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Zinc levels in children with community-acquired pneumonia: a comparative study in the context of SARS-CoV-2 infection

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It has been proven that a deficiency of zinc, can significantly weaken the body's immune response to infection. Zinc plays a key role in many immunological processes, such as the proliferation and differentiation of lymphocytes, antibody synthesis, and phagocytosis.

Aim: to assess the dynamics of zinc levels in pediatric patients with community-acquired pneumonia, taking into account the presence or absence of SARS-CoV-2 co-infection in the acute phase of the disease and the recovery period.

Materials and methods. The study included 114 children aged 6 to 18 years. The Basic group consisted of 81 patients diagnosed with community-acquired pneumonia, divided into subgroups based on the presence or absence of SARS-CoV-2 co-infection. The Control group consisted of 33 healthy children matched by age and gender. Zinc levels in serum were determined for all children. The results of the study were processed using Microsoft Excel 2013.

Results. All children in the Basic group had decreased serum zinc levels in both the acute phase and convalescent periods. Children with severe community-acquired pneumonia, regardless of viral infection, showed only a slight increase in zinc levels with standard treatment. A significant decrease in serum zinc levels was found in all children with pneumonia compared to the Control group. Patients with SARS-CoV-2 demonstrated a more pronounced zinc deficiency compared to those with pneumonia of other etiologies. During treatment, a gradual increase in zinc levels was observed in all patient groups.

Conclusions. The study revealed a decrease in zinc concentration in children with community-acquired pneumonia, both during the acute phase and during the convalescent period of the disease. Patients with SARS-CoV-2 infection had significantly lower zinc levels compared to children without detected coronavirus.

The study was carried out in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Ethical Committee for all participants in the process. The informed consent was obtained from children and parents for participation.

No conflict of interests was declared by the authors.

Keywords: community-acquired pneumonia, zinc, children, trace element, SARS-CoV-2 virus.

Рівень цинку в дітей із позалікарняною пневмонією: порівняльне дослідження в контексті інфекції SARS-CoV-2

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Доведено, що дефіцит мікроелементів, зокрема цинку, може значно послаблювати імунну відповідь організму на інфекцію. Цинк відіграє ключову роль у таких багатьох імунологічних процесах, як проліферація та диференціація лімфоцитів, синтез антитіл та фагоцитоз.

Мета: оцінити динаміку рівня цинку в педіатричних пацієнтів із позалікарняною пневмонією з урахуванням наявності або відсутності коінфекції SARS-CoV-2 у гострій фазі захворювання та періоді реконвалесценції.

Матеріали та методи. У дослідженні взяло участь 114 дітей віком від 6 до 18 років. Основну групу становив 81 пацієнт із діагнозом позалікарняної пневмонії, серед яких було виділено підгрупи залежно від наявності або відсутності коінфекції SARS-CoV-2. У контрольній групі було 33 здорових дітей відповідного віку та статі. У всіх дітей було визначено рівень цинку в сироватці крові. Результати дослідження опрацьовано з використанням програмного пакета Microsoft Excel 2013.

Результати. Усі діти основної групи мали знижений рівень цинку сироватки крові як у гострій фазі, так і в періоді реконвалесценції. Нижчі показники цинку в період розпалу та реконвалесценції мали діти з виявленим вірусом SARS-CoV-2. Діти з тяжким перебігом позалікарняної пневмонії незалежно від ураження вірусом мали незначне зростання показника мікроелемента на фоні стандартного лікування. У всіх дітей із пневмонією було виявлено статистично значуще зниження рівня цинку в сироватці крові порівняно з контрольною групою. У пацієнтів із SARS-CoV-2 простежувався більш виражений дефіцит цинку порівняно з пацієнтами з пневмонією іншої етіології. У процесі лікування спостерігалося поступове збільшення рівня цинку у всіх групах пацієнтів.

Висновки. Дослідження виявило зниження концентрації цинку в дітей, хворих на позалікарняну пневмонію, як під час гострого періоду, так і в період реконвалесценції захворювання. Окрім того, пацієнти з встановленим ураженням вірусом SARS-CoV-2 мали достовірно нижчі показники цинку порівняно з дітьми без виявленого коронавірусу.

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження погоджено етичним комітетом для всіх учасників процесу. Для участі отримано інформовану згоду від дітей та батьків.

Автори заявляють про відсутність конфлікту.

Ключові слова: позалікарняна пневмонія, цинк, діти, мікроелемент, вірус SARS-CoV-2.

