CLINICAL DESCRIPTION OF BY-EFFECTS OF ENDOCRINOTHERAPY AT SHARP RHEUMATIC FEVER

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Abstract. *The article presents the study of the clinical manifestations of side effects of corticosteroid therapy in children, with acute rheumatic fever, which was very high (73%). Hormone therapy is recommended to be prescribed with caution and only in case of severe complicated course of the disease, since stopping the introduction of hormones leads to withdrawal syndrome or to exacerbation of the process.*
Keywords: *acute rheumatic fever, glucocorticosteroids, adverse reactions.*

Introduction. From the middle of the 20th century. Glucocorticoids have rapidly entered the practice of treating rheumatic diseases, including ARF. Treatment tactics included the use of small doses of hormones (0.5–0.7 mg/kg) as a daily dose over a short course of 1–1.5 months. with a gradual reduction in the dose of the drug and its discontinuation during this period [1,2]

Glucocorticoids are effective therapeutic agents in many cases. It is necessary, however, to take into account that they can cause a number of side effects, including a complex of symptoms. Adverse reactions from the central nervous system during treatment with hormones, according to the literature, are observed most often. In children treated with corticosteroids, according to the authors' observations, ulcerative lesions of the gastrointestinal tract appear less frequently than in adults, but the prognosis in children is much more severe [3,4].

The purpose of our study was to study the clinical manifestations of side effects of corticosteroid therapy in children with acute rheumatic fever.

Materials and methods of research. The study was conducted at the bases in the cardio-rheumatology departments of the TashPMI clinic and the 4-children's city hospital in Tashkent, for the period 2014 - 18. We observed 254 children with acute rheumatic fever aged 7–15 years who were treated with corticosteroids. The children were diagnosed according to the ICD-10 classification of ARF (acute rheumatic fever) adopted in 2003.

Corticosteroids and ACTH (adrenocorticotropic hormone) were used against the background of complex treatment, mainly in the early stages of the onset of the disease or during exacerbation of the process. The duration of the course ranged from 4 to 6 weeks, sometimes more. Adverse reactions and complications during treatment with corticosteroids and ACTH that occurred in the children we observed were divided into 3 groups according to the severity of the manifestations.

Results and its discussion. The results of our studies showed that out of 254 patients, adverse reactions were identified in 185 children - in 72.8% of cases. In most children they were mild, but in 0.9%, due to deterioration of their condition, it was necessary to resort to appropriate therapeutic measures to eliminate them.

Group 1 includes milder adverse reactions that do not affect the course of the underlying disease and do not interfere with hormonal treatment. They were expressed in the appearance of

Cushingoid syndrome (rounding of the face), a transient increase in blood (maximum) pressure. Leukocytosis, the formation of age spots, acne, rashes such as folliculitis, stretch marks on the skin, menstrual irregularities, hypertrichosis, etc. were also observed.

Table 1

Adverse reactions during treatment with corticosteroids and ACTH that do not affect the course of the underlying disease in children with acute rheumatic fever

Nature of side effects reactions	Number of children with adverse reactions during treatment					
	only 207	ACTH (n-54)	Cortisone (n-24)	prednisolone (n-97)	Dexamethasone (n-53)	Triamcinolone (n-26)
Cushingoid syndrome (rounding of the face)	47	7	8	19	10	3
Leukocytosis	65	16	10	23	8	8
Transient increase in blood pressure	12	3	3	4	1	1
Pigment spots, acne,	9	2	4	1	1	1
folliculitis type rash	18	-	1	9	4	4
Stretch strips	14	-	-	11	3	-
Menstrual disorders	20	-	8	6	6	-

Most of the observed adverse reactions were short-term and usually disappeared soon after discontinuation of the hormonal drug by the end of the 3rd week, sometimes at the 5th and 6th week of treatment. However, stretch marks (striae) in the thighs, mammary glands and abdomen that appeared in girls of puberty, as well as hypertrichosis in 16 younger children, persisted for a longer time - up to 6-8 months after the end of hormonal treatment. Menstrual irregularities, expressed in delayed menstruation, were short-lived. Restoration of the menstrual cycle after completing the course of hormonal treatment was observed in 6 of them after 1 month, in 14 girls after 2 and 3 months.

There was a certain difference in the frequency and nature of the observed adverse reactions when treated with various hormonal drugs. Thus, the appearance of facial roundness, usually observed at the end of the 3rd or 4th week of treatment, was more pronounced when treated with ACTH, cortisone and prednisolone and was almost not observed when using triamcinolone. Roundness of the face was more often accompanied by a general increase in weight and increased

deposition of fat on the body; much less often, the appearance of the Cushingoid symptom was isolated.

