

LIPID METABOLISM DISORDERS IN ACUTE ALCOHOLIC HEPATITIS PATIENTS

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The complex and versatile action of alcohol on the organism is not completely studied yet (1,10). Recently, the toxic effect of alcohol on the liver is proved although one still disputes if it is direct or indirect (3,18). It is known that 95 per cent of alcohol consumed is disintegrated in the liver while the rest 5 per cent are eliminated by the kidneys and lungs (9, 11, 17). Besides cytosol alcohol dehydrogenase a microsomal ethanol oxidating system participates in alcohol liver oxidizing, too (2, 3, 9, 14, 16). The intermediate product with alcohol oxygenation — acetyl coenzyme A — exerts a favourable effect on fatty acid synthesis in hepatic cells (11, 13, 17). In any cases, alcohol causes an increased fatty acid synthesis in the liver and a reesterification of exogenic fatty acids into triglycerides (12, 13). This results in an increased cholesterol, triglycerides, lipoproteins and fatty acid synthesis as well as in the esterification of the latter into triglycerides. There is an increase mainly of the production of low density lipoproteins (LDL). Sometimes, as a cholestasis manifestation, an abnormal lipoprotein-X can be detected in the serum (20). The course of the acute alcoholic hepatitis (AAH) is often characterized by a manifested cholestatic syndrome and significant hyperlipidemia (15). S. D. Podymova (8) describes a cholestatic variation of the disease. However, it is a comparatively rare manifestation in her opinion.

Microsomal ethanol oxidation is realized at the level of smooth endoplasmic reticulum resulting in proliferation and reduction of its functional activity. These alterations have a pathogenetic importance for cholestasis development in alcoholic hepatic lesions (8).

Literature data concerning disorders of lipid metabolism in AAH patients is rather scanty and contradictory. We fail to find Bulgarian publications on this problem at all. That is why we start an investigation of these changes.

Material and methods

Our study covered a total of 30 AAH patients aged between 27 and 78 years, mean age of 48 years hospitalized in the profile Clinic of Gastroenterology, Higher Institute of Medicine, Varna, as well as 41 clinically healthy individuals aged between 21 and 72 years, mean age of 42 years. The cases were diagnosed on the basis of clinico-laboratory data and confirmed additionally by a histomorphological examination in 38 per cent of them.

Cholesterol level was estimated according to the method of Liebermann-Burhard, triglycerides — by means of the enzyme test of Boeringer, lipoproteins — by using of filter paper electrophoresis with buffer enriched in human albumin and by

estimated densitometrically, HDL-cholesterol — by precipitation with heparin-manganese reagent, LDP — cholesterol after the formula:

$$\text{LDL-cholesterol} = \text{total cholesterol} - \left(\frac{\text{triglycerides}}{5} + \text{HDL-cholesterol} \right)$$

Fatty acids were estimated by gas-liquid chromatography. Lipoprotein-X was determined by the electrophoretical semiquantitative Seidel's method on agar. Variation analysis was used in the statistical data processing.

Results and discussion

There were statistically significantly higher cholesterol, total lipids and triglycerides levels in AAH patients when compared with these of the control persons (table 1). Our results obtained were in concordance with the data report-

Table 1

Serum lipid fraction levels in AAH patients and healthy persons

Index	AAH n=30 M±m	Healthy n=20 M±m	P
Cholesterol mmol/l	6.04±1.75	4.47±0.96	<0.02
Free cholesterol %	51.0±18.0	28.0±12.0	<0.001
Esterified cholesterol %	49.0±17.0	72.0±23.0	<0.02
Free/ester. cholest. index	1.04±0.3	0.37±0.04	<0.001
Total lipids g/l	10.21±3.2	4.51±1.43	<0.001
Triglycerides mmol/l	1.93±0.47	1.29±0.23	<0.02

ed by numerous authors (4—8). The increase of free and decrease of esterified cholesterol causing a statistically significant increase of free/esterified cholesterol index in AAH patients was of greater interest. There was a disorder of cholesterol esterification probably due to the destroyed liver function.

There were considerable changes of serum lipoprotein levels. We established a statistically reliable reduction of alpha-lipoproteins and increase of beta-lipoproteins resulting in a considerable enhancement of beta/alpha-lipoprotein index in AAH patients as compared with the control levels. LDL-cholesterol and HDL-cholesterol showed also higher values but the differences were statistically insignificant. The increased LDL/HDL-cholesterol index in AAH patients indicated that LDL-cholesterol increase was stronger expressed in this case that correlated with the changes of lipoprotein fraction levels and with the higher serum lipid levels as described above (table 2).

We established that there was hyperbilirubinemia manifested to a different extent, mainly of conjugated type, in 53 per cent of the patients which was in a definite correlation with the hyperlipidemia observed. Abnormal lipoprotein-X was found out in 79 per cent of the cases as an expression of present cholestasis. It was an interesting fact that it was also established in some patients without clinico-laboratory data for cholestasis. On the grounds of that we supposed that there was a discrete intrahepatic cholestasis together with the manifested one in AAH patients.