Introduction

Community-acquired pneumonia (CAP) is a major problem worldwide because of its high prevalence and mortality. The most dangerous pathology is in the first years of life, as inflammation accounts for 14% of deaths in children under 5 years of age [16,22]. That is why most guidelines and recommendations on pneumonia are deve-

loped for children in the first 5 years of life. However, the issue of pneumonia is also relevant for older children. Global studies show that about 7% of sick children die from pneumonia at the age of 5–9 years [9,10]. According to Ukrainian researchers, the proportion of children over the age of 7 with pneumonia is about 45% [20].

Pneumonia is an inflammation of the lung tissue, usually caused by viruses, bacteria, or a combination of both. It is considered the most common cause of hospitalization among children worldwide [11,19]. The highest incidence of CAP is observed in countries with poor economies [8,10,19,20]. However, the incidence of CAP remains quite high in industrialized countries [8]. Trace elements play an important role in the development of diseases, including lung tissue pathology. After all, they are essential for the proper functioning and growth of the child's body and ensuring an adequate immune response [5,12]. One of the most important trace elements necessary for the proper functioning and growth of the child's body is zinc [13,17]. It is one of the most abundant trace elements in the human body [3]. It has an impact on pro-inflammatory reactions, the activity of the cytokines IL-1b, IL-6, and tumor necrosis factor α (TNF-α) [1,14]. The human body does not have a zinc depot, and therefore, if the micronutrient is not sufficiently supplied by the diet, it is deficient. According to the research, about 20% of the world's population has low levels of the trace element [14]. For Eastern European countries, zinc deficiency is about 10%. Low zinc levels cause a decrease in the production of antibodies and a deterioration in the immune response by increasing the production of pro-inflammatory cytokines [13,21]. At the same time, foreign studies have shown that low levels of the trace element in the body are a predisposing factor for SARS-CoV-2 viral infection in adults. They also proved an inversely proportional relationship between the severity of the disease and the level of blood metal [2,4,7].

The aim of the study was to investigate zinc levels in children at the age of 6 to 18 years with CAP with and without SARS-CoV-2 viral infection during the acute and convalescent periods.

Materials and methods of the study

The study was conducted on the basis of the Department of Infectious Diseases of the Clinical Hospital of the St. Zinaida of the Municipality and the Central Primary Health Care Centre No. 1 of the Municipality. A total of 114 patients were examined. Of these, 81 were children with CAP. The diagnosis was confirmed by medical history, recorded complaints and objective, instrumental and laboratory investigations according to the standards of care «Community-Acquired Pneumonia in Children» (2022).

Children diagnosed with CAP (Basic group) were divided into two groups according to SARS-CoV-2 viral infection. Group 1 included 52 children with severe CAP and SARS-CoV-2 infection. Group 2 consisted of 29 patients with CAP without evidence of SARS-CoV-2 virus. The Control group consisted of 33 somatically healthy children.

All children in the study had taken laboratory samples – at the acute onset and again during recovery, to determine serum zinc levels. Trace element levels were measured by atomic absorption spectrometry on an atomic absorption spectrometer.

Microsoft Excel 2013 was used for the statistical analysis of the data. A two-tailed independent Student's t-test was used to assess the differences between the means of the different groups. Differences at a significance level of $p<0.05$ were considered statistically significant.

The research was carried out in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee of the participating institution. The informed consent of the patient was obtained for conducting the studies.

Results of the study

The study showed a decrease in zinc levels in all children with CAP, regardless of SARS-CoV-2 viral infection. In the middle of the illness, the mean levels of the trace element were significantly lower in patients of the Basic group than in the Control group. Zinc levels were (7.24±0.29) μmol/L versus (14.15±0.54) μmol/L ($p<0.001$).

After the standard treatment, the blood sample was taken again and the zinc level was determined on the 7^{th}-10^{th} day of the disease. The mean level of the trace element in children of the Basic group increased gradually and was (8.11±0.29) μmol/L. However, the zinc concentration was significantly lower than in the Control group ($p<0.001$). The above data are shown in Figure.

The level of the trace element in Group 1 at baseline was (6.76±0.36) μmol/L. After treatment, the zinc level increased to (7.65±0.35) μmol/L ($p>0.05$).

