USE OF THE ADRENALIN TEST TO ASSESS SYMPATHICO-ADRENAL FUNCTION

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The effect of injection of adrenalin on the excretion of adrenalin, noradrenalin, dopamine, and DOPA in the urine was investigated in 84 subjects: 20 healthy persons and 64 patients with various forms of disturbance of autonomic nervous function. In healthy subjects changes in the excretion of the investigated substances may indicate activation of the sympathico-adrenal system and mobilization of its reserves, and the subsequent inhibition of activity in accordance with the "negative feedback" principle. In various diseases the response reaction of the sympathico-adrenal system is disturbed, and this is manifested by the predominant activation of the sympathetic component (in autonomic vascular crises), changes in the intensity of synthesis of intermediate products (in bronchial asthma), and disturbances of the "negative feedback" effect (in juvenile hypertension).

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If small doses of adrenalin are injected into an animal, fluctuations in the tone of the autonomic nervous system develop [2-4], and on this basis the adrenalin test has been introduced into clinical practice to determine the state of function of the autonomic nervous system [1]. However, no attempt has yet been made to study the complex relationships existing within the catecholamine group (the relationship between adrenalin, noradrenalin, dopamine, and DOPA) in the internal medium injection of exogenous adrenalin into man.

The object of the present investigation was to study the action of exogenous adrenalin on the urinary excretion of adrenalin, noradrenalin, dopamine, and DOPA in healthy subjects and in patients with various disturbances of functions of the autonomic nervous system.

EXPERIMENTAL METHOD

Observations were made on healthy adults and adolescents (altogether 20 persons) and also on adult patients with autonomic vascular paroxysms of hypothalamic origin, children with bronchial asthma, and young persons with juvenile hypertension (altogether 64 patients). Catecholamines and DOPA were determined by the method of Matlina and co-workers [5] in samples of urine collected every 4 h throughout the day (1st, 2nd, and 3rd) and in the night sample (4th) collected after a period of 12 h. Adrenalin was injected subcutaneously in a dose of 0.3-0.5 ml of a 0.1% solution after the first sample had been collected.

The investigations were carried out as follows. Changes in the excretion of catecholamines and DOPA without injection of adrenalin were studied in each subject on the first day, because it is well known that the excretion of catecholamines shows a definite 24-hour rhythm with the changes reaching a maximum during the day and a minimum at night. The results were expressed in nanograms per minute and in percentages of the morning sample of urine. The experiments were repeated on the day of injection of the adrenalin. The first sample of urine was collected before injection of adrenalin, and subsequent samples after its injection. These results also were expressed in nanograms per minute and as percentages of the sample of urine. To demonstrate the action of adrenalin with exclusion of the effect of 24-hour fluctuations in the substances tested, percentages obtained on the day of injection of adrenalin were divided by the indices on the control days, and these results in turn were expressed as percentages.

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TABLE 1. Changes in Excretion of Adrenalin, Noradrenalin, Dopamine, and DOPA After Injection of Adrenalin (M ± m)

