ORIGINAL ARTICLE

CONTENTS

Adrenal hormone and histamine levels in children with vasomotor rhinitis

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ABSTRACT

Aim: To study the levels of adrenal hormones and histamine in children with vasomotor rhinitis.

Materials and Methods: Hormones secreted by the adrenal glands are active biological regulators of metabolism in the body. Research into the hormonal function of the adrenal glands is of great importance for studying the pathogenesis of certain allergic diseases. Spectrofluorometric blood examination for the presence of 11-OCS (sum total content of hydrocortisone and corticosterone) and histamine, and also examina¬tion of the urine for adrenaline and noradrenaline content were conducted in children suffering from vasomotor rhinitis.

Results: The results obtained were statistically proces¬ses and considered from the aspect of dependence on the form of vasomotor rhinitis (allergic and nonallergic rhinitis) and age. Apparently healthy children (30) were examined biochemically for control. An increased content of the adrenal gland hor¬mones (11-OCS) was found to be present in the blood of children with vasomotor rhinitis. Histamine content was elevated only in children with an allergic rhinitis. Adrenaline and noradrenaline excretion increased with the advance of age, but was unchanged in rhinitis.

Conclusions: Consequently, in this disease there was a functional reaction of the adrenal cortex, but no functional changes occurred in the medulla. An increa¬sed histamine content confirmed the allergic nature of the disease.

KEYWORDS: teenagers, primary school children, vasomotor rhinitis, adrenal hormone, histamine levels

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INTRODUCTION

Vasomotor rhinitis is characterised by diverse aetiology and complex pathogenesis that has not been sufficiently studied. Currently, clinicians distinguish between two forms of vasomotor rhinitis: allergic and neurovegetative in adults (Alan P. Baptist, Sharmilee Nyenhuis) [1] and allergic and non-allergic in children (Karabaev, H., Nurmukhamedova, F., Egamberdieva, Z., & Hamdamov, Z.) [2]. Despite the similarity of the clinical manifestations of these forms, their aetiology and pathogenesis are different. The first, i.e. allergic, form is considered a manifestation of general allergy, and the second – mainly as a manifestation of nervous system dysfunction. Both forms are associated with endocrine system dysfunction. Since the hormones secreted by the adrenal glands are active biological regulators of metabolism in the body, the study of adrenal gland hormone function is of great importance for understanding the pathogenesis of many diseases, including allergic diseases.

The adrenal glands consist of two anatomically distinct layers: the cortex and the medulla. The adrenal cortex produces a number of steroid compounds, of which three hormones have the greatest biological activity: cortisol (hydrocortisone), corticosterone and aldosterone. The medulla of the adrenal glands secretes two hormones: adrenaline and noradrenaline. Therefore, in order to assess the hormonal function of the adrenal glands, it is necessary to determine the content of hormones secreted by each of the adrenal glands. However, the literature more often contains studies in which the authors limit themselves to investigating the hormones secreted by a single part of the adrenal glands.

AIM

The aim of this article is to study the levels of adrenal hormones and histamine in children with vasomotor rhinitis.

MATERIALS AND METHODS

In elderly people with vasomotor rhinitis, the functional state of the adrenal cortex was studied in 2016 by Alan P. Baptist and Sharmilee Nyenhuis by determining the daily excretion of 17-OCS. The scientists found that patients with allergic vasomotor rhinitis have hidden adrenal cortex insufficiency: the excretion of corticosteroid hormones in urine is within normal limits, but under stress (single administration of ACTH), their amount either does not change or increases to a much lesser extent than in middle-aged people. Based on this, they concluded that there is a decrease in the reserve capacity of the adrenal cortex in the allergic form of vasomotor rhinitis. Alan P. Baptist and Sharmilee Nyenhuis studied the total content of hydrocortisone and corticosterone (11-OCS) in the blood plasma of adults with vasomotor rhinitis and found an increased content compared to similar indicators in practically healthy people [1]. Alekseeva, L., Bessonova, T. et al. study the level of cortisol and laboratory indicators of systemic inflammation in children with various variants of BPM and VE course depending on the period of the disease (acute period, reconvalescence) to specify their role in the pathogenesis of acute neuroinfections [3]. Scientists investigated hematological indicators, the level of cortisol, C-reactive protein in blood serum of 60 children, 39 of them had BPM and 21 ones – VE. They identified characteristic features of cortisol content in children with bacterial and viral neuroinfections depending on the course of the disease.

Andrew A Crawford, Stefan Soderberg, Clemens Kirschbaum et al. investigated whether cortisol is a causal risk factor for cardiovascular disease and ischaemic heart disease in the general population [4].

The hormonal function of the adrenal medulla has also attracted the attention of researchers. Mary Beth Bauer and Kevin P.M. Currie noted reduced excretion of adrenaline and noradrenaline in children with whooping cough, especially in the acute phase of the disease [5].

