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SOME ASPECTS OF LIPID METABOLISM IN TUBERCULOSIS

M. M. Abdel Kader*, M. T. Abdel Aziz, M. A. Shawky,
M. Abdel Hakim, M. Amr and I. Soultan

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INTRODUCTION

Low serum lipids were observed in cachectic states produced by prolonged starvation observed in inmates of concentration camps in the second world war, or by chronic wasting disease, e.g. carcinomas and tuberculosis. It was also proposed that resolution of the tuberculous process by chemotherapy might induce a reversion to higher serum lipid levels, which were known to be low in tuberculosis[1].

It was also shown that a low incidence of coronary atherosclerosis occurred in tuberculosis, despite the relatively high-lipid and high-caloric diets taken by tuberculous patients[2].

The biochemical aspect of pulmonary function was a subject of active research in the last 20 years[3]. The intermediary metabolism of the lung, with regards to oxygen consumption, in relation to carbohydrates, lipids, proteins and nucleic acids was thoroughly studied[4].

These phenomena suggest a fundamental relationship between pulmonary tuberculosis and lipid metabolism. This work was therefore conducted to study some aspects of lipid metabolism in tuberculosis.

MATERIALS AND METHODS

137 male and female individuals comprised the experimental subjects of this work. These were classified into two groups:

Group A: 77 males and females of an age ranging from 14~65 years classified as follows:

(1) 14 normal males and females as controls from the working staff of the university hospital who subsisted on the same hospital diet offered to the tuberculous patients.

(2) 16 patients suffering from minimal T.B. lesion (stage I).

(3) 23 patients suffering from moderately advanced T.B. lesions (stage II).

(4) 24 patients suffering from far-advanced T.B. lesions (stage III).

The classification of stage I, II, III were satisfied according to the national tuberculous association of America (1961).

From all these subjects, plasma and serum samples were taken after an overnight fast. The following lipid components were assayed:

a) Total serum lipids and serum lipoprotein pattern by paper electropheresis[5].

b) Plasma cholesterol, both free and esterified[6].

c) Plasma phospholipids[7].

d) Plasma triglycerides[8].

Group B: 60 subjects classified as:

1) 20 normal subjects.

2) 20 patients with active pulmonary tuberculosis.

3) 20 patients after quiescence during treatment from T.B.

From all these subjects samples of serum were taken after overnight fasting for serum lipase estimation by sigma method (Kit No. 800—Tietz 1959).

* From the Biochemistry and Chest Departments Faculty of Medicine, Cairo University.

Table 1. The Mean Value of Blood Lipid Component in Normals & Tuberculous Patients

	Total lipids mg %	Cholesterol mg %			Phospho lipids mg %	Trigly-cerides mg %	Lipoprotein pattern			
		Free	Ester	Total			Beta	Alpha	Non mobile	β/α
Normals	511.4	88.40	89.80	178.1	170.2	93.30	53.8	29.30	19.60	1.8
S.D. ±	55.3	10.88	13.52	21.23	9.6	12.8	4.2	4.01	4.2	0.36
S.E. ±	14.78	2.9	3.6	5.67	2.6	3.4	1.2	1.15	1.2	0.1
Stage I	571.2	59.90	113.5	209.4	139.7	132.30	45.2	25.30	29.50	1.8
S.D. ±	67.5	37.8	20.8	55.2	30.8	15.6	6.2	5.7	8.2	0.59
S.E. ±	19.8	10.1	5.8	15.3	7.9	3.4	1.68	1.54	2.22	0.16
P.	<0.05	<0.5	<0.01	<0.1	<0.01	<0.01	<0.01	<0.01	<0.11	<0.01
Stage II	515.0	78.50	88.3	166.8	140.2	141.2	39.9	29.50	30.60	1.35
S.D. ±	79.0	28.3	89.6	55.0	17.5	30.2	3.3	10.6	6.36	0.34
S.E. ±	18.3	6.58	20.84	12.79	3.65	7.37	0.767	2.465	1.479	0.079
P.	<0.9	<0.3	<0.9	<0.5	<0.01	<0.01	<0.01	<0.9	<0.01	<0.01
Stage III	481.5	70.40	74.9	145.4	135.5	139.38	51.2	23.7	25.4	2.327
S.D. ±	64.8	11.1	13.6	19.7	28.4	32.9	8.5	6.1	8.2	0.75
S.E. ±	13.2	2.3	2.8	4.0	5.8	6.7	1.7	1.2	1.7	0.15
P.	<0.2	<0.01	<0.01	<0.01	<0.01	<0.01	<0.2	<0.01	<0.01	<0.01