Subject	No. of subjects	Substance studied	Sample of urine	Time after injection of adrenalin (in h)	Excretion (in ng/min)		P
					Control day	Day of experiment	
Healthy adults aged 20-45 years	10	Adrenalin	2nd	0-4	6.0 ± 1.2	23.2 ± 5.0	< 0.05
		Adrenalin	4th	8-20	2.6 ± 0.2	1.3 ± 0.4	< 0.02
		Noradrenalin	2nd	0-4	6.9 ± 0.7	13.8 ± 3.6	> 0.05
Patients aged 20-45 years with autonomic vascular crises of hypothalamic origin	22	Adrenalin	2nd	0-4	6.6 ± 0.8	16.2 ± 4.2	< 0.05
		Noradrenalin	2nd	0-4	8.0 ± 1.5	18.7 ± 4.7	< 0.05
		Dopamine	3rd	4-8	488.0 ± 125	213.0 ± 51	< 0.05
		DOPA	2nd	0-4	28.9 ± 4.8	17.2 ± 3.2	< 0.05
Children aged 4-5 years with bronchial asthma	32	Adrenalin	2nd	0-4	1.1 ± 0.22	6.76 ± 0.77	< 0.01
		Noradrenalin	2nd	0-4	2.76 ± 0.45	7.95 ± 1.26	< 0.01
Healthy adolescents aged 16-18 years	10	Dopamine	2nd	0-4	138.1 ± 28.2	77.9 ± 13.3	> 0.05
		Adrenalin	2nd	0-4	7.38 ± 1.47	31.34 ± 2.8	< 0.01
			3rd	4-8	7.41 ± 0.92	13.45 ± 2.45	< 0.05
			4th	8-20	3.73 ± 0.56	8.52 ± 1.4	< 0.01
Adolescents aged 16-18 years with juvenile hypertension	12	Adrenalin	2nd	0-4	9.23 ± 1.25	32.2 ± 3.74	< 0.01
		Adrenalin	3rd	4-8	6.69 ± 0.91	11.76 ± 1.52	> 0.01
		Adrenalin	4th	8-20	3.48 ± 0.35	9.42 ± 1.83	< 0.01
		Noradrenalin	2nd	0-4	16.25 ± 3.38	26.4 ± 4.2	> 0.05
		Noradrenalin	3rd	4-8	12.1 ± 1.6	24.6 ± 2.28	< 0.01
		Noradrenalin	4th	8-20	8.79 ± 1.65	18.15 ± 3.44	< 0.05

EXPERIMENTAL RESULTS

Only the results of investigations in which statistically significant changes (expressed in nanograms/min) are given in Table 1, and the results (in percentages) obtained by the method described above are illustrated in Fig. 1.

The concentration of adrenalin excreted in the urine of the healthy persons after injection of adrenalin, expressed as a percentage of the control day was 344, and the corresponding figures for noradrenalin was 201 and for DOPA 156% (2nd sample of urine). Changes in the excretion of adrenalin and noradrenalin were statistically significant. The excretion of dopamine was not significantly altered. In the next samples of urine a consistent decrease in the content of adrenalin, noradrenalin, dopamine, and DOPA was observed, the decrease in the adrenalin level being statistically significant.

In healthy adolescents, just as in the adults, injection of adrenalin caused an increase in its excretion in the 2nd sample of urine (to 436%). Subsequently the excretion of adrenalin remained high, but less so than in the 2nd sample of urine. The excretion of adrenalin was increased after the adrenalin test to 134%, but in subsequent tests its concentration fell.

In the urine of patients with autonomic vascular crises, collected after injection of adrenalin (2nd sample), the adrenalin concentration was increased by a much smaller degree over its level on the control day than in the healthy subjects (to 175%). Meanwhile the excretion of noradrenalin was rather higher than in the healthy subjects (240%). The excretion of DOPA fell to 69% but the excretion of dopamine remained essentially unchanged. In subsequent samples of urine the excretion of all catecholamines and DOPA showed small but consistent decreases.

In the children with bronchial asthma a more marked increase in the adrenalin excretion was observed than in the healthy subjects (up to 698%). The excretion of noradrenalin also was increased, changes in the DOPA content in the urine followed the same direction, but the dopamine excretion was reduced. In adolescents with the juvenile form of hypertension, the excretion of adrenalin after the adrenalin test was increased on the average up to 376% (2nd sample). Subsequently the excretion of adrenalin fell gradually, but just as in the healthy subjects it remained at a level slightly higher than in the controls. The noradrena-