A transient increase in blood pressure in the range of 10-20 mm was more pronounced during treatment with ACTH, cortisone and prednisolone and was rarely observed during treatment with triamcinolone. Leukocytosis as a manifestation of the side effects of hormones was observed in approximately 35% of patients at the end of the 1st and beginning of the 2nd week of treatment, was equally often observed when using various corticosteroids and ranged from 10,000-13,000, reaching 25,000 in only 2 children. At the same time, there was no deterioration in the general condition, increased activity of the rheumatic process, or signs of any new infection. After reducing the corticosteroid dose, the leukocyte count in the blood returned to normal.

Adverse reactions also included severe tachycardia, increased blood pressure, significant weight gain (more than 2 kg per course of treatment), disruption of the nervous system in the form of anxiety, headache, increased excitability, insomnia, euphoria or depression. The most common of them, as can be seen in Table 2, were tachycardia and hypertension, which does not contradict the literature data. They usually appeared in the 2nd and 3rd weeks of hormonal treatment and were more often observed when using cortisone and prednisolone. In most children, tachycardia and hypertension decreased or disappeared as the drug dose was reduced. When these phenomena persisted, had an adverse effect on the activity of the cardiovascular system, and the need to continue hormonal treatment was obvious, additional antihypertensive agents such as reserpine, raunatin, and dibazole were used. When using the latter, adverse reactions to hormones usually disappeared quickly, which made it possible to continue and complete the necessary course of hormonal treatment.

A tendency toward significant weight gain was observed with the use of primarily cortisone and ACTH. This was due not only to changes in fat, carbohydrate and protein metabolism, but also to significant changes in mineral-water metabolism, especially retention of sodium and water salts, decreased diuresis and increased potassium excretion, which contributed to weight gain and sometimes the appearance of edema. To a lesser extent, weight gain was observed with the use of prednisolone and dexamethasone, and with treatment with triamsinolone, even the opposite reaction—weight loss—was observed, which is likely due to increased sodium excretion and diuresis. According to our observations, a small number of children (7.7%) treated with corticosteroids experienced symptoms of increased excitability, insomnia and euphoria, which usually appeared by the end of the 2nd week of treatment and were more often observed when taking cortisone and administering ACTH. We did not observe any mental disorders.

We included complications associated with a decrease in immunological reactions in the 3rd group of side effects during treatment with corticosteroids. Suppression of tissue resistance to bacterial and purulent infection, which is associated with their ability to reduce the reaction of lymphoid and other tissues to infectious and any damaging influences, reduces the inflammatory reaction of tissues and inhibits the formation of antibodies.

Such reactions were observed in 11% of children. The most frequently observed exacerbation of chronic focal infection - chronic tonsillitis, sinusitis, etc. In some children, infectious diseases of a strepto-staphylococcal nature such as pyoderma, phlegmon of the forearm, aphthous stomatitis, etc. were observed. In the majority of our children (67%), the phagocytic activity of leukocytes decreased and the complementary energy of the blood decreased.

Table. 2

Adverse reactions during treatment with corticosteroids and ACTH, adversely affecting the course of the underlying disease in children with acute rheumatic fever

Nature of side effects reactions	Number of children with adverse reactions during treatment					
	only 207	ACTH (n-54)	Cortisone (n-24)	prednisolone (n-97)	Dexamethasone (n-53)	Triamcinolone (n-26)
Tachycardia	78	10	34	26	5	3
hypertension	80	11	27	29	8	5
obesity	33	11	12	5	3	2
Astheno-vegetative disorder	16	5	3	4	1	3

Among 254 children treated by us with corticosteroids, 3 girls (0.95%) were found to have fresh gastric ulcers, which did not manifest themselves clinically during life. These children were admitted with a severe, continuously relapsing course of acute rheumatic fever with symptoms of pancarditis and polyserositis, severe valvular lesions of the heart, circulatory failure of II-B and III degrees. Despite active complex treatment with prednisone, they were unable to stop the steady progression of the rheumatic process, which resulted in death. In addition, in 3 more children with a similar severe course of acute rheumatic fever, old stomach ulcers were identified, which worsened during the period of hormonal treatment and ended in perforation with intestinal bleeding in 1 child. Unfortunately, it was not possible to establish the beginning of their occurrence; Apparently, their course was previously asymptomatic.

Conclusion. Despite the positive effectiveness of hormone therapy in severe ARF, side effects are very often observed and account for a very high rate (73%). Therefore, it is recommended to prescribe hormone therapy with caution, since stopping its administration leads to withdrawal syndrome or an exacerbation of the process.

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