The average global incidence of abusive alcohol consumption in the families of the probands (first and second degree relatives) reaches 32%, with an unbalanced sex ratio (predominance of males)
3. The monitoring of metabolic profiles for probands (average concentrations of alcohol and acetaldehyde in peripheral blood after provoked alcohol ingestion) is supporting the theory of inheritance for the genetic predisposition in alcoholism in what concerns the addiction/resistance to alcohol.

REZUMAT

Incidența declarată a cazurilor de alcoolism confirmă nu doar caracterul "familial" al acestora dar, ca o caracteristică generală, heterogenitatea distribuției interfamiliale în ciuda subiectivității relative a relatărilor. Calculele oferă posibilitatea primară de a constata că incidența medie globală a consumatorilor alcoolici/abuzivi în rudenia de grad I sau II a probanzilor ajunge la valoarea de 32%, cu repartizare inegală între grupuri departajate după sexul probandului. Există argumente puternice în susținerea unei componente genetice, dar abordările simple tradiționale ale investigării tulburărilor cu transmitere mendeliana nu pot fi aplicate direct.

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