

BIO-MEDICAL RESEARCH
DOCUMENT DESCRIPTION FORM

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 1980 0063267 UC
 year as-1961- File number Sub-Index
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#155. GLUCOCORTICOID FUNCTION OF THE ADRENAL CORTEX IN PATIENTS WITH
CHRONIC INTOXICATION WITH CERTAIN UNSATURATED CHLORINATED HYDROCARBONS

Ye. P. Rumyantseva and L. A. Goryacheva (Dzerzhinsk)
Affiliate of the Gor'kiy Institute of Occupational Hygiene
and Occupational Diseases

Translation of: "Glyukokortikoidnaya Funktsiya Kory Nadpochechnikov
u Bol'nykh s Khronicheskoy Intoksikatsiyey Nekotorymi Nepredel'nymi
Khlorirovannymi Uglevodorodami," Gig. Truda, 12, pp. 16-19, 1968.

R&S 109924

GLUCOCORTICOID FUNCTION OF THE ADRENAL CORTEX IN PATIENTS WITH CHRONIC INTOXICATION WITH CERTAIN UNSATURATED CHLORINATED HYDROCARBONS

Ye. P. Rumyantseva and L. A. Goryacheva (Dzerzhinsk)

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Gig. Truda, 12, pp. 16-19, 1968.

The hormones of the adrenal cortex take active participation in the so-called adaptation syndrome which provides the capacity of the organism to withstand the constantly changing conditions of the environment. From data of the literature it is known that different toxic substances (gasoline, octane, benzene, lead, aniline, carbon sulfide, carbon tetrachloride, mercaptophos, etc.) cause changes in the functional condition of the adrenal cortex (N. A. Minkina, L. I. Geller; L. E. Gorn; N. L. Kanner, and others). Most authors note hyperfunction during the acute effect of toxic substances, while with the chronic effect they note hypofunction of the adrenal cortex.

We studied the glucocorticoid function of the adrenal cortex in patients with chronic intoxication with unsaturated and chlorinated hydrocarbons (ethylene, propylene, trichlorethylene, and vinyl chloride). 105 patients ranging in age from 28 to 52 years were under observation. The stage of their work and contact with the indicated substances ranged from 2-15 years. Most of them were in contact with several products and were subjected to long term exposure to them in small concentrations.

With respect to clinical symptoms, chronic intoxication of unsaturated and chlorinated hydrocarbons, notwithstanding a certain specificity of effect, occurred monotypically predominantly in the form of changes in the nervous system. V. A. Antonyuzhenko demonstrated that monotypicity of the clinical picture of chronic intoxication with the given poisons is caused by their overall capacity to induce narcosis. This characteristic, which consists in primary manifestations of the narcotic effect of the named substances, is explained by this author as being due to the long term effect of the substances in small concentrations. Moreover, it is also necessary to take into account the fact that most patients work in contact with several substances simultaneously. In regard to this, the clinical picture and the results of the investigation of the functional condition of the adrenal cortex are presented for all patients.

During the clinical examination the workers complained of headache, dizziness, heightened fatigue, sleep disorders, decrease in memory capacity, sweatiness, paresthesia, and pain in the extremities, instances of paling of the finger tips and toes, edema of the fingers and toes, pain and unfavorable sensations in the region of the heart. The objective investigation revealed significant polymorphism of the neurological symptoms. The most constant symptoms were disorders of pain

sensation -- hypo- or hyperalgesia of the "glove" and "stocking" type, frequently associated with elements of hyperpathia. Vegetative-vascular changes were frequently noted, taking the form of pathological changes of dermographism, local angiodystonic crises of the Reyno type, asymmetries of blood pressure, inclination to hypotony lability of pulse and disorder of the cardiac rhythm. The combination of these disorders created the characteristic picture of vegetative-sensory polyneuritis or toxic angioneurosis, dependent upon the degree of pronouncement of any particular syndrome. Frequently there was asymmetry of the tendinous reflexes with their regeneration. Moreover, disorders of the cranio brain innervation were observed -- disorder of sensitivity in the face along the courts of the trigeminal nerve, weakness of convergence, tremor of the eyeball and nystagmus, anisocoria, instability of glance and flattening of the nasolabial plica. This symptoms complex indicates the appearance of toxic encephalopathy. All patients, with respect to the severity of intoxication, comprised two groups. In the first of these, the syndrome of vegetative-sensory polyneuritis was usually detected against a background of astheno-vegetative symptoms, while in the second group there were usually symptoms of toxic encephalopolyneuritis (V. A. Antonyuzhenko).

