COMBINED EFFECT OF IPRONIAZID AND HIGH ALTITUDE ON LIPID METABOLISM IN HEALTHY RABBITS AND RABBITS WITH EXPERIMENTAL ATHEROSCLEROSIS

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Administration of iproniazid (2 mg/kg) daily for 30 days had little effect on lipids of the blood plasma, liver, and aorta of healthy rabbits, but produced a significant decrease in the concentrations of cholesterol and total lipids in these tissues in rabbits receiving cholesterol for 75 days and reduced the severity of atherosclerosis of the aorta in animals kept in the plains and in the mountains. Iproniazid increased the blood concentration of nonesterified fatty acids, and in 4 of 27 rabbits with atherosclerosis it produced hyperbilirubinemia.

The beneficial effect of monoamine oxidase inhibitors (nialamide) in the initial period of development of experimental atherosclerosis in rabbits [2, 5] and of iproniazid in human patients with atherosclerosis [2] has been demonstrated.

The effect of a course of small doses of iproniazid, of a therapeutic order for man, on rabbits with experimental atherosclerosis was investigated at low and high altitudes.

EXPERIMENTAL METHOD

Male rabbits weighing 2.5-3.5 kg received cholesterol (0.5 g/kg) daily with their food for 75 days. Some of the rabbits were given iproniazid (2 mg/kg daily for 30 days) by gastric tube 45 days after the beginning of cholesterol feeding. The same experiments were repeated on the Tyuya Ashu Pass (3200 m above sea level). The concentrations of total cholesterol [3], phospholipids [4], and total lipids were determined in the blood plasma, the liver, and abdominal aorta [7], and the concentration of nonesterified fatty acids (NEFA) in the plasma was also estimated [6]. The severity of the atherosclerosis was assessed by planimetry of the thoracic aorta [1]. The effect of a 30-day course of iproniazid in the same dose on lipid metabolism was also investigated in healthy rabbits.

EXPERIMENTAL RESULTS

In healthy rabbits iproniazid lowered the total lipid level in the liver by 15% but had no effect on the other indices of lipid metabolism (Table 1).

Both in the plains and in the mountans, iproniazid lowered the concentrations of cholesterol and total lipids in the plasma, aorta, and liver,and increased the NEFA level in the plasma of rabbits with experimental atherosclerosis. In the plains, a decrease in area of the thoracic aorta occupied by atherosclerotic plaques was observed (from 40±9 to 22±5%; $P = 0.05$) and the incidence of cases of mild atherosclerosis (in which less than 30% of the surface area of the thoracic aorta was affected) was increased from 33 to 70% of cases. In the plains, iproniazid reduced the area of lipoidosis of the thoracic aorta from 48±9 to 34±4%, and in the mountains from 57±3 to 43±4% ($P < 0.05$).

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TABLE 1. Effect of Iproniazid on Lipid Concentration in Blood Plasma, Liver, and Aorta of Healthy Rabbits and Rabbits with Atherosclerosis

Rabbits	No. of rabbits	Blood plasma			NEFA in plasma (in μeq/ml)	Abdominal aorta		Liver		
		cholesterol (in mg/100 ml)	phospholipids (in mg/100 ml)	total lipids (in mg/100 ml)		cholesterol (in mg %)	phospholipids (in mg %)	cholesterol (in mg %)	phospholipids (in mg %)	total lipids (in mg %)
Healthy	12	42±1.6	88±3	267±15	0.56±0.04	99±4	370±10	392±17	1373±46	4661±225
Receiving iproniazid alone	5	38±2.4	92±4	251±16	0.71±0.08	95±6	382±14	376±13	1370±63	3980±175
P		0.5	0.5	0.5	> 0.05	0.5	0.5	0.5	0.5	< 0.05
Receiving cholesterol (in Frunze)	9	998±71	429±16	4680±290	1.14±0.05	214±11	442±16	2430±242	1400±71	8105±460
Receiving cholesterol and iproniazid (in Frunze)	10	770±51	386±11	3770±256	1.21±0.09	184±8	405±9	2081±180	1296±80	7180±279
P		<0.05	>0.05	< 0.05	0.5	<0.05	> 0.05	0.2	0.2	0.1
Receiving cholesterol (Tyuya Ashu Pass)	14	1397±81	484±27	4920±229	1.21±0.07	245±11	434±14	2824±146	1484±36	8796±330
Receiving cholesterol and iproniazid (Tyuya Ashu Pass)	14	992±61	436±17	3900±136	1.42±0.05	201±4	397±12	2210±222	1317±42	7220±171
P		< 0.001	0.2	< 0.01	< 0.01	< 0.01	> 0.05	< 0.05	< 0.01	< 0.001

Consequently, a 30-day course of small daily doses of iproniazid, starting 45 days after placing the rabbits on an atherogenic diet, definitely improved the state of lipid metabolism and reduced the severity of atherosclerotic lesions in the aorta.

The course of iproniazid caused hyperbilirubinemia in 3 of the 15 rabbits with atherosclerosis in the mountains and in one of the 12 rabbits in Frunze, which was not observed in rabbits with atherosclerosis not receiving iproniazid. These 4 rabbits also had an increased concentration of bilirubin in lipid extracts from the liver.

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