LIPID METABOLISM IN DIENCEPHALIC SYNDROME OF THE ITZENKO-CUSHING TYPE AND IN ITZENKO-CUSHING'S DISEASE

G. Varbanov

Lipid metabolism regulation is effected by the neuroendocrine system (3, 11, 16, 17, 24). An inportant role in this respect is attributed to the system hypothalamus — hypophysis — adrenal cortex. The hypothalamus exerts its influence on lipid metabolism intensity through the endocrine glands.

In 1964, Lee (cit. 5, 10) succeeded in isolating from the hypophysis of animals and humans a fraction with peptide structure, coined with the term lipotropin. This free of STH and ACTH-content polypeptide has a pronounced lipolytic effect. (21, 22). Lipotropin has been demonstrated in the blood of humans after receiving large fat amounts with the food. This substance is never detected in the blood of patients with hypopituitarism and in post-hypophysectomy conditions (21). In 1956, Leytes and co-workers (cit. 1, 10) isolated an analogical substance from the hypophysis of animals, denominated adiposin. The latter lipolytic substance is also known as lipomobilizing factor (11,12) or hormone (27). Hartman (1947) isolated a «fatty» factor from the adrenal cortex promoting the mobilization of lipids from the fat deposits towards the liver (cit. 6). The regulatory effect on fat metabolism exerted by a number of hormones, such as ACTH, STH, TTH, GTH etc has been accordingly proved. The adrenals likewise participate actively in the regulation of lipid metabolism.

ACTH has a pronounced lipolytic effect — it lowers the level of serum cholesterol (4, 10, 11, 16, 20, 25, 26, 28). Furthermore, it stimulates the mobilization of fats from the deposits, and their utilization in the tissues (19,18). On the contrary, Adlersberg et al (cit. 20) do not rule out the possibility of cholesterol level increase, intense fatty deposition in the tissue, and their redistribution. Literature data concerning the lipomobilizing effect of glycocorticoids are controversial: e. g. it is claimed equally that they may enhance (18), as well as inhibit lipolysis (7). Under the influence of glycocorticoids, the blood cholesterol level rises (4, 15, 23). Leytes (8) and Stork (29) established that cortisone exerts no influence on lipolysis, in vitro, whereas, in vivo, it accounts for its insignificant inhibition. Most probably, glycocorticoids do not have an independent, immediate lipomobilizing effect, but rather a permissive effect, on the factors promoting mobilization and utilization of fats (9, 11, 19). Leytes and Davtyan (9) observed a permissive effect of cortisone in terms of the lipomolibizing action of epinephrine.

Hyperpituitarism is characterized by an increased blood level of cholesterol, phospholipids and beta-lipoproteins, whereas in hypopituitarism the listed above indicators are reduced or within normal limits (17). Ganelina (24) established a considerable rise of the cholesterol and total lipids content in

the blood, and reduced lipoprotein lipase activity in patients with diencephalic syndrome. In Itzenko-Cushing's disease, similarly an overall increase of the serum lipid level and endogenic heparin level, not correlating with the lowered activity of lipoprotein lipase, is established (13, 14). The mechanisms of the described above lipid metabolism disorders are not sufficiently well clarified, with a great importance being attributed to the lowered lipoprotein lipase activity (14).

It is the purpose of the present work to study the activity of lipoprotein lipase, and the changes in serum lipids' content in diencephalic syndrome of the Itzenko-Cushing type, and in Itzenko—Cushing's disease.

Material and methods

The heparin test was dispensed in a series of 14 patients with diencephalic syndrome of the Itzenko-Cushing type, in 10 patients with Itzenko-Cushing's disease, and in 17 clinically healthy individuals.

We accepted that it was a matter of diencephalic syndrome of the type of Itzenko-Cushing's disease in cases of primary lesion in the hypothalamus area with disturbed function of the system hypothalamus-hypophysis-adrenal cortex, and appearance of early, not invariably clearly manifested symptoms, characterictic of the disease of Itzenko-Cushing. The consistent involvement of the adrenal cortex in the pathological process of the above described disorders was interpreted as presence of Itzenko-Cushing's disease (3).

The heparin test and the methods employed in the study of serum lipids were outlined in an earlier work (2).

Results

Among the patients with diencephalic syndrome of the Itzenko-Cushing type, compared to patients with Itzenko-Cushing's disease (Table 1), a statistically significantly lower level of cholesterol, total lipids, phospholipids, beta-lipoproteins, endogenic heparin and blood sugar was established, at considerably enhanced lipoprotein lipase activity. As far as triglyceride and non-esterified fatty acids content is concerned, no essential difference is found between the two morbid conditions.

In the group of patients with diencephalic syndrome of the Itzenko-Cushing type, as compared to healthy individuals, a statistically significantly lower cholesterol and endogenic heparin level is established, and a higher level of beta-lipoproteins. The other findings show a lower lipoprotein lipase activity, and higher level of total lipids and triglycerides, but the latter difference proved statistically insignificant (Table 1).