The method of studying glucocorticoid function of the adrenals included the Thorn test, determination of the content of leucocytes in the peripheral blood and of 17-oxycorticosteroids in the daily urine. The investigations were conducted before and after loading with ACTH hormone, which was administered intramuscularly in a dose of 20 units. The urine was collected over the course of the day from the moment of administration of ACTH. The Thorn test was studied by us in 103 patients. The investigations showed that in 34 of the 103 persons with chronic intoxication with unsaturated and chlorinated hydrocarbons this test was altered. In 33 persons of these the level of eosinophils decreased by 10-40%, in 1 patient the content of eosinophils following the administration of ACTH, on the other hand, increased (inverse reaction). Changes in the Thorn test were most frequently observed in persons with the more pronounced form of intoxication. Thus, if in the first group an altered test existed in 26.4% (18 of 68) patients, in the second group a negative test was revealed in 45.6% (16 of 35) patients.

According to data of the literature (L. I. Yegorova and L. N. Siryatskaya; Ye. V. Sergel'; V. F. Zaytsev; G. V. Kudryavtsev; L. M. Petrenyuk), neutrophilic leucocytosis (without an increase in the content of rod-nucleated forms), lymphopenia and monocytopenia in response to the administration of ACTH can also serve as a criterion for maintenance of glucocorticoid function of the adrenals. In our observations, leucocytosis following the administration of ACTH was absent in 37 (35.8%) of the patients, and somewhat more frequently (43% of the cases) in the second group. In 18 persons following the administration of ACTH, leucocytosis was slight (an increase of 500-800 leucocytes). The negative reaction to ACTH simultaneously according to both indices (eosinophils and leucocytes) was recorded in 24 (23.3%) of the examinations; of these in 19% of the patients of the first group and in 31.4% of the patients in the second group. Of 18 persons, we observed the character of the leucogram in response to the administration of ACTH. Of 10 of these the reaction was normal and was manifested by a significant decrease in the content of lymphocytes and monocytes. In 3 persons the level of lymphocytes decreased while the level of monocytes remained as before. In 5 patients the content of lymphocytes and monocytes practically did not change. Among 66 persons the Thorn test and the content of leucocytes were studied in dynamics over the course of 2 years. Each patient was subjected to 4-5 blood analyses. The dynamic observation demonstrated that the character of the Thorn test was not constant; however a tendency toward the negative reaction was maintained.

The urinary corticosteroids were determined by us after the Reddy method in the modification of Yu. N. Gurskiy and G. V. Ordynets. In order to make the limits of the norm more exact with respect to fluctuations of 17-oxycorticosteroids, their content was studied in 20 patients. Their level varied from 3 to 12.5 mg per day, which corresponds with the data of the literature (G. Ya. Sharanova and Yu. K. Skripkina, P. A. Kanner). Spontaneous content of 17-oxycorticosteroids was studied by us in 105 patients. This content fluctuated within wider limits than among healthy people (from 1.8 to 30 mg per day). In a majority (73) of the patients, spontaneous content of 17-oxycorticosteroids was 3-12 mg, which corresponds to normal indices. In 32 (30.4%) of the examined patients there were deviations with respect to the content of 17-oxycorticosteroids: in 19 people this index had increased to 14-30 mg, while in 13 it decreased to 1.8-2.6 mg. Deviations in the content of 17-oxycorticosteroids were more frequently revealed in persons with the more pronounced symptoms of intoxication (in the first group in 26.1% of those examined, in the second group in 39%).

The investigation of spontaneous content of 17-oxycorticosteroids was inadequate to form a judgement concerning hypo- or hyperfunction of the adrenal cortex. The elevated level of 17-oxycorticosteroids can be combined with exhaustion of the reserve capacities of the organ, while decreased excretion of 17-oxycorticosteroids is also possible with maintenance of potential reserves of the adrenal cortex (G. Ya. Sharapova). The most complete concept of the functional condition of the adrenals can be obtained only during an investigation of the excretion of 17-oxycorticosteroids in response to functional loading with ACTH. According to data of the literature, stimulating the adrenals with ACTH causes a daily increase in the content of 17-oxycorticosteroids which is 2 fold. Cope and Bleak observed an increase in the level of 17-oxycorticosteroids by 21.8-25.7 mg per day following the administration of 50 units ACTH. In our observations of healthy people, the content of 17-oxycorticosteroids in response to the administration of 20 units ACTH increased by 10-20 mg per day. The results of studying the daily secretion of hormones by the adrenals in response to the administration of ACTH in 87 healthy people are shown in the table.

