

PHTHIVAZID AND CHOLESTERIN METABOLISM

Iu.M. Ostrovskii, D.Z. Kagan and A.A. Iaroshevich

From the Polotsk City Hospital (Chief Physician E.M. Polygalina) and the

Polotsk Tuberculosis Dispensary (Chief Physician N.Ia. Krengauz)

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The biosynthesis of cholesterol in the body is effected by a number of reactions as a result of which are formed high aliphatic hydrocarbons (squalene), which later undergo cyclic transformation into a phenanthrene ring [3]. The chain of this precursor of cholesterol is formed as a result of the action of acetyl-coenzyme A [7].

Study of the effect on metabolism of the derivatives of isonicotinic acid hydrazide, to which group phthivazid belongs, has shown that these drugs may interfere with the formation of acetyl-coenzyme A [1, 4].

TABLE 1

Serum Cholesterol Content in Patients with Pulmonary Tuberculosis Treated with Phthivazid

Serial No.	Patient's name	Cholesterol (mg %)	
		before giving phthivazid	on the 3rd day of phthivazid therapy
1	B-a	155	134
2	P-o	162	162
3	R-la	130	120
4	B-n	166	144
5	G-s	125	90
6	Kh-o	148	126
7	K-k	157	119
8	Sh-ch	144	125
9	Zh-v	165	165
10	P-a	174	133
11	Ia-k	133	124
12	K-l	161	130
13	P-a	147	106
14	S-o	168	126
15	Ia-o	100	89
16	B-o	139	96
17	K-sh	120	99
18	Sh-a	134	111
19	L-o	158	144
20	S-ch	134	119
21	M-v	160	148
22	S-v	94	85
23	L-a	114	132
24	L-v	148	131
Average		143	123

There is evidence of possible weakening of the resynthesis of ATP during isoniazid therapy [9]. The most likely explanation of this is that withdrawal of the acetyl residue for the requirements of acetylation of the isoniazid [5, 6] may affect the synthesis of cholesterol.

In the literature accessible to us we were unable to find any investigations of this problem, yet changes in the serum cholesterol content are often used by phthisiologists as a reliable indication of the control of the course of a tuberculous infection. It is generally considered that with successful treatment of tuberculosis the serum cholesterol content rises.

EXPERIMENTAL METHOD

The aim of our investigation was to study the changes in the serum cholesterol content in a group of patients with pulmonary tuberculosis (of the chronic fibrocavernous type) under treatment with phthivazid. Estimation of cholesterol was done on admission of the patients to hospital before starting phthivazid and later (in the majority of patients) on the third day of therapy (1 to 1.5 g per day). A small group of patients was examined on the 3rd, 15th and 30th days of treatment.

At the beginning of the investigation all the patients were in a phase of flare-up of infiltration. We did not separate the patients according to the form and extent of the lesion, since the action of phthivazid on cholesterol metabolism was the same in all the patients.

EXPERIMENTAL RESULTS

As a rule on the third day of phthivazid therapy the serum cholesterol level fell. Out of 24 patients examined the drug showed this effect in 21. In two patients the serum cholesterol level remained unchanged and only in one did it rise (Table 1).

During observations for one month (eight patients) it was found that the cholesterol level gradually begins to rise, but even on the 30th day of treatment, on the day before discharge, when the majority of the patients were in a satisfactory condition, the serum cholesterol concentration did not exceed its original level (Table 2).

TABLE 2

Serum Cholesterolin Content in Patients with Pulmonary Tuberculosis Treated with Phthivazid

Serial No.	Patient's name	Before giving phthivazid	Day of phthivazid therapy		
			3rd	15th	30th
1	K-1	161	130	147	154
2	S-o	168	126	139	159
3	B-o	139	96	119	124
4	K-sh	120	99	—	121
5	S-ch	134	119	136	122
6	M-v	160	148	141	164
7	S-v	94	85	92	109
8	L-v	148	131	166	—
Average		140	115	134	136

The results obtained are confirmed by others reported in the literature. A case has been reported of the use of isoniazid in treating cholesterolin pleurisy arising in a patient with tuberculosis. The course of treatment led to an alteration in the character of the disease, with a fall in the cholesterolin concentration [8]. It is likely that phthivazid acts in the same way as isoniazid. High doses of phthivazid also lower the cholesterolin level [2].

Thus, changes in the serum cholesterol level in patients with pulmonary tuberculosis are the result not only of the pathological process but also of drug therapy, and this must be taken into account by the clinician.

SUMMARY

The authors studied the effect of phthivazid on the synthesis of cholesterol in the organism of tuberculous patients. It was established that in the majority of patients (21 of the 24) the therapeutic doses of phthivazid decrease the cholesterol level from 143 mg % (before administration of phthivazid) to 123 mg %, on the average by the third day. With prolonged treatment by phthivazid (one month) the cholesterol level gradually approaches its initial value (but never exceeds it).

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