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Features of the microelement status in children with acute urticaria

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Background*: The increase in the occurrence of allergic dermatoses, especially in young children, is one of the urgent problems of pediatrics. The development of allergic reactions may be caused by changes in microelements balance of the body.* ***Objective****: Our aim was to study the features of the microelement status in children with acute urticaria.* ***Methods****: A comparative study included patients with acute urticaria of varying severity and healthy children (I and IIA groups of health). Study of microelement was carried out in hair samples by X-ray analysis.* ***Results****: The study revealed lower content of zinc in hair in patients with urticaria (n = 40) (48 compared to 146 mcg/g in 23 children of control group, p < 0.001). It also revealed lower content of calcium (447 and 2428 mcg/g respectively; p = 0.001) as well as higher content of sulfur (33860 and 26447 mcg/g respectively; p = 0.001) and potassium (537 and 312 mcg/g respectively; p = 0.001). Differences in the iron, nickel, copper, and chlorine content in hair in comparable groups were not detected. There was no association of microelements content with a burdened hereditary allergologic anamnesis.* ***Conclusion:*** *Children with urticaria have dismicroelemntosis, characterized by a decrease in zinc and calcium content, and an increase in the concentration of sulfur and potassium.*
Keywords*: children, urticaria, microelements.*

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Rationale

One of the relevant problems of pediatrics is the steadily increasing prevalence of allergic diseases in early age children [1]. Urticaria and the Quincke edema are 2nd in prevalence among all allergic diseases after bronchial asthma [2, 3]. The prevalence of urticaria among the adult population is 1-5%, int he child population it reaches 6% [4]. Its most often causes are infections, usage of medicines, food allergens and stings of hymenopterous insects [5].
The development mechanisms of allergic dermatoses, which have to do with regulation disorders on behalf of the central nervous system and pathological changes in the digestive organs, are the most studied ones for the moment [6 ,7]. At the same time, it is known that changes in the body's trace element status can influence the course of immunological processes. Such disorders can lead to immune-deficiency states and changes in the oxidizing-reducing processes at cellular level, which leads to the development of allergic reactions [8]. For this reason, the influence of dismicroelementosis on child health has actively been discussed over the past few years [9, 10]. At the same time, the prevalence of micro- and macro-elemental misbalance in Russian children over the past decades is due mainly to the changes in the nutrition ration and an unfavorable ecological situation [11, 12].

A number of studies have shown the connection between the contents of micro-elements and the development of allergic diseases [13-15]. The analysis of certain micro-elements has shown the significance of certain substances int he genesis of allergic diseases: chrome (allergic skin lesions, dermatitis and eczema) [16, 17], copper (risk of developing bronchial asthma, allergic dermatosis, vitiligo) [16], calcium, selene, iodine, manganese, zinc (formation of bronchial hyperreactivity in children, influence on the longitude and severity of the atopic process) [18]. An elemental status misbalance (a decrease in the concentrations of calcium, iron, nickel, copper with normal concentrations of zinc and sodium) was noticed in early age children suffering from obstructive bronchitis [19]. A deficit in the contents of essential elements has been established in more than 90% of atopic dermatitis patients (zinc - in 85%, sulphur - in 73%, calcium and iron - in 70% of patients; excess levels of toxic and potentially toxic elements was registered in 2/3 of children, with regard to nickel - in every tenth child) [20]. At the same time, the presence and expression level of elemental status misbalance has not been studied in children with urticaria before.
The aim of our investigation was to study the characteristics of trace element status in children with acute urticaria.

Methods

STUDY DESIGN

A comparative case-control investigation was conducted.

INCLUSION CRITERIA

Inclusion criteria:

- patients with a confirmed diagnosis «acute urticaria»;
- age between 2 and 12 years;
- residing in the research area (Rostov district) for not less than 2 years.