SECRETION OF 17-OXYCORTICOSTEROIDS FOLLOWING ADMINISTRATION OF ACTH

1) Группа больных	5) Число Солнских	21) Уровень 17-оксикортикостероидов									
		6) увеличился (нормальная реакция)				11) не изменился (отрицательная реакция)				16) снизился (инверсная реакция)	
		7) % больных	8) $M \pm \sigma$ (в мг/сутки)		12) % Солнских	13) $M \pm \sigma$ (в мг/сутки)		17) % Солнских	18) $M \pm \sigma$ (в мг/сутки)		20) 11КВ всего
			9) до введения АКТГ	10) после введения АКТГ		14) до введения АКТГ	15) после введения АКТГ		19) до введения АКТГ	20) после введения АКТГ	
2) 1-я	55	15(27.2)	6.3 ± 1.4	24.9 ± 4.1	29(52.7)	7.4 ± 1.55	7.2 ± 1.4	11(20)	14.6 ± 2.9	6.2 ± 0.9	
3) 2-я	32	9(28.0)	6.1 ± 1.5	21.3 ± 3.2	11(34.4)	6.8 ± 1.4	6.5 ± 1.6	13(40.6)	17.3 ± 3.6	6.7 ± 1.4	
4) Всего	87	24(26.4)	6.2 ± 1.35	24.7 ± 4.2	43(49.5)	7.1 ± 1.25	7.0 ± 1.4	24(27.9)	16.1 ± 3.6	6.5 ± 1.2	

Key: 1, Group of patients; 2, First; 3, Second; 4, Total; 5, Number of patients; 6, Increased (normal reaction); 7, % of patients; 8, $M \pm \sigma$ (in mg/days); 9, Prior to administration of ACTH; 10, Following administration of ACTH; 11, No change (negative reaction); 12, % of patients; 13, $M \pm \sigma$ (in mg/days); 14, Prior to administration of ACTH; 15, Following administration of ACTH; 16, Decrease (inverse reaction); 17, % of patients; 18, $M \pm \sigma$ (in mg/days); 19, Prior to administration of ACTH; 20, Following administration of ACTH; 21, Level of 17-Oxycorticosteroids.

The normal reaction of the adrenal cortex, according to the materials of investigations of 17-oxycorticosteroids, was revealed in only 23 (26.4%) of the patients, and with approximately the same frequency in both groups. In half (43 of 87) of the patients the reaction of the adrenal cortex to the administration of ACTH was absent. The content of 17-oxycorticosteroids in these patients almost remained unchanged in comparison with the original data. This indicates a decrease in function of the adrenal cortex. In 21 persons an inverse reaction was observed. Following the administration of ACTH, the daily content of 17-oxycorticosteroids in their urine not only did not increase, but, on the other hand, decreased by 5-15 mg, which indicates inadequate initial and potential reserves of the adrenal cortex. The inverse reaction basically occurred in persons with a high original content of 17-oxycorticosteroids, more frequently in the second group, among patients with more pronounced forms of intoxication (in 20% of the first group and in 31.2% in the second group).

The results of investigating the Thorn test were compared by us with the data of studying the 17-oxycorticosteroids. The absence of reaction with respect to the adrenal cortex in response to the administration of ACTH, according to the materials of investigating the 17-oxycorticosteroids, was revealed more frequently (73%) than according to the data of the Thorn test (48.2%). Simultaneously, a change in the indices of the Thorn test (level of eosinophils and leucocytes) and the 17-oxycorticosteroids occurred in 47% of the patients, more frequently in the second group (60%) coinciding than in the first group (40%).

The obtained results indicate inadequate functioning of the adrenal cortex in patients with chronic intoxication of unsaturated and chlorinated hydrocarbons. The physiological load with ACTH permitted us to reveal latent deficiency of the adrenal cortex, the exhaustion of present and potential capacities of this organ.

Conclusions

1. In patients with chronic intoxication with unsaturated and chlorinated hydrocarbons (according to the data of investigating the Thorn test, the content of leucocytes and 17-oxycorticosteroids), there is disruption of the glucocorticoid function of the adrenals, which is characterized by exhaustion of present and potential capacities of the organ.
2. An investigation of the secretion of 17-oxycorticosteroids in response to the administration of ACTH is a more sensitive test of the functional condition of the adrenal cortex than the Thorn test.
3. The known relationship between the functional condition of the adrenal cortex and the severity of intoxication was noted.

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R&S 109929