Upon comparison of the serum lipids blood content and lipoprotein lipase in the groups under study and in patients with acromegaly (2), it was found out that among the patients with Itzenko-Cushing's disease, the level of cholesterol, total lipids and beta-lipoproteins was the highest, and the activity of lipoprotein lipase — the lowest.

Under the influence of the heparin administered in patients with diencephalic syndrome of the Itzenko-Cushing type (Table 2), a statistically significant reduction of the blood content of cholesterol, total lipids, phospholipids, triglycerides and beta-lipoproteins occurs, along with an increase of

non-esterified fatty and endogenic heparin. In cases with Itzenko-Cushing's disease heparin exert an analogical effect (Table 3).

Table 1

Correlation between the Content of Serum Lipids, Endogenic Heparin, Lipoprotein Lipase and Blood Sugar in Patients with Diencephalic Syndrome of the Itzenko-Cushing Type, Itzenko-Cushing's Disease and in Clinically Healthy Subjects

	Diencephal. syndrome n=14 M±r	Itzenko—Cushing n=10 M±r	P	Clinically healthy n=17 M±r	P
Cholesterol mg %	204±43	234±98	<0.01	223±37	<0.01
Total lipids mg %	583±102	645±207	<0.02	568±73	>0.1
Phospholipids mg %	198±21	227±64	<0.05	196±26	>0.1
Triglycerides mg %	182±84	183±102	>0.1	153±44	>0.1
β-lipoproteins FU	51±19	64±32	<0.05	40±11	<0.02
Non-esterified f. a. μ M/ml	0.57±0.25	0.54±0.22	>0.1	0.52±0.1	>0.1
Lipoprotein lipase μ M/ml	1.62±1	1.11±0.6	>0.1	2.40±0.42	>0.1
Endogenic heparin U/ml	6±2	9±2	<0.001	9±0.6	<0.001
Blood sugar mg %	104±15	118±29	<0.05	105±14	>0.1

Table

Heparin Effect on the Blood Content of Lipids in Patients with Diencephalic Syndrome of the Itzenko-Cushing Type

	n	Pre-heparin value M±r	Post-heparin value M±r	P
Cholesterol mg %	14	204±43	192±54	<0.01
Total lipids mg %	14	583±102	516±95	<0.001
Phospholipids mg %	14	198±21	190±24	<0.02
Triglycerides mg %	14	182±84	132±76	<0.001
β-lipoproteins FU	14	51±19	37±13	<0.001
Non-esterified f. a. μ M/ml	13	0.57±0.25	0.90±0.36	<0.001
Lipoprotein lipase μ M/ml	13		1.62±1	
Endogenic heparin U/ml	14	6±2	8±1.7	<0.001

Table 3

Heparin Effect on the Blood Content of Lipids in Patients with Itzenko-Cushing's Disease

	n	Pre-heparin value M±r	Post-heparin value M±r	P
Cholesterol mg %	10	234±98	205±78	<0.01
Total lipids mg %	10	645±207	565±163	<0.01
Phospholipids mg %	10	227±64	193±42	<0.02
Triglycerides mg %	10	183±102	160±87	>0.1
β-lipoproteins FU	10	64±32	44±25	<0.001
Non-esterified f. a. μ M/ml	9	0.54±0.22	1.04±0.63	<0.01
Lipoprotein lipase μ M/ml	9		1.11±0.61	
Endogenic heparin U/ml	10	9±2	11±2.4	<0.001

Discussion

The results of our study point to presence of a serious lipid metabolism derangement in the groups under observation.

In cases with diencephalic sundrome, Ganelina (24) noted an increase of cholesterol and total lipids mainly, and a reduction of lipoprotein lipase activity. In our series of diencephalic syndrome patients, in comparison with healthy subjects, the cholesterol level appears to be lower and the endogenic heparin content as well which correlates with the reduced lipoprotein lipase activity. The lowered cholesterol level and the moderately raised levels of the other lipid indicators in our series are most probably attributable to the enhanced ACTH production, to its lipolytic and cholesterol-level reducing effect. This is in harmony with the observations made by various authors (4, 11, 16, 28). It is by no means ruled out that at this particular stage of the disease, parallel to the increase of ACTH, the activity of the lipomobilizing hormone of the hypophysis (adiposin) is also enhanced, and exerts an additional influence on serum lipids.

Similar to other authors (14), we too established a particularly low lipoprotein lipase activity which does not correlate with the normal endogenic heparin level. The lipoprotein lipase fall is most likely due to the increased activity of its inhibitors. We are propense to accept that the considerable variations in lipid fractions, observed among the Itzenko-Cushing's disease patients, are caused by the lowered activity of lipoprotein lipase in these patients.

