INFLUENCE OF ESSENTIAL PHOSPHOLIPIDS (EPL) ON SELECTED BIOCHEMICAL PARAMETERS OF LIPID METABOLISM IN RATS CHRONICALLY EXPOSED TO AMMONIUM FLUORIDE VAPOURS

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SUMMARY: The influence of essential phospholipids (EPL) on selected lipid parameters in rats chronically exposed to ammonium fluoride vapours was studied. The content of total lipids, cholesterol, and triglycerides in serum, and the content of cholesterol and triglycerides in liver homogenate were measured. An advantageous influence of EPL on disorders in lipid metabolism due to ammonium fluoride was found.

Key words: Ammonium fluoride; Essential phospholipids; Fluoride intoxication, Lipid metabolism.

Introduction

Lipid disorders are known to be one of the major risk factors in premature atherosclerosis. They have become an object of interest for multidisciplinary studies since lipids and lipoproteins are important in basic metabolic processes.

Lipid metabolism in the organism may be affected not only by disease processes but also by exogenous factors such as pollution of the environment by fluorine compounds. The effect of fluoride on fatty acid changes can be studied from different aspects, *e.g.*, absorption, bioavailability, oxidation and "de novo" pathway synthesis (1). In turn, essential phospholipids (EPL), through their effects on the activity of key enzymes needed in lipid transformations, are also able to regulate lipid metabolism. Moreover, phospholipids are one of the substrates in the esterification of cholesterol and they take part in the transport of lipids in plasma. Therefore, the decision was made to investigate if, and to what extent, the essential phospholipids (EPL) influence lipid metabolism in animals chronically exposed to ammonium fluoride vapours. Among many fluorine compounds used for animal intoxication, ammonium fluoride was chosen due to its ability to penetrate cells (2).

Materials and Methods

Sixty male Wistar rats of initial 300 g body wight were used in the study. The animals were divided into 6 groups of 10. Essential phospholipids (EPL) (Rhone-Poulenc Rorer, Nattermann Group).

Group I: control.

Group II: received EPL at 30 mg/kg of body weight.

Group III: received EPL at 100 mg/kg of body weight.

Group IV: intoxicated by ammonium fluoride (NH_4F).

Group V: intoxicated by ammonium fluoride and receiving EPL at 30 mg/kg of body weight.

Group VI: intoxicated by ammonium fluoride and receiving EPL at 100 mg/kg of body weight.

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During the entire duration of the study the animals were allowed free access to water and standard type of feed. EPL in definite doses was added to the balls of feed which were given to the animals every day prior to location in the intoxication chamber. Humidity, temperature and ventilation (10 m^3/hr) conditions within the chamber were controlled. Ammonium fluoride was passed into the chamber as an aerosol in a concentration of 2 mg F^-/m^3 of air. The concentration of fluoride ions in the chamber was controlled through the use of an ion-selective fluorine electrode (PN-83/2-04093,07). The rats were exposed for 5 hours daily, 5 days a week for 6 months. The content of total lipids, cholesterol and triglycerides in serum, and the content of cholesterol and triglycerides in liver homogenate were measured.

Results and Discussion

The results of these studies are presented in Tables 1 and 2. In the experiment described it was concluded that the amount of total lipids in rat serum clearly rises after intoxication with NH_4F and falls slightly under the influence of essential phospholipids (EPL) administration. In the exposed groups which were at the same time protected by EPL administration, the total lipid content fell to values obtained in the control.

Cholesterol content in serum rises under the influence of fluoride intoxication and is normalized after EPL administration. Triglycerides content in serum falls under the influence of essential phospholipids in non-exposed animals, and rises significantly after NH_4F exposure. Administration of EPL at 100 mg/kg body weight decreases the content of triglycerides in serum.

Measurement of liver homogenate contents showed decreasing cholesterol after chronic exposure to NH_4F vapours and a normalizing tendency of cholesterol content due to essential phospholipids (EPL). Amounts of triglycerides in liver homogenate decreased after administration of EPL at 100 mg/kg of body weight and increased significantly in exposed animals. Simultaneous administration of NH_4F and EPL at 100 mg/kg body weight returned triglycerides to the initial values.