Table 2. Serum Lipase in Tuberculosis
(Tietz units/mℓ serum)

	Normals	Active T.B.	After treatment
Means	0.565	0.220	0.345
St. D.	0.120	0.030	0.022
St. E.	0.020	0.006	0.0049
P		<0.01	<0.01

RESULTS

The results are presented in tables 1 & 2. It is clear that there is apparent changes in the lipid components of the blood during the different stages of pulmonary tuberculosis, namely an increase in total lipids which was significant only in stage 1. Total cholesterol, free and esters, decreased significantly only in stage III of the disease; significant reduction in phospholipids was shown in all stages of the disease. A highly significant increase was shown in the non-mobile fraction in all stages of T.B. The α-lipoprotein was significantly decreased only in stage III while β-lipoprotein showed a significant decrease only in stage I & II.

DISCUSSION

Definite changes tookplace in total and fractional lipids in the different stages of pulmonary tuberculosis studied.

In the first stage of the disease, the slight increase in total serum lipids could be explained on the basis of increased lipid mobilization accompanying the loss of weight of the tuberculous patients. These findings confirm the work of Guillermand[9] who reported a condition of hyperlipemia in eight cases suffering from pulmonary tuberculosis. He attributed this condition to the functional defect of liver and lung parenchyma leading to disturbed lipid metabolism. Misra[10], however, reported decreased serum total lipids in tuberculous patients.

However, total lipids reverted to their normal values during the advancement of the disease, which could be explained on the basis of the significant decrease in phospholipids and cholesterol during the different phases of the disease (Table 1).

The significant decrease in total, free and esterified cholesterol in the far advanced tuberculosis observed in this work might be due to a defect in hepatic function. This also might explain the low incidence of coronary atherosclerosis observed in tuberculosis by Straus[2]. Our findings confirm those of Muckherjee[11] who

showed the same phenomenon in the mouse and rabbit; however, increased levels of cholesterol ester were observed[12].

Kondo et al.[12] reported that blood levels of cholesterol esters increased markedly in the mouse with the development of tuberculous lesions.

Theon et al.[13] showed an increase in free cholesterol and lipoproteins in rabbits infected with *Mycobacterium bovis*. The discrepancy between the results shown in animals and human might be explained on the basis of species differences.

The low serum cholesterol levels observed in far advanced tuberculosis might be due to diminished synthetic capacity of the liver to produce either cholesterol of lipoproteins, increased utilization or degradation of cholesterol by the tissues of the body.

The significant decrease in phospholipids observed during the advancement of the disease (Table 1) could be explained on the basis of derangement in liver function with regards to phospholipid biosynthesis; this observation confirms Brinda Ban[14] findings in tuberculous patients.

The lipoprotein pattern in tuberculous patients, on the basis of the observed changes in lipid components, was markedly deviated from normal. The significant decrease in the β-lipoproteins could be explained on the basis of observed decrease in the phospholipids and cholesterol fraction (Table 1). The changes observed in the different lipoprotein fractions are due to the observed changes in the decreased levels of phospholipids and cholesterol and increased concentrations of triglycerides.

The marked reduction observed in serum lipase activity in the tuberculous patients explains the significant increase noticed in plasma triglycerides. This, also, might explain the marked increase in non-mobile fraction of the electrophoretic pattern of serum lipoproteins, in the far advanced disease. The decreased activity of serum lipase in tuberculosis might be explained on the basis of a deficiency of heparin synthesized by the reticuloendothelial system which is affected directly by the tuberculous lesions in the lung.

It has been postulated[15] that the lung, by virtue of its reticuloendothelial function, may, in some way similar to the liver, operate to inactivate the circulating lipoprotein lipase.