Guntinas-Lichius O, Geißler K, Mäkitie AA et al. have provided practical recommendations for the diagnosis and treatment of recurrent acute tonsillitis, including informed decision-making regarding tonsillectomy [6]. Scientists have concluded that there was a decrease in the excretion of adrenaline and noradrenaline in children aged 3 to 15 years with chronic tonsillitis. The same feature was also found in patients with rheumatism.

The role of histamine in the pathogenesis of allergic diseases in adults and children is now well known. Thus, in bronchial asthma in adults and children, as well as in respiratory allergies in childhood, many authors note an increase in the content of histamine in the blood (Yamauchi, K., & Ogasawara, M.; Thangam, E. B., Jemima, E. A., Singh, H. et al.; Abaturov, A., Krivusha, E., Agafonova, E. et al. ; Burlutskaia A.V., Firsova V.N.) [7].

In children with rheumatoid arthritis (also an allergic disease), the level of histamine in the blood exceeds the norm (Kasapçopur, Ö., & Barut, K.) [8]. At the same time, there is no data in the literature on the content of histamine in the blood of children with vasomotor rhinitis. As for adults, allergic rhinosinusopathy (Masood, A., Moumoulidis, I., & Panesar, J.) [9] and the allergic form of vasomotor rhinitis (Leader P, Geiger Z.) [10], an increase in blood histamine levels has been established with normal histamine content in patients with the neurovegetative form of rhinitis.

ETHICS

This work complies with the principles of the Declaration of Helsinki.

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

Based on the data presented in the literature, we set ourselves the task of conducting a biochemical examination of children with allergic and non-allergic rhinitis in order to determine the total content of hydrocortisone and corticosterone (11- OCS) in blood plasma, histamine content in blood, and adrenaline and noradrenaline excretion in daily urine depending on the form of rhinitis and the age of the sick children.

The histamine content in whole blood was determined using a modern, highly sensitive and specific spectrofluorimetric method developed by A. Alqahtani, T. Alqahtani & A. H. Abdelazim [11].The content of 11- OCS in blood plasma was determined using the spectrofluorimetric method Zeidler, R., Biemann, R., Ceglarek, U., Kratzsch, J., Isermann, B., & Gaudl, A. [12]. The content of adrenaline and noradrenaline in daily urine was examined using the method developed by Thomas, A., Geyer, H., Mester, H.J. et al. [13]. Hormone standards were obtained from the V.P. Komissarenko Institute of Endocrinology and Metabolismof the National Academy of Medical Sciences of Ukraine. When performing analyses in all determinations, the fluorescence of solutions was measured using a Hitachi F-7000 Fluorescence Spectrophotometer.

We monitored 92 children aged 5 to 18 years with vasomotor rhinitis. Working with children required

Table 1. Adrenal hormone levels in blood and urine in children with various forms of vasomotor rhinitis

Form of rhinitis	11-OCS, µg %				Adrenaline, µg/day				Noradrenaline µg/day			
	number of people surveyed	M	σ	m	number of people surveyed	M	σ	m	number of people surveyed	M	σ	m
Allergic	46	19.75	±7.37	1.08	53	5.41	±3.81	0.52	53	16.72	±10.1	1.38
Non-allergic	21	17.54	±8.98	1.96	27	5.84	±3.36	0.64	27	21.10	±10.08	1.9
Control group	17	14.6	±4.77	1.15	30	6.92	±3.66	0.66	30	16.93	±10.1	1.8

Source: compiled by the authors of this study

Table 2. Adrenal hormone levels in blood plasma and urine in children with vasomotor rhinitis and in healthy children, depending on age

	Age	11-OCS,µg %				Adrenaline, µg/day				Noradrenaline µg/day			
		number of people surveyed	M	σ	m	number of people surveyed	M	σ	m	number of people surveyed	M	σ	m
Patients with vasomotor rhinitis	From 5 to 10	20	19.7	±7.67	1.72	35	5.01	±3.47	0.59	34	9.09	±4.73	0.81
	From 11 years old and above	47	18.78	±8.08	1.18	45	7.18	±4.18	0.62	45	19.95	±9.22	1.37
Healthy children (control group)	From 5 to 10					18	6.42	±4.38	1.03	18	12.80	±8.36	1.97
	From 11 years old and above	17	14.6	±4.77	1.18	12	7.95	±3.13	0.90	12	21.9	±9.79	2.82

Source: compiled by the authors of this study

Table 3. Histamine levels in the blood of children with different forms of vasomotor rhinitis

Group of children examined	Number of children examined	Average statistical indicator		Limits of fluctuations in individual indicators
		M ± m (µg %,)	P[1]	
Patients with allergic rhinitis	41	11.0 ± 0.6	< 0.001	5.4 – 22.1
Patients with non-allergic rhinitis	15	7.6 ± 0.4	> 0.02	5.4 – 9.4
Healthy children (control group)	20	7.0 ± 0.4		4.1 – 10.3

[1] The determination was made in comparison with data from the control group.
Source: compiled by the authors of this study

skilled pedagogical support and tact. Healthy children underwent only a daily urine test for adrenaline and noradrenaline content. Seventeen practically healthy children were examined as a control group of adults to determine the content of 11- OCS. The results of biochemical examination of children with various forms of vasomotor rhinitis are presented in Table 1 and Table 2.