The statistically significantly lower blood sugar level ($p<0.02$) in the healthy subjects, relative to patients with Itzenko—Cushing's disease, point to the existence of a close interrelation betveen carbohydrate and lipid metabolism in this affection.

Under the effect of heparin, a considerable lipolysis takes place, involving all the lipid fractions, in both groups of patients under study. Usually, such a lipolytic effect is exerted by heparin in association with a severe lipid metabolism disturbance.

The substantial increase in practically all lipid fractions of the blood in Itzenko-Cushing's disease may be used as an additional test in the diagnosis of the condition.

REFERENCES

1. Антонова, Е. Е. *Бюлл. экспер. биол.*, 1970, 11, 63—65. — 2. Върбанов, Г. Първа научно практ. конф. Окр. болница — Варна, юни, 1971. — 3. Гинчерман, Е. З. *Пробл. эндокрин.*, 1966, 2, 44—51. — 4. Досев, Ил. *Вътр. бол.*, 1969, 5, 580—583. — 5. Колев, Д. Хормони, 1972, С., Наука и изкуство. — 6. Лейтес, С. М. Физиолог. и патол. жировой ткани 1954, М. Медгиз. — 8. Лейтес, С. М. Патофизиология жирового обмена, 1964, М. — 8. Лейтес, С. М., Н. К. Давтян. Матер. III Всесоюзна конф. — Химия и обмен углеводов, Москва, 1965, 314—321. — 9. Лейтес, С. М., Н. К. Давтян. *Бюлл. экспер. биол. и мед.*, 1965, 2, 55—56. — 10. Лейтес, С. М. Актуални пробл. във вътр. мед., 1967, С., Мед. и физк. — 11. Липовецкий, Б. М. *Пробл. эндокрин.*, 1971, 5, 50—54. — 12. Липовецкий, Б. М., И. Ф. Гольдмахер, И. И. Дмитриева, Т. Е. Козловa-Лавриненко. *Кард.*, 1967, 12, 82—86. — 13. Лобанова, А. М. *Пробл. эндокрин. и гормонотер.*, 1966, 3, 11—14. — 14. Малыгина, С. И., Р. М. Пархимович. *Пробл. эндокрин.*, 1970, 3, 37—40. — 15. Пенчев, Пв. Ендокрино-

логия, 1968, С., Мед. и физк. — 16. Попов, А. В. *Пробл. эндокрин. и гормонотер.*, 1965, 4, 92—95. — 17. Пронин, Ю. И., М. Я. Лауфер, *Тер. арх.*, 1966, 7, 39—41. — 18. Прохорова, М. И., З. Н. Тупикова. Большой практикум по углев и липидному обмену, 1965, Л. — 19. Цанев, А. Н. *Вътр. бол.*, 1962, 2, 54—57. — 20. Якубовская, В. И., И. А. Рыковская. *Пробл. эндокрин.*, 1968, 3, 64—68. — 21. Anselmino, K. J., F. Hoffman, Dtsch. med Wschr., 1965, 90, 39, 1967—1701. — 22. Csch, G., J. Fovenui, E. Goth, L. Graf, G. Tamasi. *Orv. Hetul.*, 1969, 110, 27, 1540. 23. Felt, V., Cs. Gastroeut. Vyz. 1963. 51—57. — 24. Ganelina, I. E., J. M. Krajwski, G. P. Deragina. *Z. ges. inn. Med.*, 1966, 21, 16, 488—496. — 25. Gries, F. A., H. Bethge. *Metabolism.* 1967, 16, II, 967—976. — 26. Ho, R.J., H. C. Meng. *Metabolism*, 1964, 13, 4, 361—364. — 27. Lelek, I. *Z. arztl. Fortbild.*, 1963, 1, 56—60. — 28. Stock, K., E. Westermann. Naynyn-Schmiedebergs. *Arch. exp. Path. Pharmak.*, 1965, 251, 5, 488—502. — 29. Stork, A., E. Fabian, J. Sponarova. *Enzymol. biol. clin.*, 1968, 9, 4, 256—260.

ЛИПИДНЫЙ ОБМЕН ПРИ ДИЭНЦЕФАЛЬНОМ СИНДРОМЕ ТИПА БОЛЕЗНИ ИЦЕНКО—КУШИНГА И ПРИ БОЛЕЗНИ ИЦЕНКО—КУШИНГА

Г. Вырбанов

РЕЗЮМЕ

Липопротеиновая липаза, эндогенный гепарин и сывороточные липиды исследованы у 14 больных с диэнцефальным синдромом типа Иценко-Кушинга, у 10 больных с болезнью Иценко—Кушинга и у 17 клинически здоровых лиц.

У больных с болезнью Иценко—Кушинга по сравнению с больными с диэнцефальным синдромом установлены статистически значимые более высокие величины холестерина, общих липидов, фосфолипидов, β-липопротеинов и эндогенного гепарина. Налицо серьезное нарушение липидного обмена, касающееся всех липидных фракций.