Tayeau[16] observed that stress, caused by great number of diseases, and particularly acute tuberculosis, would lead to a significant increase in plasma glycoprotein. Stress conditions will also stimulate hypersecretion of adrenaline ACTH and corticosteroids which activate the extracellular collagenase enzyme leading to liberation of peptides from connective tissues[17]. These peptides will initiate the biosynthesis of fibrinogen and glycoproteins in liver with an accompanying increase in the plasma glycoproteins[18]. Glycoproteins are inhibitors of the clearing factor lipoprotein lipase. Triglycerides are therefore not hydrolysed and accumulate in plasma[19][20].

This hypothesis explains clearly the decreased activity of the serum lipase accompanied by the increased levels of triglycerids in tuberculous patients.

Further work should be carried out to explain the observed changes in the lipid metabolism in tuberculosis.

SUMMARY

In active tuberculosis there is a significant decrease in plasma phospholipids in the 3 stages of tuberculosis, compared to normal, due to liver affection while there is a significant increase in plasma triglycerides in the 3 stages of active tuberculosis due to decrease in the serum lipase activity. Total serum lipids increased significantly in stage I of the active disease but without a significant difference shown in stage II & III of the active disease. Total plasma cholesterol showed a significant decrease in stage III of the active disease without a significant difference appearing in stage I & II.

Free plasma cholesterol showed a significant decrease in stage III of the disease without a significant difference observed in stage I & II.

Cholesterol ester showed a significant increase in stage I of the active disease, to decrease significantly in stage III without a significant change in stage II. Phospholipids, however, were significantly decreased during the different stages of the disease.

Serum lipoprotein pattern showed a highly significant increase in the non-mobile fraction in all stages of

tuberculosis, most probably due to the increase of triglycerides. The α-lipoprotein fraction showed a highly significant decrease in stage III of the active disease, with insignificant changes in stage I & II.

The β-lipoprotein fraction decreased significantly in stage I & II with insignificant change in stage III.

Serum lipase activity decreased significantly in active tuberculosis and significantly increased after treatment but not up to the level in normal persons.

REFERENCES

1) Cook, R.P.: Cholesterol, Academic Press, New York, 1958.
2) Straus, R., Wurm, M., Myers, W.E. and Salkin, D.: Amer. J. Clin. Path., 37 : 339, 1962.
3) Clements, J.A.: Fed. Proc., 33 : 2231, 1974.
4) Tierney, D.F.: Fed. Proc., 33 : 2232, 1974.
5) Swahn, B.: Scand. J.Clin. Lab. Invest., 4 : 98, 1952.
6) Sackett, G.E.: J. Biol. Chem., 24 : 227, 1925.
7) Youngburg, G.E. and Youngberg, M.V.: J. Lab. Clin. Med., 16 : 158, 1930.
8) Sigma Tentative Technical Bulletin, No.405, August, 1971.
9) Guillermand, J.: Le Poumon et Le Coeur 27 : 377, 1971.
10) Misra, U.K. and Jenkitasubrumanian, T.A.: Indian. J. Biochem., 1 : 159, 1964.
11) Muckherjee, K.L.: J. Indian. Med. Ass., 16 : 404, 1964.
12) Kondo, E., Murohashi, T., Kanai, K. and Kubota, S.: Japan. J. Med. Sci. Bull., 24 : 345, 1971.
13) Theon, C.C., Karlson, A.G. and Ellefson, R.D.: J. Infect. Dis., 127 : 408, 1973.
14) Ban, B.: Amer. J. Tuberc., 72 : 71, 1955.
15) Popjak, G. and Beekmans, M.L.: Biochem. J., 47 : 233, 1950.
16) Tayeau, F.: Exp. Ann. Biochim. Med., 16 : 215, 1954.
17) Houck, J.C., Johnston, J. and Jacob, R.A.: Biochem., Pharm-March, p.19, 1968.
18) Jayle, M.F., Engler, R. and Degrelle, H.: Exp. Ann. Biochem. Med., 30 : 142, 1970.
19) Tayeau, F., Jouzier, E. and Tixier, M.: Bull. Acad. Med., 151 : 521, 1967.
20) Tayeau, F., Jouzier, E. and Sechet, J.: Bull. Acad. Med., 155 : 819, 1971.