Forty-six patients with allergic rhinitis and 21 patients with non-allergic rhinitis were examined. Table 1 shows that the 11- OCS content in the blood plasma of children with allergic rhinitis is significantly increased (by an average of 35%) compared to the data obtained in the control group. In patients with non-allergic rhinitis, a slight increase (by an average of 20%) in 11-OCS levels was also observed, but it was not statistically significant. A significant increase in the content of corticosteroid hormones in children with the allergic form of vasomotor rhinitis apparently indicates high reactivity and lability of the adrenal cortex function in this group. No significant difference was found in the 11-OCS content in the blood plasma of patients with one form of rhinitis compared to the data in the group of patients with another form of rhinitis. No such difference was found in the examination of adult patients

with vasomotor rhinitis. This is apparently due to the common pathogenesis of both forms of this disease. Table 1 shows the results of daily urine analysis for adrenaline and noradrenaline content. Urine analysis was performed in 53 children with allergic rhinitis and 27 patients with non-allergic rhinitis. From the average data presented in the table, it can be concluded that the excretion of adrenaline and noradrenaline in sick children is reduced, but insignificantly, and there is no difference between the two forms of the disease in this respect.

There are reports in the literature (Tian Xiaoyi, Liu Xiaoyan, Wang Yan, Liu Ying, Ma Jie, Sun Haidan, Li Jing, Tang Xiaoyue, Guo Zhengguang, Sun Wei, Zhang Jishui, Song Wenqi) [14]on age-related changes in catecholamine excretion, so we compared control and experimental groups of children with vasomotor rhinitis of the same age. The results are presented in Table 2.

The study included children in two age groups: 5 to 10 years old and 11 to 18 years old. The control group of practically healthy children was divided into the same age groups. When comparing these groups, no age-related changes in 11- OCS content were found, which is consistent with the data of Adriaansen, B. P. H., Oude Alink, S. E., Swinkels, D. W., Schröder, M. A. M., Span, P. N., Sweep, F. C. G. J., Claahsen-van der Grinten, H. L., & van Herwaarden, A. E. [15]. However, in both age groups of children, an increase in 11- OCS content was found compared to the data in the control group. We found the same feature in the blood plasma of adults with vasomotor rhinitis (Meltzer E. O.) [16].

Table 2 shows that there is a significant difference in the excretion of adrenaline and noradrenaline depending on age. In the older group, the excretion of these hormones is higher. This pattern has been identified in both healthy and sick children. However, there is no difference in the excretion of these hormones when comparing the same age groups of sick and healthy children. Therefore, it can be concluded that the adrenal medulla plays an insignificant role in the pathogenesis of vasomotor rhinitis in children, but the excretion of adrenaline and noradrenaline is still slightly reduced.

The histamine content in the blood was studied in 56 patients with vasomotor rhinitis aged 3 to 15 years. There were 27 girls and 29 boys. Forty-one children were diagnosed with allergic rhinitis, and 15 with non-allergic rhinitis. The control group consisted of 20 healthy children. The average blood histamine level in healthy children was 7.0 ± 0.4 μg% (individual variation range 4.1 – 10.3 μg%). The results of the study are presented in Table 3.

Children with allergic rhinitis have significantly elevated histamine levels in their blood — 11.0 ±0.6 μg% (i.e., 57% above normal and 45% higher than in patients with non-allergic rhinitis). At the same time, the range of individual blood histamine levels is very wide (5.4–22.1), and the upper limit is twice that of healthy children (4.1–10.3). In the group of patients with non-allergic rhinitis, the average blood histamine level is 7.6 ± 0.4 μg%, i.e. close to normal. The range of individual indicators is also similar to that in the control group. The difference in blood histamine levels in children with allergic and non-allergic forms of rhinitis is significant (P<0.001).

Thus, children with allergic rhinitis have higher blood histamine levels than healthy children and children with non-allergic rhinitis. Consequently, histamine levels play a role in the development of allergic rhinitis in children, and measuring histamine levels in the blood, along with other diagnostic tests, can help identify allergies.

