

Clinical-Pathogenetic Justification Of Therapy In Children With Nosocomial Pneumonia By Correcting The Microelemental Status

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ABSTRACT

The aim of the study was to identify and evaluate abnormalities in the exchange of immunological, macro and microelements, as well as to develop methods for their correction in the treatment of nosocomial pneumonia in children. The microelement composition of the blood of healthy children and patients with out-of-hospital and nosocomial pneumonia was studied by neutron activation analysis. The data obtained show that with nosocomial pneumonia, the violation of the trace element status is more pronounced in comparison with healthy children. The developed 3-step method of treatment with the use of an immunomodulatory drug and vitamin-mineral complex Vitrum kids, based on the basic therapy, improves the healing process and normalizes the microelement status of children.

1. INTRODUCTION

Respiratory diseases are one of the most pressing medical and social problems of modern medicine. Of these, pneumonia is the most common pathology affecting various age groups of the population. A high incidence rate is often associated with a complicated and protracted course of the disease. Pneumonia is one of the leading causes of death in children worldwide. It kills an estimated 1.1 million children under the age of five each year. Pneumonia is divided into out-of-hospital and nosocomial. Community-acquired pneumonia occurs in a child under normal conditions, nosocomial after 72 hours of hospital stay or within 72 hours after discharge [1].

Despite modern antibacterial drugs with improved antimicrobial properties, complex diagnostic issues remain unresolved, the reasons for the increase in the frequency of severe complications and deaths in pneumonia have not been fully deciphered. Over the past years, a rapid increase in the resistance of pneumonia pathogens to antibacterial drugs has been observed throughout the world [2].

Actual scientific research aimed at an in-depth study of the patterns of etiopathogenesis of pneumonia open up prospects for the timely diagnosis of adverse outcomes, improvement of metabolic therapy, since success in the treatment of pneumonia, as is known, depends not only on the use of antibacterial agents. It is important to search for new affordable drugs that can restore trophic disorders in the lung tissue and supplement the treatment and rehabilitation programs for this category of patients.

The important role of trace elements in the life of the human body is beyond doubt. In recent years, a significant number of studies have accumulated on the study of the effect of trace

elements on metabolism. The imbalance of trace elements depends on the biogeochemical characteristics of that of anthropogenic pollution. The content of elements in the environment can affect the micro and macroelement composition of the biological media of the body and create serious problems for the health of children. Negative factors of anthropogenic impact, including excessive intake of heavy metals and deficiency of vital chemical elements, as well as unfavorable living conditions, contribute to a decrease in human health factors.

The stability of the chemical composition of the human body is one of the most important and prerequisites for its normal functioning. Elemental homeostasis is a particular form of the general homeostatic system of the body, the disturbances of which are reflected in the body's ability to adapt in extreme conditions [4,5].

Micro- and macroelements are involved in most biochemical reactions in the body, in the regulation of water-salt metabolism, etc. Their role is especially great as activators of enzymes, without which it is difficult to imagine at least one process in a child's body. Micro- and macroelements are structural components of enzymes, their active catalytic centers. Inorganic ions are especially in demand by the immune system, since most of its constituent components cannot fully perform their functions without the active work of enzymatic systems. Thus, a sufficient microelement reserve is the key to the full functioning of the immune system.

The aim of the study was to identify and evaluate abnormalities in the exchange of immunological, macro and microelements, as well as to develop methods for their correction in the treatment of nosocomial pneumonia in children.

2. MATERIALS AND METHODS

Clinical laboratory, immunological and microelement status of children with nosocomial pneumonia were carried out. The study of the microelement status of the organism of children was carried out according to the quantitative study of the content of trace elements in whole blood by the method of neutron activation analysis.

The proposed neutron activation method allows with high sensitivity and productivity to determine more than 25 elements in one weighed portion of the sample, while the sample preparation is quite simple and does not require decomposition. All measurements of samples irradiated at the nuclear reactor of the Institute of Nuclear Physics of the Academy of Sciences of the Republic of Uzbekistan were carried out on a high-purity germanium detector with a high-resolution computerized gamma spectrometer. Data processing was carried out using the GENIE 2000 program.

To assess the magnitude of the error in determining the elements, an analysis of a comparison sample provided by the International Atomic Energy Agency (IAEA), NN-1 is a hair homogenate with a certified content of elements. The accuracy of the analysis results was determined by comparing the data obtained (Table 1).

Table 1. Assessment of the accuracy of the analysis results.

Microelement	Certified content, $\mu\text{g} / \text{g}$	Found, $\mu\text{g} / \text{g}$
Ag	0.19 ± 0.060	0.21 ± 0.064
Co	6.0 ± 1.2	5.5 ± 0.49
Cr	0.27 ± 0.16	0.28 ± 0.080
Hg	1.7 ± 0.24	1.8 ± 0.50
Fe	24 ± 9.8	26 ± 4.8
Sb	0.030 ± 0.010	0.033 ± 0.010
Se	0.35 ± 0.040	0.32 ± 0.062
Rb	3.8 ± 0.80	4.2 ± 0.56
Zn	170 ± 32	180 ± 15

The analysis of the results obtained by the K-factor method showed the high reliability of the neutron activation analysis technique.

