EFFECT OF THE MONOAMINE OXIDASE INHIBITOR IPRONIAZID ON THYROID FUNCTION IN HEALTHY RABBITS WITH EXPERIMENTAL ATHEROSCLEROSIS

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Administration of iproniazid to rabbits in a daily dose of 2 mg/kg for one month increases absorption of I^{131} by the thyroid gland and also increases the concentration of protein-bound iodine in the thyroid and blood plasma. Experimental atherosclerosis, produced by feeding cholesterol to rabbits, lowers the indices of thyroid function, whereas a course of iproniazid given to rabbits with experimental atherosclerosis restores these indices to normal.

Iproniazid, a monoamine oxidase inhibitor of the hydrazine group, induces the accumulation of biogenic amines in the brain and other tissues [13-15, 17], produces changes in the mental state [9, 16] and function of certain endocrine glands [3, 8, 10], influences metabolism [4, 5, 15], and is used in the treatment of certain mental and physical diseases [1, 6, 7, 11, 12, 16].

The object of the present investigation was to study the effect of iproniazid on thyroid function.

EXPERIMENTAL METHOD

The concentration of protein-bound iodine (PBI) in the blood plasma and thyroid gland [2], the weight of the gland, and its uptake of I^{131} during the 6 h after injection of an indicator dose were determined in male rabbits weighing 2.5-3.5 kg.

Control animals received water by mouth for 30 days, while the experimental rabbits received a solution of iproniazid in a daily dose of 2 mg/kg during the same period. The effect of this course of ipro-

TABLE 1. Changes in Thyroid Function in Healthy Rabbits and Rabbits with Experimental Atherosclerosis Receiving Iproniazid (2 mg/kg daily for one month; M ± m)

Group of animals	Number of animals	Weight of rabbits (g)	PBI in blood plasma (μg%)	Weight of thyroid		PBI in thyroid gland (mg %)	Absorption of I^{131} in % of dose administered	
				in mg	in mg/kg body weight		10 mg gland tissue	whole gland
Control (Frunze)	12	2820±101	1,92±0,05	144±8	51±3	3,49±0,11	0,82±0,06	11,8±1,3
Receiving iproniazid (Frunze)	5	2610±51	2,29±0,08	169±12	65±5	3,66±0,13	1,04±0,07	18,2±2,0
P			0,01	>0,05	<0,05	0,2	<0,05	0,02
Receiving cholesterol (Frunze)	9	2814±181	1,69±0,14	145±11	52±3	2,71±0,07	0,60±0,06	8,7±1,0
Receiving cholesterol and iproniazid (Frunze)	10	3190±136	1,80±0,11	157±13	55±4	3,00±0,15	0,66±0,06	10,4±1,4
P			0,5	0,5	0,5	>0,05	0,5	0,2
Receiving cholesterol (Tyuya-Ashu Pass)	14	2820±113	1,56±0,07	136±7	48±2	2,41±0,13	0,40±0,06	5,3±0,8
Receiving cholesterol and iproniazid (Tyuya-Ashu Pass)	14	2650±101	1,93±0,09	176±12	65±4	3,39±0,11	0,86±0,15	15,4±2,6
			0,001	0,01	0,001	0,001	0,001	0,001

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niazid was also studied on rabbits receiving cholesterol in a daily dose of 0.5 g/kg body weight with the diet for 45 days before and during the course of iproniazid, and also on rabbits with experimental atherosclerosis kept at a high altitude (at the Tyuya-Ashu Pass, altitude 3200 m above sea level). The existence of atherosclerosis was demonstrated by the macroscopic picture of the aortic wall and the cholesterol concentration in the aortic wall, blood, and liver. The atherosclerotic lesions in the aorta were equally severe in animals kept in the mountains and on the plain.

EXPERIMENTAL RESULTS

In healthy rabbits the course of iproniazid increased the absorption of I^{131} by the thyroid tissue significantly (by 54%). The weight of the thyroid and the PBI concentration in it and in the plasma were increased, but not by a statistically significant degree ($P > 0.05$; Table 1). These results show that iproniazid stimulates the iodine-concentrating function of the thyroid but has no effect on the formation of thyroid hormone. Thyroid activity, when inhibited in atherosclerosis (in animals kept on the plain), was stimulated by iproniazid. Although the degree of this stimulation was not statistically significant (compared with animals receiving cholesterol only), it was sufficient to obliterate the differences from the control animals.

In animals with atherosclerosis and kept at a high altitude, iproniazid significantly stimulated both the iodine-concentrating and the hormone-forming activity of the thyroid.

In the interpretation of these results, it must be remembered that the effect of a course of small doses of iproniazid, equivalent to human therapeutic doses, was investigated, and the compound was given in the late period of development of alimentary atherosclerosis, when thyroid function was definitely inhibited, especially in the animals kept at a high altitude.

These results suggest that stimulation of thyroid function may play an important role in the genesis of the catabolic action of iproniazid and other monoamine oxidase inhibitors of the hydrazine group on metabolism.

LITERATURE CITED

1. V. I. Bobkova and M. G. Khovanskaya, Ter. Arkh., No. 1, 27 (1965).
2. P. P. Giatsintova, Izvest. Akad. Nauk Kirgizsk. SSR, Seriya Biol. Nauk, 2, No. 6, 95 (1960).
3. V. G. Zoryan, Effect of Iproniazid, Indopan, and Reserpine on the Pituitary–Adrenal System, Candidate's Dissertation, Moscow (1966).
4. B. M. Kopytin, A. D. Dzhumaliev, V. S. Rodina, et al., Abstracts of Proceedings of the First Conference of Biochemists of the Central Asian Republics and Kazakhstan [in Russian], Alma-Ata (1966), p. 162.
5. B. M. Kopytin, V. S. Rodina, A. D. Dzhumaliev, et al., Proceedings of the First Scientific Biochemical Conference of Omsk Medical Institute [in Russian], Omsk (1967), p. 58.
6. B. P. Kushelevskii and A. N. Kokosov, Kardiologiya, No. 5, 46 (1961).
7. I. A. Levina, E. A. Gruzina, et al., Klin. Med., No. 10, 44 (1963).
8. N. K. Popova, Farmakol. i Toksikol., No. 2, 166 (1965).
9. A. P. Savinskaya, Zh. Nevropat. i Psikhiat., No. 12, 1462 (1959).
10. P. S. Brown, J. Endocrinol., 35, 161 (1966).
11. T. Cesarman, J. Clin. Exp. Psychopath., 19, 169 (1958).
12. P. Cossio, Ann. New York Acad. Sci., 80, 1009 (1959).
13. S. M. Hess, B. G. Redfield, and S. Udenfriend, J. Pharmacol. Exp. Ther., 127, 178 (1959).
14. O. Hornykiewicz, Wien. Klin. Wschr., 76, 289 (1964).
15. A. Pletscher, Dtsch. Med. Wschr., 86, 647 (1961).
16. G. Zbinden, Am. J. Cardiol., 6, 1121 (1960).
17. E. A. Zeller, J. Biol. Chem., 214, 267 (1955).