The «acute urticaria» diagnosis was verified according to the Federal clinical recommendations concerning urticaria diagnosis and treatment [21]. Urticaria activity was determined using the UAS 7 (Urticaria Activity Score 7). The expression of the main disease symptoms (number of rashes and itching intensity) was evaluated by the patients and their parents every 24 hours over 7 consecutive days (table 1) [21].

Table 1. Evaluating urticaria activity using the UAS 7 scale

Score	Blisters	Itching
0	No	No
1	Light stage (<20 blisters/24 hrs)	Light stage (present, but not causing anxiety)
2	Moderate stage (20–50 blisters/24 hrs)	Moderate stage (causes anxiety, but does not affect daily activity and sleep)
3	Intensive (>50 blisters/24 hrs, or large merging blisters)	Intensive (severe itching, causing enough anxiety and disrupting daily activities and sleep)

EXCLUSION CRITERIA:

- urtricary rashes, persisting for more than 6 weeks;
- presence of autoimmune diseases.

The control group was composed of I and IIa health group children, permanently residing in the Rostov region. They were examined at the same time as the main group at the polyclinic department of the Rostov-on-Don state hospital number 2.

REALIZATION CONDITIONS

The study was conducted over the period from November 2014 to November 2015 at the pediatric department of the Rostov State Medical University and at the pediatric somatic department of the city child

hospital number 2, Rostov-on-Don.

LABORATORY STUDIES

The amount of micro-elements (S, Ca, Fe, Ni, Zn, Cl) in children with acute urticaria was analyzed. The amount of micro-elements was determined in the hair of the back side of the head using the Total reflected X-Ray Fluorescence analysis (TXRF) method [22, 23]. The average length of investigated hair was 2 cm, which corresponds to the period of accumulating micro-elements over the period of approx. 1 month [24].

Probes were prepared using the wet combustion method. 10 mg of hair was diluted in nitrous acid, proportion - 1 mg per 10 mcl during 10 minutes. In order to speed up the dilution process, the test tube was held in a muffle furnace at 60 ºC for 15 minutes. 10 mcl of the ICP multi-element standard solution [24] vanadium ions with a concentration of 1 mg/cm^3 and 40 mcl of bidistilled water were added to the 5 vcl hair dilute. The prepared probes were applied to a quartz wafer in the form of 3 drops 10 mg each in turns. In order to fully fix the solution on the wafer surface, the prepared probes were placed into a furnace until fully dried for 10 minutes. The surveillance x-rax fluorescent spectres for the K_α- and K_β-lines were registered using the AMPTEK (Germany) energy-dispercing spectrometer with a molibdane anode. Spectres were being registered in the 0 to 36.91 keV range, which is in correspondence with the elements being determined (from S to Zn). The spectre registration exposition in one point was 300 s.

ETHICAL EXPERTISE

The study was approved by the Local ethical committee of the Rostov State Medical University (protocol no. 19/14 from 11 Dec 2014). An informed consent to participation in the study was obtained from all parents of the children involved.

STATISTICAL ANALYSIS

The data was processed using the STATISTICA v. 7.0 software (StatSoft Inc., USA). The quantitative data was described using the median (25th; 75th percentile). The differences of values of quantitative indexes in independent samples were evaluated using the Mann-Whitney criteria. The comparison result was considered statistically significant at $p < 0.05$.

Results

STUDY PARTICIPANTS

The study included 40 children (21 girl, 19 boys) with acute urticaria and 23 healthy children. The groups were comparable by sex - 21 (53%) and 12 (52%) girls ($p = 0.813$) - and age 6.6±3.4 и 6.5±3.3 years of age, correspondingly ($p =0,967$). A mild form of urticaria (local skin lesions, no itch or weak itching) was diagnosed in 8 (20%), moderate urticaria (spread skin lesions 2-score itching) in 28 (70%), severe course (generalized skin leasion, expressed itching) was determined in 4 (10%) of children from the main group. In 12 (30%) children the development of urticaria was combined with the appearance of Quincke edema attributes. 2 patients had atopic dermatitis, 2 - allergic rhinitis, 1 - bronchial asthma. Urticaria at a more early age was noticed in 20 (50%) children. In 18 (45%) children urticaria was triggered by food, in every third child - 12 (30%) - acute respiratory infection, in 6 (15%) - medicines. In every 10th case ($n = 4$) the cause of urticaria could not be established.