3. RESULTS

To determine the balance of essential trace elements, whole blood of 20 practically healthy children and 50 sick children aged 1 to 13 years from different regions of Uzbekistan was studied. Table 2 shows the results of the analysis of the content of elements in healthy children.

Table 2. The content of elements in healthy children in comparison with the reference values, $\mu\text{g} / \text{g}$

Microelement	Healthy (n=20)	Range of normal contents
Br	7.6±0.82	7.4-18
Ca	350±40	300-400
Cl	12200±60	12000-16000
Co	0.016±0.0021	0.015-0.24
Cr	0.24±0.010	0.22-0.63
Fe	2200±130	2100-3400
K	9300±85	8500-10000
Mn	0.21±0.016	0.068-0.43
Na	8100±45	7200-10000
Rb	6.6±0.60	4.6-14
Se	0.51±0.042	0.48-0.97
Zn	28±1.4	21-40

The content of trace elements in healthy children is within the normal range. During the development of the disease, the content of elements in the whole blood of sick children changes (Table 3). When considering changes in the content of elements in community-acquired and nosocomial pneumonia, it was revealed that practically healthy children differ from children with pneumonia in higher blood levels of bromine, calcium, cobalt and manganese and lower levels of iron and zinc, in comparison with the content of elements in the healthy group. children (Table 3)

Comparison of the mean values between the groups of healthy children and those suffering from outside and inside hospital pneumonia made it possible to reveal a significant decrease in the values of iron content from 2200 ± 130 to 1800 ± 110 . A similar situation is observed for the average values of zinc content: 28 ± 1.4 - for practically healthy children and up to 21 ± 0.76 - for children with nosocomial pneumonia. Comparison of the contents of zinc and iron in groups 2 and 3 allows us to conclude that in the group with nosocomial pneumonia, the process of the development of the disease is aggravated.

Children with pneumonia are characterized by increased calcium values up to 880 ± 54.0 , which is 2.5 times higher than in the healthy group and manganese values up to 0.63 ± 0.021 (3 times). The increased content of these elements contributes to a decrease in the body of iron and zinc, which are characterized by increased fatigue, drowsiness, and decreased activity.

Analysis of the data obtained (Table 3) also indicates an increase in the bromine content from 7.6 ± 0.82 - for healthy children to 14 ± 1.9 - for children with the development of nosocomial pneumonia and cobalt from 0.016 ± 0.0021 - for healthy children to 0.092 ± 0.0034 - for children with the development of nosocomial pneumonia. Probably, this

tendency is associated with the neuro-somatic activity of the child's body during the period of illness and stay in the hospital, although these values are within the range of normal contents. Comparison of the content of trace elements shows that in children with nosocomial pneumonia it is most pronounced, from which it follows that the course of the disease is more severe.

Table 3. Average contents of elements in sick and healthy children, $\mu\text{g} / \text{g}$

Microelement	Healthy (n=20)	Community-acquired pneumonia (n=25)	Nosocomial pneumonia (n=25)
Br	7.6±0.82	13±2.5	14±1.9
Ca	350±40	690±65	880±54
Cl	12200±60	12600±420	11700±85
Co	0.016±0.0021	0.090±0.0015	0.092±0.0034
Cr	0.24±0.010	0.36±0.041	0.35±0.022
Fe	2200±130	1900±35	1800±110
K	9300±85	8300±170	8500±130
Mn	0.21±0.016	0.62±0.013	0.63±0.021
Na	8100±45	9700±170	9700±110
Rb	6.6±0.60	7.4±0.25	7.5±0.034
Se	0.51±0.042	0.41±0.013	0.37±0.028
Zn	28±1.4	22±0.61	21±0.76

In order to choose the most optimal treatment, there were 3 approaches: basic treatment, basic therapy and an immunostimulating drug and the third - basic therapy, then an immunostimulating drug, then a vitamin-mineral complex (1 month).

As an immunostimulating drug, Polyoxidonium was used, which has an immunomodulatory effect, increases the body's resistance to local and generalized infections. The basis of the mechanism of the immunomodulating action of the drug is a direct effect on phagocytic cells and natural killer cells, as well as stimulation of antibody production. Along with the immunomodulatory effect, Polyoxidonium has a pronounced detoxifying antioxidant activity and the ability to remove toxins from the body.

Vitrum was used as a vitamin-mineral complex, containing 13 vitamins and 10 minerals: iron, calcium, zinc, selenium, manganese, chromium, etc.

Table 4 shows the average values of trace elements in whole blood in all studied groups.

