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## ENTEROSORBENTS THERAPY IN CHILDREN WITH ASTHMA LIVING IN POOR SANITARY CONDITIONS

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**SUMMARY:** According to recent epidemiological and toxicological data, children living in poor sanitary conditions develop abnormal physical characteristics, such as morphological abnormalities and chronic diseases of the Central Nervous System and the respiratory, cardiovascular, musculoskeletal, endocrine and digestive Systems. Among the substances of industrial origin, an important role is played by metals that accumulate in the tissues and organs. The toxic effects are due to the type of metal, its concentration, the concurrence of other pathological factors and the general health conditions (immune reactivity, hypersensitivity, etc.). The study was conducted on 236 children suffering from mild asthma (experimental Group) living in areas close to metallurgical plants. The composition of the air – concerning the percentage of manganese, chrome, lead and nickel – was found to have values at the upper limits of standard. The control Group, homogeneous for age, gender and residential area, consisted of 41 children. In order to reduce the blood concentrations of the considered toxic metals, 4 enterosorbents were tested and prescribed for 2 consecutive weeks of therapy: Enterosgel<sup>®</sup>, Polysorb<sup>™</sup>, Polyphepan, and activated charcoal. – Enterosgel<sup>®</sup> - blood tests. Decrease from baseline: Mn = 12%; Ni = 64 %; Pb = 20 %; Cr = 56 %. – Polysorb<sup>™</sup> - blood tests. Decrease from baseline: Mn = 24%; Ni = 65%; Pb = 20 %; Cr = 66%. – Polyphepan - blood tests. Decrease from baseline: Mn = 0 %; Ni = 51 %; Pb = 12%; Cr = 61 %. – Activated charcoal - blood tests. Decrease from baseline: Mn = 0 %; Ni = 69 %; Pb = 10 %; Cr = 44%. Data reveal that the use of Enterosgel<sup>®</sup> and Polysorb<sup>™</sup> for 2 consecutive weeks allows to obtain a significant reduction – compared to the controls – of the amount of Cr and Ni (56-66%) and Mn and Pb (12-24%) in the blood of asthmatic children living in poor sanitary conditions.

**KEY WORDS:** ENTEROSORBENTS, ENTEROSGEL<sup>®</sup>, MANGANESE, NICKEL, LEAD, CHROME, POLLUTION.

General health status of the population resident in the industrialized areas is mostly determined by the sanitation level.

This correlation is observable especially in children.

Recent data of epidemiological and clinical studies at our disposal show that children living in precarious hygienic and sanitary conditions experience various deviations from the reference in physical development (mismatch regarding somatometry, physiometry, morphology, age and gender indicators, dyssynchrony in the time of formation of secondary sexual characteristics, etc.), higher prevalence of morphological and functional anomalies, chronic diseases of CNS and Apparatus / Systems such as respiratory, cardio-vascular, musculoskeletal, endocrine and digestive.

Among the toxic industrial substances that engender health problem, an important role is reserved for heavy metals. On entering the body through food or respiratory tract, the metals are excreted more slowly compared to organic compounds, undergo biotransformation and can be accumulated in organs and tissues, which influence the parameters of population health.

The range of toxic effects of the metals on the molecular, cellular, and systemic tissue level is largely determined by such factors as: 1) concentration in organs and tissues; 2) combination with other pathological factors; 3) the previous state of the child's health; 4) the child's immune reactivity; 5) the presence of genetically determined hypersensitivity.

- Currently pathogenesis mechanisms related to the role of metals in the development of allergic diseases of respiratory apparatus and skin, endocrine diseases, as well as diseases of musculoskeletal system, the gastrointestinal tract, cardiovascular System and nervous system have become known.

One of the treatment methods of diseases associated with the effect of chemical factors is the so called "elimination therapy", among which the use of intestinal adsorbents (enterosorbents) is the most widespread.

Of particular importance is elimination therapy of patients with allergy associated with the presence of toxic chemical substances of industrial origin (e.g. heavy metals).

Heavy metals cause body sensitization and intoxication.

To render the intestinal adsorption the most effective and safe method for the pediatric practice is - therefore – a major issue.

- The purpose of this research is to perform a comparative evaluation of the efficacy of elimination therapy using various enterosorbents in children with asthma living in the environments polluted with metals.

Research objectives:

- 1) To define the parameters of elimination effect of the intestinal adsorbents for metals (manganese, chrome, lead and nickel);
- 2) To evaluate comparative effectiveness of enterosorbents tested.

## PATIENTS AND METHODS

The study was conducted with participation of 236 children (experimental group) suffering from mild asthma and not suffering from concomitant gastrointestinal diseases, living in the geographic area next to metallurgical plants.

- The air of the residence territory of the children was found to contain quantities exceeding the limits permitted under the Russian standards (maximum permissible emission PEL): manganese up to 2.19 PEL, chromium up to 1.1 PEL, lead up to 3-5 PEL, nickel up to 1.1 PEL.