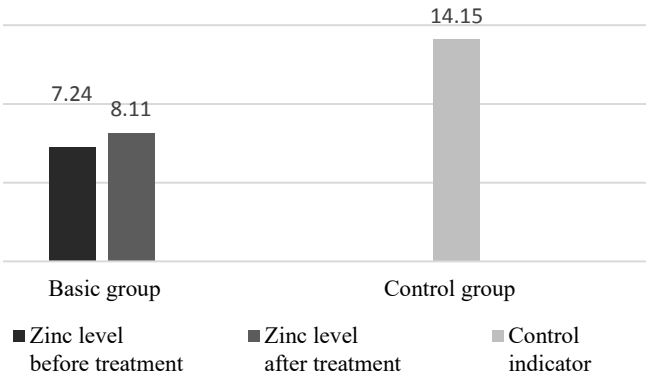

Fig. Zinc levels in the body of the studied children, μmol/L

In Group 2, the trace element level in the acute phase was (8.10±0.49) μmol/L. According to the results of the standard treatment, an increase in zinc levels during the convalescence period was found at the level of (8.9±0.48) μmol/L ($p>0.05$).

A comparative analysis of zinc levels in children with CAP depending on SARS-CoV-2 viral infection revealed a significant decrease in the concentration of trace element in patients with confirmed coronavirus infection both during the exacerbation period and convalescence against the background of standard treatment. A detailed description of zinc levels in the studied children is given in Table.

According to the results of the study, children with CAP, regardless of SARS-CoV-2 viral infection, had lower zinc levels compared to healthy children of the same age. In addition, a significant decrease in the concentration of the trace element was found in patients with proven SARS-CoV-2 viral infection compared to children who had negative test results for coronavirus infection.

Low serum zinc levels in paediatric patients with CAP are the result of impaired protective functions of the body. The trace element is involved in the immune response at various stages and in the functioning of both innate and acquired immunity.

Discussion

The publication reflects the comparative characteristics of zinc concentration in the blood of paediatric patients with CAP with and without SARS-CoV-2 viral infection. Existing scientific data indicate that zinc plays an important role in the functioning of defense mechanisms and is an important indicator of the immune response [5,12,14]. The works by various scientists have shown that children suffering from inflammatory diseases of the respiratory tract and have reduced levels of the trace element [2,4,7,15,21,23]. Previous studies have shown that zinc levels in adults are quite low when they are affected by the SARS-CoV-2 virus [6,18]. These data are confirmed by the results of our study, which showed statistically significant differences in the concentration of the trace element between patients with CAP and clinically healthy children. In addition, our data further demonstrate that zinc levels are worse in CAP patients with SARS-CoV-2 viral infection compared to CAP patients without SARS-CoV-2 viral infection.

Conclusions

A significant decrease in zinc concentration was observed in all children with CAP during the acute phase of the disease. Patients with established SARS-CoV-2 viral infection and CAP had significantly lower mean zinc levels in the acute phase of the disease compared to children without SARS-CoV-2 viral infection. During the recovery period, the mean zinc levels increased in children with CAP against the background of standard treatment. However, zinc levels in children with CAP remained significantly lower than in the Control group during the recovery period. Concentrations of the trace element were significantly lower in the group of CAP patients with SARS-CoV-2 viral infection.

Thus, in cases of suspected community-acquired pneumonia in children, it would be appropriate to determine the serum zinc level for possible further

Table

Zinc concentration in children in dynamics

Period of disease	Groups		
	I	II	Control
Period of acute onset	6.76±0.36 $p_{1-2}<0.05$ $p_{1-3}<0.001$	8.10±0.49 $p_{2-3}<0.05$	14.15±0.54
Period of convalescence	7.65±0.35 $p_{1-2}<0.05$ $p_{1-3}<0.001$	8.9±0.48 $p_{2-3}<0.05$	

correction of the trace element concentration to facilitate a faster recovery.

Prospects for further research. Further research could be aimed at investigating the efficacy of zinc supplementation in children with CAP, especially those with SARS-CoV-2 viral infection.