Table 4. Average content of elements in patients with nosocomial pneumonia after treatment, $\mu\text{g} / \text{g}$

Microelement	Healthy (n=20)	Nosocomial pneumonia	Basic therapy	Basic therapy and PO	Basic therapy, PO, Vitrum
Br	7.6±0.82	14±1.9	13±0.96	13±1.1	11±1.0
Ca	350±40	880±54	800±75	680±55	450±56
Cl	12200±60	11700±85	11900±120	12000±160	12500±110
Co	0.016±0.0021	0.092±0.0034	0.089±0.0071	0.079±0.0061	0.078±0.0058
Cr	0.24±0.010	0.35±0.022	0.35±0.021	0.36±0.019	0.37±0.021
Fe	2200±130	1800±110	1800±120	2000±220	2400±130
K	9300±85	8500±130	8500±150	8700±170	8900±76
Mn	0.21±0.016	0.63±0.021	0.62±0.034	0.56±0.031	0.35±0.024

Na	8100±45	9700±110	9800±130	8900±120	8500±94
Rb	6.6±0.60	7.5±0.54	7.7±0.68	7.8±0.58	7.8±0.61
Se	0.51±0.042	0.37±0.028	0.39±0.024	0.42±0.028	0.49±0.032
Zn	28±1.4	21±0.76	23±1.9	26±1.9	32±2.1

Analysis of the content of the studied elements, depending on the various approaches of the therapy, revealed that the content of chlorine, sodium, potassium and rubidium practically does not change and is within the limits for healthy children. The use of basic therapy with the immunostimulating drug Polyoxidonium improves the iron content by 1.1 times, and with the additional inclusion of the vitamin and mineral complex Vitrum kids by 1.3 times, at the same time, the calcium content, on the contrary, decreases initially by 1.3 times, and then 1.9 times and approaches normal values. In the course of treatment, the zinc content is normalized - with the use of an immunostimulating drug by 1.2 times, and with the additional use of a vitamin-mineral complex by 1.5 times. The content of bromine in the course of treatment is reduced by 1.3 times, and manganese by 1.8 times compared with patients with nosocomial pneumonia. The content of selenium during treatment with the addition of a vitamin-mineral complex approaches the reference values for healthy children.

The performed correlation analysis showed a significant inverse reliable correlation between the indicators of FAN and SD4 + ($r = 0.49$, $p < 0.001$), IgA and SD20 + ($r = 0.50$, $p < 0.001$), SD16 + and TNF α ($r = 0.50$, $p < 0.001$), there is a correlation between Cu and SD20 + and LPO ($r = 0.59$, $p < 0.001$). The results of studies of the microelement status showed a positive correlation between the content of CD16 + and Se ($r = 0.50$, $p < 0.001$), CD20 +, Zn and Cu ($r = 0.50$, $p < 0.001$), CD20 + and Fe ($r = 0.52$, $p < 0.001$), TNF α and Zn ($r = 0.48$, $p < 0.001$), CD4 + and Se ($r = 0.48$, $p < 0.001$), a significant positive correlation was also found between the IgA and Se levels ($r = 0.50$, $p < 0.001$), IL 8 and Zn ($r = 0.44$, $p < 0.001$), IL6 and Zn ($r = 0.44$, $p < 0.001$), IL 4 and Se ($r = 0.45$, $p < 0.001$), IL8 and TNF α ($r = 0.45$, $p < 0.001$), IL4 and IgA ($r = 0.45$, $p < 0.001$). A direct strong relationship was found between selenium concentration and natural killer cells ($r = 0.64$, $p < 0.001$). In patients with a severe course of nosocomial pneumonia, there was an increase in the identified correlations, that is, the influence of a violation of the trace element balance on the parameters of immunity was more strongly traced.

Thus, during the three-stage treatment, the indicators of iron, zinc, selenium increase. These trace elements increase the immune status, improve the processes of hematopoiesis, and accelerate the healing process. In turn, a decrease in the values of calcium, bromine and manganese normalizes the nervous-somatic system. All this allows us to conclude that the timely inclusion of an immunostimulating drug in the basic therapy with the subsequent addition of a vitamin-mineral complex leads to an improvement in the outcome of the disease, normalizing the elemental status of children.

4. CONCLUSION

The microelement composition of the blood of healthy children and patients with out-of-hospital and nosocomial pneumonia was studied by neutron activation analysis. The data obtained show that with nosocomial pneumonia, the violation of the trace element status is more pronounced in comparison with healthy children. The developed 3-step method of treatment with the use of an immunomodulatory drug and vitamin-mineral complex Vitrum kids, based on the basic therapy, improves the healing process and normalizes the microelement status of children.

Acknowledgements

We are grateful to the staff members of Nationwide Specialized Scientific and Practical Medical Center of Pediatrics of the Ministry of Health of the Republic of Uzbekistan and Urgench branch of the Tashkent Medical Academy for the cooperation and support in our research. The participants kindly gave full written permission for this report.

CONSENT

Written informed consent was obtained from all participants of the research for publication of this paper and any accompanying information related to this study.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

FUNDING

No funding sources to declare.

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