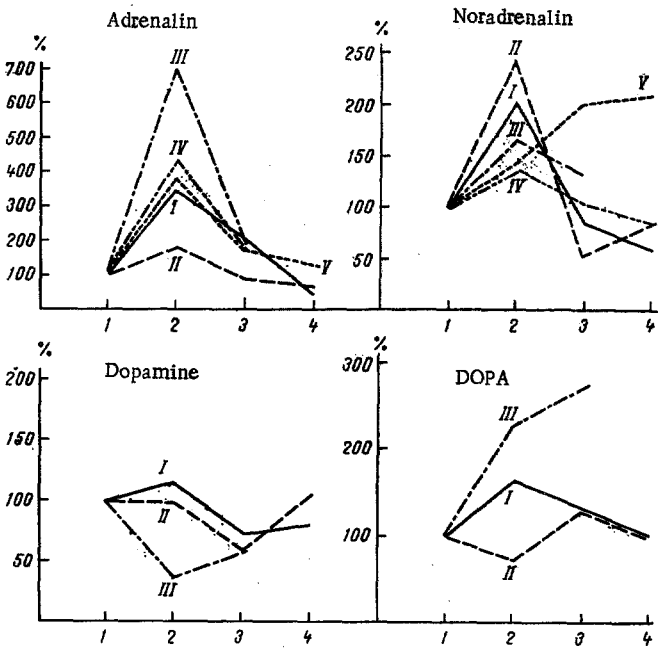

Fig. 1. Effect of injection of adrenalin on excretion of adrenalin, noradrenalin, dopamine, and DOPA. I) Healthy subjects; II) patients with autonomic vascular crises of hypothalamic origin; III) children with bronchial asthma; IV) healthy adolescents; V) adolescents with juvenile hypertension. 1, 2, 3, 4) Samples of urine. Results expressed as percentages of indices for 1st sample of urine and as a ratio of the corresponding results on the control days of investigation (see "Experimental Method").

lin excretion was increased to 143% (2nd sample), and in subsequent samples, in contrast to the healthy adolescents, it remained increased by a statistically significant margin (201 and 209%).

According to the literature, adrenalin injected into the body disappears rapidly from the blood stream and 3-5% of it is excreted in the urine in an unchanged form [8-15].

The results show that during the first few hours after injection of adrenalin into adult subjects its excretion was increased on the average by 3.8% of the dose injected. However, comparison of clinical manifestations produced by injection of adrenalin with the level of adrenalin-like substances in the blood suggests that the increase in the adrenalin concentration in the urine during the first few hours after its injection may be due not only to excretion of exogenous hormone, but also to activation of the sympathico-adrenal system [1].

The same mechanism probably lies at the basis of the increase in the excretion of noradrenalin and DOPA which we observed in the first few hours after the adrenalin test. The possibility likewise cannot be ruled out that exogenous adrenalin may displace noradrenalin from the nerve endings [6, 7, 11, 16]. The decrease in the excretion of catecholamines and DOPA by healthy subjects in the 2nd-4th samples of urine collected after injection of adrenalin may be explained by subsequent inhibition of the sympathico-adrenal system by exogenous adrenalin in accordance with the "negative feedback principle."

In patients with autonomic vascular paroxysms of hypothalamic origin the excretion of adrenalin in the sample of urine collected after the adrenal test was increased to a lesser degree than in the healthy subjects. However, the noradrenalin excretion was increased more. This may be due to the higher reactivity of the sympathetic (nervous) component of the sympathico-adrenal system and to insufficient activation of the hormonal (adrenal) component. Another possibility is that the more active uptake of adrenalin by the nerve endings than normally and the more intensive displacement of noradrenalin from them may

play an important role. It may thus be considered that in patients with periodic autonomic vascular paroxysms the catecholamine metabolism is disturbed, and the cause or effect of this is a disturbance of the mechanisms regulating the state and activity of the sympathico-adrenal system. In children with bronchial asthma, in contrast to healthy subjects, a marked dissociation was observed between the direction of the changes in the excretion of adrenalin, noradrenalin, dopamine, and DOPA in the first samples of urine collected after injection of adrenalin. Whereas the excretion of adrenalin, noradrenalin, and DOPA was increased, the excretion of dopamine fell. This suggests that in children with bronchial asthma dissociation occurs between the intensity of formation of the various intermediate products of biosynthesis of the catecholamines appearing after activation of the sympathico-adrenal system by exogenous adrenalin.

In patients with juvenile hypertension, in contrast to healthy adolescents, no decrease took place in the excretion of adrenalin and noradrenalin in the 3rd and 4th samples of urine. In them the "negative feedback" effect, so clearly marked in the healthy adolescents, was evidently weak. This may be important in the pathogenesis of the disease.

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