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REFERENCES/ЛІТЕРАТУРА

1. Arigliani M, Spinelli AM, Liguoro I, Cogo P. (2018). Nutrition and Lung Growth. Nutrients. 10(7): 919. doi:10.3390/nu10070919.
2. Finzi E. (2020). Treatment of SARS-CoV-2 with high dose oral zinc salts: a report on four patients. Int J Infect Dis: IJID: Off Publ Int Soc Infect Dis. 99: 307-309. doi: 10.1016/j.ijid.2020.06.006.
3. Gammoh NZ, Rink L. (2017). Zinc in Infection and Inflammation. Nutrients. 9(6): 624. doi: 10.3390/nu9060624.
4. Ghanei E, Baghani M, Moravvej H, Talebi A, Bahmanjahromi A, Abdollahimajd F. (2022). Low serum levels of zinc and 25-hydroxyvitmain D as potential risk factors for COVID-19 susceptibility: a pilot case-control study. European journal of clinical nutrition. 76: 1297-1302. doi: 10.1038/s41430-022-01095-5.
5. Gombart AF, Pierre A, Maggini S. (2020). A Review of Micronutrients and the Immune System-Working in Harmony to Reduce the Risk of Infection. Nutrients. 12(1): 236. doi:10.3390/nu12010236.
6. Guido Cereda et al. (2022). Zinc as a Neuroprotective Nutrient for COVID-19 – Related Neuropsychiatric Manifestations: A Literature Review, Advances in Nutrition. 13(1): 66-79, doi: 10.1093/advances/nmab110.
7. Heller RA, Sun Q, Hackler J, Seelig J, Seibert L, Cherkezov A et al. (2021). Prediction of survival odds in COVID-19 by zinc, age and selenoprotein P as composite biomarker. Redox Biol. 38: 101764. doi: 10.1016/j.redox.2020.101764.
8. Hu T, Sarpong EM, Song Y, Done N, Liu Q, Lemus-Wirtz E et al. (2023). Incidence of non-invasive all-cause pneumonia in children in the United States before and after the introduction of pneumococcal conjugate vaccines: a retrospective claims database analysis. Pneumonia (Nathan). 15(1): 8. doi: 10.1186/s41479-023-00109-5.
9. Institute of Health Metrics and Evaluation. (2019). Global Burden of Disease Study, 2019. URL: http://ghdx.healthdata.org/gbd-2019.
10. Kevat PM, Morpeth M, Graham H, Gray AZ. (2022). A systematic review of the clinical features of pneumonia in children aged 5-9 years: Implications for guidelines and research. J Glob Health. 12: 10002. doi: 10.7189/jogh.12.10002.
11. Kirolos A, Blacow RM, Parajuli A, Welton NJ, Khanna A, Allen SJ et al. (2021). The impact of childhood malnutrition on mortality from pneumonia: a systematic review and network meta-analysis. BMJ Glob Health. 6(11):e007411. doi: 10.1136/bmjgh-2021-007411.
12. Knebusch N, Mansour M, Vazquez S, Coss-Bu JA. (2023). Macronutrient and Micronutrient Intake in Children with Lung Disease. Nutrients. 15(19): 4142. doi: 0.3390/nu15194142.
13. Kramarov S, Yevtushenko V, Yevtushenko O. (2021). The value of zinc in infectious diseases in children. Actual Infectology. 8(1): 17-24. doi: 10.22141/2312-413x.8.1.2020.196167.
14. Luan R, Ding D, Xue Q et al. (2023). Protective role of zinc in the pathogenesis of respiratory diseases. Eur J Clin Nutr. 77: 427-435. doi: 10.1038/s41430-022-01191-6.
15. Pechugina VV, Usachova OV. (2023). Modern ideas about the importance of providing zinc in infectious diseases in children. Modern Pediatrics. Ukraine. 3(131): 97-103. doi: 10.15574/SP.2023.131.97.
16. Popovsky EY, Florin TA. (2022). Community-Acquired Pneumonia in Childhood. Encyclopedia of Respiratory Medicine. 6: 119-131. doi: 10.1016/B978-0-08-102723-3.00013-5.
17. Sakulchit T, Goldman RD. (2017). Zinc supplementation for pediatric pneumonia. Can Fam Physician. 63(10): 763-765. PMID: 29025801; PMCID: PMC5638472.
18. Skalny AV et al. (2020). Zinc and respiratory tract infections: Perspectives for COVID-19 (Review). International journal of molecular medicine. 46(1): 17-26. doi: 10.3892/ijmm.2020.4575.
19. United Nations International Children's Emergency Fund. (2023). Pneumonia in children: Everything you need to know. URL: https://www.unicef.org/stories/childhood-pneumonia-explained.
20. Volosovets O, Bolbot Y, Abaturov O, Kryvopustov S, Besh L, Stoieva T et al. (2020). Dynamics of the incidence rate of pneumonia in children in Ukraine over the past 20 years. Med. perspekt. 25(4): 174-181. URL: https://journals.uran.ua/index.php/2307-0404/article/view/221680.
21. Wessels I, Pupke JT, von Trotha KT, Gombert A, Himmelsbach A, Fischer HJ et al. (2020). Zinc supplementation ameliorates lung injury by reducing neutrophil recruitment and activity. Thorax. 75(3): 253-261. doi: 10.1136/thoraxjnl-2019-213357.
22. World Health Organization. (2022). Pneumonia in children. Geneva. URL: https://www.who.int/news-room/fact-sheets/detail/pneumonia.
23. Yang M, Li Y, Yao C, Wang Y, Yan C. (2023). Association between serum copper-zinc ratio and respiratory tract infection in children and adolescents. PLoS ONE. 18(11): e0293836. doi: 10.1371/journal.pone.0293836.

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