All children were aged from 7 to 12 years ( $9.3 \pm 1.5$ ).

The control group consisted from 41 children with mild bronchial asthma without concomitant organic diseases of the gastrointestinal tract. The ages of the children in the control group ( $9.8 \pm 1.1$  years) and gender distribution were similar to those of the experimental group ( $p = 0.4-0.9$ ); also the area was the same. No significant differences related the socioeconomic status of the families of children were under study ( $p = 0.1-0.8$ ).

In addition to clinical and functional standards according to International Consensus on Asthma - 2011, in children of both groups were made blood count regarding manganese, nickel, lead and chromium. The analyzes were performed at T0 and immediately after and of treatment (15 days of therapy).

Chemical and analytical studies were performed by atomic adsorption spectrophotometry [spectrophotometer Analyst - Perkin Elmer (USA)] and plasma mass spectrophotometry for inductive coupling-ISP-MS – Agilent 7500cx (USA) sec. Guidelines (MUK 4.1.2104-06; 4.1.2105-06; 4.1.2106-06; 4.1.2773-10).

In both groups the specific therapy of bronchial asthma was carried out according to the Guidelines of International Consensus on Pediatric Asthma-2011.

The children in the experimental group were treated with four different enterosorbents in the doses recommended for a period between 1 and 14 days in addition to specific therapy.

During the study the following sorbents have been used:

- a) Silicon-based enterosorbent Enterosgel® biological (68 children);
- b) Silicon-based enterosorbent PolysorbTM (56 children);
- c) lignin Enterosorbent based Polyphepan (54 children);
- d) Adsorbent based on activated carbon (58 children).

## RESULTS

From the values of blood count it was found that the levels of manganese ( $0.025 \pm 0.001$  mg / dm), chromium ( $0.041 \pm 0.003$  mg / dm), nickel ( $0.43 \pm 0.16$  mg / dm) and lead ( $0.145 \pm 0.001$  mg / dm) in the experimental group did not differ statistically compared to that control group (manganese  $0.027 \pm 0.001$  mg / dm,  $p = 0.99$ ; chrome  $0.045 \pm 0.001$  mg / dm,  $p = 0.99$ ; nickel  $0.45 \pm 0.12$  mg / dm,  $p = 0.96$ ; lead  $0.141 \pm 0.001$  mg / dm,  $p = 0.99$ ), which were, however, much higher compared with the reference standard (manganese  $0.0109$  mg / dm;  $p < 0.01$ ; chrome  $0.028$  mg / dm;  $p < 0.01$ ; nickel  $0.12$  mg / dm;  $p < 0.01$ ; lead  $0.1$  mg / dm;  $p < 0.01$ ) (Table 1).

The basic treatment of bronchial asthma in the control group did not substantially change the value of the metals in blood. On day 15 of treatment, the level of manganese was  $0.024 \pm 0.001$  mg / dm (initially  $0.027 \pm 0.001$  mg / dm,  $p = 0.89$ ); chromium  $0.042 \pm 0.001$  mg / dm (initially  $0.045 \pm 0.001$  mg / dm,  $p = 0.86$ ); nickel  $0.046 \pm 0.09$  mg / dm (initially  $0.45 \pm 0.12$  mg / dm,  $p = 0.99$ ); lead  $0.138 \pm 0.001$  mg / dm (initially  $0.141 \pm 0.001$  mg / dm,  $p = 0.93$ ).

In all cases, the blood level of each metal tested remained significantly exceeding in relation to the reference standard levels ( $p < 0.01$ ). In the experimental group the combined use of specific treatment of bronchial asthma and enterosorbents has within 15 days contributed to reduce significantly the blood level of the metals studied (Table 2).

- By using enterosorbent Enterosgel® the level of manganese in the blood decreased, compared to the baseline, by 12% and reached the value of  $0.022 \pm 0.004$  mg / dm ( $p = 0.81$ ), although it did not reach the limit of the reference value ( $p = 0.04$ ); the content of nickel decreased by 64% ( $0.156 \pm 0.021$  mg / dm,  $p = 0.03$ ), next to the reference level ( $p = 0.05$ ); level of lead decreased by 20% and reached  $0.116 \pm 0.008$  mg / dm ( $p = 0.05$ ), which corresponded to the reference value ( $p = 0.62$ ); the content of chromium, on the completion of elimination therapy, was  $0.018 \pm 0.004$  mg / dm, 56% below baseline ( $p = 0.03$ ) and there was no significant difference compared with the reference value ( $p = 0.84$ ).

- In children given PolysorbTM, manganese content in the blood is decreased by 24% and reached  $0.019 \pm 0.003$  mg / dm ( $p = 0.04$ ), still staying above the reference value ( $p = 0.03$ ); nickel decreased by 65% ( $0.151 \pm 0.021$  mg / dm,  $p = 0.02$ ), next to the reference value ( $p = 0.05$ ); lead was reduced by 20%, reaching a value of  $0.116 \pm 0.013$  mg / dm ( $p = 0.05$ ), corresponding to the reference value ( $p = 0.62$ ); the chromium content on the completion of elimination therapy was  $0.014 \pm 0.002$  mg / dm, 66% lower than the baseline ( $p = 0.02$ ) and there was no significant difference compared to the reference value ( $p = 0.51$ ).