MAIN RESULTS OF THE STUDY

It was established that the children in the main group had a lower concentration of zinc and calcium and a higher concentration of sulphur and potassium as compared to the controls (table 2). There was no difference in the concentration of such elemnts as iron, nickel, copper and chlorine in the compared groups. Also, there was no difference in the concentration of micro-elements between patients with aggravated and non-aggravated hereditary allergic anamnesis.

Table 2. The concentration of micro-elements (mkg/gr) in the hair of healthy children and acute urticaria patients

Index	Control group (n =23)	Urticaria patients (n =40)	p
S	26 447 (20 527; 32 153)	33 860 (27 713; 37 670)	0,001
K	312 (230; 360)	537 (402; 719)	0,001
Ca	2428 (558; 6389)	447 (278; 1266)	0,001
Fe	70 (34; 170)	68 (34; 87)	0,228
Ni	17 (6; 22)	14 (8; 45)	0,814
Zn	146 (90; 190)	48 (23; 72)	0,001
Cu	18 (18; 22)	25 (19; 30)	0,145
Cl	1233 (781; 1563)	899 (443; 1337)	0,218

Discussion

MAIN RESULT SUMMARY

It was established that an acute urticaria-type allergic reaction is characterized in children by a change in the trace element status, a symptom of which is the change in micro-element concentration in the hair, especially the decrease in zinc and calcium concentrations.

DISCUSSION OF THE MAIN RESULT

We chose hair to be the investigted biosubstrate due to its ability to accumulate trace elements over the period of its growth. Thus, the concentration of micro-elements in the hair reflects their concentration in the body over a long period of time (2-3 months) [25]. Other types of biosubstrates (blood, urine) participate actively in metabolism, while their contents depend on the ration. As a result, the fluctuation of mineral concentration in these biosubstrates reflect the state of the body over a limited time period [25].

A comparative analysis of results acquired over the course of this study has shown the following. According to the data obtained by korean scientists, there is a connection between the level of zinc concentration decrease and the level of atopic dermatitis severity [13], while according to our data there is an overall decrease of this element in cases of acute urticaria, which does not depend upon the clinical symptoms and the prevalence of skin elements. It has was also been said that there is an association between chronic idiopathic urticaria and the Plummer-Vinson syndrome [15], however we did not find such a pattern in our study.

Also we did not detect a valid difference in copper concentration in cases of acute urticaria as compared to the controls, while, according to literature, an increase in copper concentration predisposes to the development of allergic diseases [16]. Also, we noticed that patients with acute urticaria have a decreased concentration of calcium, which corresponds with similar changes noted in cases of bronchial asthma [18]. Hence, this hypomicroelementosis may be a universal indicator of a developing allergic process.

We did not find any significant changes in nickel concentrations over the course of the study. However, most authors point out that and excess of this potentialy toxic element can lead to the disorder becoming chronic, in particular with regard to atopic dermatitis [20].

STUDY LIMITATIONS

The hair of most patients was taken during the spring-summer period, which might reflect the trace

elemental status during other seasons.

Conclusion

The course of urticaria in children is characterized by change in the concentration on micro-elements, i.e. a decrease in the concentration of zinc and calcium, as well as an increase in the concentration of sulphur and potassium in hair. The established trace element characteristics have nothing to do with the severity of the disease, nor with an anamnesis aggravated by allergic disease.

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Conflict of interest

The authors declared they have no competing interests to disclose.

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