The observed increase of total lipids in serum under chronic exposure to fluorine compounds has a proven biochemical basis. As mentioned above, fluorine influence on lipid metabolism is complicated. It can be studied under the aspects of bioavailability, metabolism and synthesis. Bioavailability was defined by Ebersdobler (3) as the usage of foodstuffs after digestion and absorption. The bioavailability of fluorides is influenced mainly by their absorption in the digestive tract, which is significantly increased in the presence of food fats (1). This may be indicative of the lipophilic character of the fluoride ion.

The weakening of lipid metabolism by fluorides is due to repression of the activity of a number of enzymes responsible for lipid transformation: triglyceride lipase (4,5), some nonspecific esterases (6,7), and the complete blockage of pyrophosphatase activity (8,9), which causes repression in the oxidation of fatty acids. During chronic exposure to ammonium fluoride vapours, administration of essential phospholipids (EPL) clearly improves biochemical lipid parameters, decreasing the content of total lipids to their initial values. This is consistent with observations by other authors (10). The observations can be explained by the activating influence of

EPL on lipoprotein lipase (LPL) (11) and its liver fraction (HTGL) (12), an enzyme which facilitates lipoprotein uptake from the plasma by the lipid tissue.

On the basis of available publications it is difficult to ascertain a significant increase in the content of cholesterol in serum under the influence of fluoride ions. Administration of EPL normalizes these values. It seems that the cause is the activating action of EPL on lecithin-cholesterol acetyltransferase (LCAT) (13), an enzyme which through esterification of cholesterol regulates its metabolism and circulation. The content of triglycerides in serum decreases under the influence of EPL. The increase of triglyceride levels due to NH_4F is caused, among other reasons, by blockage of triglyceride lipase activity (4, 5).

TABLE 1. Influence of EPL on some lipid parameters in serum of rats chronically exposed to NH_4F vapours

PARAMETERS	Group I $\bar{x} \pm SD$	Group II $\bar{x} \pm SD$	Group III $\bar{x} \pm SD$	Group IV $\bar{x} \pm SD$	Group V $\bar{x} \pm SD$	Group VI $\bar{x} \pm SD$
TOTAL LIPIDS (mg/dL)	270 ± 13,7	263 ± 8.68	256 ± 11.7	333 ± 16.9*	256 ± 17.9	252 ± 8.67
TOTAL CHOLESTEROL (mmol/L)	1.158 ± 0.11	1.410 ± 0.14	1.305 ± 0.17	2.582 ± 0.1*	1.378 ± 0.1	1.462 ± 0.06*
TRIGLYCERIDES (mmol/L)	0.73 ± 0.059	0.62 ± 0.09	0.68 ± 0.06	1.08 ± 0.028*	1.03 ± 0.06*	0.68 ± 0.069

$\bar{x}$ mean value
SD standard deviation
* statistically significant ($p < 0.01$) compared to control

TABLE 2. Influence of EPL on some lipid parameters in liver homogenate in rats chronically exposed to NH_4F vapours

PARAMETERS	Group I $\bar{x} \pm SD$	Group II $\bar{x} \pm SD$	Group III $\bar{x} \pm SD$	Group IV $\bar{x} \pm SD$	Group V $\bar{x} \pm SD$	Group VI $\bar{x} \pm SD$
CHOLESTEROL (mg/L g of tissue)	2.39 ± 0.21	2.18 ± 0.15	2.36 ± 0.17	1.79 ± 0.17*	1.90 ± 0.11*	2.09 ± 0.11
TRIGLYCERIDE (mg/L g of tissue)	12.7 ± 0.95	12.3 ± 0.84	7.0 ± 1.09*	15.3 ± 2.11	15.3 ± 2.11	11.9 ± 1.68

$\bar{x}$ mean value
SD standard deviation
* statistically significant ($p < 0.05$) compared to control

Conclusions

1. Increases in the contents of lipid fractions in serum of animals exposed to ammonium fluoride vapours show disorders in lipid metabolism.
2. Essential phospholipids (EPL) have an advantageous effect in chronic intoxication with ammonium fluoride, normalizing the lipid metabolism.

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