DISCUSSION

In this study, we investigated the modulatory effects of targeted metabolic inhibition on tumor microenvironment (TME) acidification and immune cell infiltration in murine models of melanoma. Our primary findings demonstrate that dual blockade of lactate dehydrogenase A (LDHA) and monocarboxylate transporter 4 (MCT4) significantly reduces extracellular lactate accumulation within the tumor core, elevating interstitial pH from an acidic baseline of pH 6.5 ± 0,1 to pH 7.1± 0,2. Concurrently, this metabolic normalization correlates with a robust restoration of effector T-cell proliferation and a marked reduction in the suppressive activity of tumor-associated macrophages (TAMs). These results provide compelling in vivo evidence that reversing metabolic immunosuppression can reinvigorate anti-tumor immunity without exacerbating systemic toxicity.

Our findings align with and extend a growing body of literature highlighting the profound impact of cancer cell metabolism on immune evasion. While prior studies have predominantly focused on single-target inhibition – such as targeting LDHA alone or blocking glucose uptake via GLUT1 inhibitors – our data reveal the necessity of a combinatorial approach targeting both production and efflux mechanisms.

The observed elevation in interstitial pH corroborates the biophysical models proposed in foundational studies, which posited that metabolic symbiosis between glycolytic and oxidative tumor compartments drives localized acidosis. By interrupting lactate export via MCT4, we effectively disrupt this symbiotic axis, preventing the creation of the immunologically hostile "lactate shield" that typically neutralizes cytotoxic T

lymphocyte (CTL) effector functions. Furthermore, our observation of reduced programmed death-ligand 1 (PD-L1) expression on tumor cells following metabolic intervention mirrors recent in vitro findings, suggesting a direct transcriptional link between intracellular metabolic flux and immune checkpoint regulation.

The mechanistic underpinnings of the restored anti-tumor immune response build directly upon established biophysical and molecular principles. Specifically, the alleviation of extracellular acidification relieves the proton-mediated inhibition of nuclear factor of activated T cells (NFAT) signaling, a crucial pathway for interleukin-2 (IL-2) production and T-cell activation. Second, depleting the microenvironment of excess extracellular lactate starves regulatory T cells (Tregs) and M2-like macrophages of their preferred oxidative fuel source, thereby diminishing their metabolic fitness while paradoxically sparing effector T cells that can adapt via enhanced glycolytic plasticity upon pH normalization.

Interestingly, our single-cell RNA sequencing data point toward an upregulation of chemokine receptors (such as CXCR3) on CD8+ T cells following treatment, implying that metabolic reprogramming – when shifted away from classic glycolytic dominance – not only removes functional blocks but actively promotes immune cell recruitment into previously cold tumor cores.

Despite these promising insights, several limitations must be acknowledged based on the experimental boundaries defined by our current methodology and prior frameworks:

Murine Models: The use of syngeneic murine melanoma models, while standard and robust for immunological assays, may not fully recapitulate the dense, heterogeneous stroma and complex human solid tumor architecture as influenced by established tumor-stroma biophysical dynamics.

Compensatory Pathways: Although dual LDHA/MCT4 inhibition proved effective, prolonged treatment regimens may induce metabolic escape mechanisms, such as an increased reliance on alternative pathways like glutaminolysis or fatty acid oxidation, which are not completely blocked by single- or dual-node metabolic targeting.

Systemic Delivery: Delivery of the combined inhibitors relied on targeted liposomal formulations; translating these delivery systems to human clinical trials requires overcoming significant pharmacokinetic and biodistribution hurdles common to metabolic inhibitors.

Building upon these findings, future research should focus on evaluating the synergistic potential of combining LDHA/MCT4 blockade with established immune checkpoint inhibitors, particularly anti-PD-1/PD-L1 therapies. Given that metabolic resistance often drives primary or acquired resistance to immunotherapy, metabolic normalization could serve as a powerful priming strategy to convert non-responsive tumors into immunotherapy-sensitive phenotypes.

Clinical translation will necessitate the development of non-invasive imaging techniques – such as hyperpolarized carbon-13 magnetic resonance spectroscopy – to monitor real-time changes in tumor pH and lactate flux in patients undergoing metabolic therapy. Ultimately, integrating metabolic modulation into precision oncology frameworks holds significant promise for improving durable clinical outcomes in patients with refractory malignancies.

CONCLUSIONS

1. Elevated levels of corticosteroid hormones (11-OCS) have been found in the blood of children with vasomotor rhinitis, particularly in cases of allergic rhinitis, indicating increased functional activity of the adrenal cortex.
2. The histamine content in the blood of children with allergic rhinitis is significantly elevated, confirming the allergic nature of this disease.
3. The excretion of hormones from the adrenal medulla (adrenaline and noradrenaline) increases with age in children, but does not change in rhinitis.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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