Table 2

Serum lipoprotein levels in AAH patients and healthy persons

Indexes	AAH n=30 M±m	Healthy n=20 M±m	P
β-lipoproteins PE	84±22	42±4	<0.001
α-lipoproteins %	14±2.7	34±7.7	<0.001
β-lipoproteins %	86±29	66±3.8	<0.02
β/α-lipoprot. index	6.14±1.72	1.94±0.76	<0.001
LDL-Cholesterol mMol/l	3.59±0.66	2.83±0.57	>0.10
HDL-Cholesterol mMol/l	1.39±0.34	1.27±0.33	±0.10
LDL/HDL Cholesterol index	2.60±0.45	2.20±0.37	±0.10

We found out a statistically significant lower level of palmitic, stearic, oleic, linolenic, and arachidonic acid, as well as of total free fatty acids (FFA) in AAH patients as compared with that of the controls (table 3). There was an insigni-

Table 3

Comparison of individual FFA in AAH patients and healthy persons

FFA μMol/l	AAH n=12 M±m	Healthy n=41 M±m	P
Myristic	15.2±12.7	9.4±0.2	>0.10
Palmitic	69.2±54.6	146±30	<0.001
Palmitoleic	13±7.3	11±7.3	>0.10
Stearic	30±11	53±16	<0.001
Oleic	84±48.5	167±59	<0.001
Linolenic	33±24	98±40	<0.001
Arachidonic	10±5.5	36±20	<0.001
Total FFA	269±135	520±158	<0.001

ficant increase of myristic and palmitoleic acids both. Total FFA reduction was mainly on the account of polyunsaturated fatty acids. There was a certain tendency towards saturated fatty acid increase. These changes in the proportion of individual FFA had a steatogenic effect.

The percentage distribution of individual FFA in AAH patients and healthy persons showed similar relationships.

The fatty acid composition of triglycerides in AAH patients did not demonstrate any significant differences with the control one of healthy persons (table 4) excepting a statistically higher palmitoleic acid level in AAH patients. Similar changes were observed in the percentage distribution of individual fatty acids as components of triglycerides, too.

It is well known that consumption of large amounts of alcohol intensifies lipolysis resulting in FFA level increase. On the contrary to that, we establish its reduction in AAH patients. It is rather difficult to explain satisfactorily these changes. Probably, other factors and mechanism are also involved except the

Table 4

Comparison of individual fatty acids in triglycerides
in AAH patients and healthy persons

Fatty acids in triglycerides mMol/l	AAH n=12 M±m	Healthy n=41 M±m	P
Myristic	5.0±2.2	5.2±1.1	> 0.10
Palmitic	40.6±16	35±10.3	> 0.10
Palmitoleic	8.9±4.9	4.4±0.8	< 0.02
Stearic	6.5±3.7	5.5±0.9	> 0.10
Oleic	41.7±24.7	50.9±20.5	> 0.10
Linolenic	24.6±21.9	22±13.1	> 0.10
Arachidonic	2.4±2.1	1.5±0.9	> 0.10
Total fatty acids	130±74.6	139±13.8	> 0.10

rdirect alcohol influence. A dynamic follow-up of these indexes is required covering various terms after alcohol consumption. It is possible that this assessment can elucidate these problems. A serious damage of the liver and of its function sets in with AAH and a disturbance of FFA synthesis can be, therefore, supposed in this respect. In our previous investigations (19) we report a reduced lipoprotein lipase activity in patients with alcoholic hepatic steatosis. Probably, alcohol suppresses the activity of this enzyme and of lipolysis, respectively resulting in FFA liberation reduction, by unknown mechanisms.

In conclusion we summarize that there is a serious disorder of lipid metabolism most probably related to the immediate alcohol influence, liver damage and present cholestasis in AAH patients.

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НАРУШЕНИЯ ЛИПИДНОГО ОБМЕНА У БОЛЬНЫХ ОСТРЫМ АЛКОГОЛЬНЫМ ГЕПАТИТОМ

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Р Е З Ю М Е

Исследованы нарушения липидного обмена у 30 больных острым алкогольным гепатитом и у 41 здорового лица.

У больных острым алкогольным гепатитом устанавливается статистически значимо более высокий уровень холестерина, общих липидов, триглицеридов и бета-липопротеинов, причем устанавливается незначительное повышение холестерина в липопротеинах низкой плотности. У 79 % больных обнаруживается наличие липопротеина-X. Результаты показывают более низкий уровень пальмитиновой, стеариновой, олеиновой, линолевой и арахидоновой кислот, как и тотальных свободных жирных кислот.

Автором сделан вывод о серьезном нарушении липидного обмена у больных острым алкогольным гепатитом.