- In children given Polyphedan, the content of manganese in the blood did not change and was equal to  $0.025 \pm 0.003$  mg / dm ( $p = 0.99$ ); the content of nickel reduced, compared to the baseline, by 51% ( $0.0212 \pm 0.0023$  mg / dm,  $p = 0.04$ ), but remained above the reference value ( $p = 0.03$ ); level of lead decreased only by 12%, with a value of  $0.127 \pm 0.011$  mg / dm ( $p = 0.66$ ), and was higher than the reference level ( $p = 0.04$ ); the content of chromium at the end of elimination therapy decreased by 61% ( $0.016 \pm 0.006$  mg / dm,  $p = 0.04$ ) and did not show significant difference compared to the reference value ( $p = 0.72$ ).

- In the group treated with activated charcoal, the blood level of manganese after the therapy did not change and was  $0.026 \pm 0.002$  mg / dm ( $p = 0.99$ ); the content of nickel decreased by 69% compared with the baseline ( $0.135 \pm 0.011$  mg / dm,  $p = 0.03$ ) and was next to the reference value ( $p = 0.056$ ); the level of lead decreased only by 10%, equal to  $0.130 \pm 0.009$  mg / dm<sup>3</sup> ( $p = 12:06$ ) and it was above the reference level ( $p = 0.04$ ); the content of chromium at the end of elimination therapy decreased by 44% ( $0.023 \pm 0.009$  mg / dm,  $p = 0.02$ ) with no significant difference from the reference value ( $p = 0.76$ ).

In general, the results of the study have shown that the effects of elimination of manganese, nickel, lead and chromium with Enterosgel® and PolysorbTM have been by 1.3 times higher in comparison with the results of Polyphedan and activated carbon.

The lowest elimination percentages for the studied enterosorbents, are attributable to lead (from 10 to 20%) and manganese (from 0 to 24%), while the elimination of nickel and chrome has reached proportions ranging from 44% to 69%.

Thus, use of Enterosgel® and PolysorbTM allows to obtain a significant reduction in blood levels of chromium and nickel (56-66%) and reduction of 12-24% of the level of manganese and lead within 15 days of treatment, to support the effectiveness of elimination therapy in children with bronchial asthma.

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ТАВ. 1

Metal	Experimental group	Control group	Reference values	p1	p2	p3
Managanese (Mn)	0.025±0.001	0.027±0.001	0.0109±0.0006	<0.01	<0.01	0.99
Nickel (Ni)	0.43±0.16	0.45±0.12	0.08-0.12	<0.01	<0.01	0.96
Lead (Pb)	0.145±0.001	0.141±0.001	0.1	<0.01	<0.01	0.99
Chrome (Cr)	0.041±0.003	0.045±0.001	0.007-0.028	<0.01	<0.01	0.99

Presence of heavy metals in the blood of the children of the two groups before treatment, mg/dm<sup>3</sup> (M ± m).

p1 - significance of the differences between the values of the experimental group and the reference value.

p2 - significance of the differences between the values of the control group and the reference value.

p3 - significance of the experimental group and the control group

TAB. 2

Enterosorbents	manganese		nickel		lead		chrome		p1	p2	p3	p4
	Hematic value before the elimination therapy											
	0.025±0.001		0.43±0.16		0.145±0.001		0.041±0.003					
	Hematic value by the end of the elimination therapy; % of reduction in comparison with the baseline											
Value	%	Value	%	Value	%	Value	%					
Enterosgel®	0.022±0.004	12	0.156±0.021	64	0.116±0.008	20	0.018±0.004	56	0.04	0.05	0.62	0.84
Polysorb™	0.019±0.003	24	0.151±0.022	65	0.116±0.013	20	0.014±0.002	66	0.03	0.05	0.62	0.51
Polyphedan	0.025±0.003	0	0.212±0.023	51	0.127±0.011	12	0.016±0.006	61	0.01	0.03	0.04	0.72
Active charcoal	0.026±0.002	0	0.135±0.011	69	0.130±0.009	10	0.023±0.009	44	0.01	0.05	0.04	0.756
Reference values (N.Tits, 2003)	0.0109±0.0006		0.08-0.12		0.1		0.007-0.028					

Presence of heavy metals in the blood of children of the experimental group after treatment with enterosorbents, mg / dm (M ± m).

p1 - significance of differences for blood manganese at the end of elimination therapy compared to the reference values.

p2 - significance of differences for blood nickel at the end of elimination therapy compared to the reference values.

p3 - significance of differences of blood lead at the end of elimination therapy compared to the reference values.

p4 - significance of differences of blood chrome at the end of elimination therapy compared to the reference values.