THE STATE OF THE ERYTHRON SYSTEM IN ACUTE PNEUMONIA IN CHILDREN

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Annotation
Changes in the erythron system in acute pneumonia in children occurring against the background of iron deficiency anemia of varying degrees determine the severity of the underlying disease. Using phase-contrast microscopy, morphological changes in erythrocytes, life expectancy, average size and its functional state were studied, which confirm the relationship between the severity and clinical course of the disease. Identification of common pathogenetic mechanisms of the formation of these pathological conditions allows us to optimize the ongoing treatment.

Keywords: children, acute pneumonia, erythron system, iron deficiency anemia, diagnosis, treatment.

Introduction
Currently, acute pneumonia (AP) is of particular relevance for a general practitioner due to its high prevalence in the pediatric population [1, 4]. It is known that in the prevalence, course and outcome of pneumonia, a large role belongs to the state of the reactivity of the child's body. The latter often depends not only on the course of pneumonia itself, but also on conditions that are the so-called "unfavorable premorbid background" - malnutrition, rickets, anemia, etc. [8, 13, 17].

The development of pneumonia in some children and its absence in others, despite the presence of the same viral and microbial agents, has always forced pediatricians to look for additional factors that help reduce the resistance of the macroorganism [5, 6, 12]. These undoubtedly include iron deficiency anemia, which, even in a mild form, predispose to the occurrence of severe and recurrent respiratory diseases. The frequency of iron deficiency states is observed in 44% of young children [2, 3]. According to WHO data, it has been established that the prevalence of iron deficiency anemia (IDA) among the most vulnerable groups of the population, such as pregnant women and children, is 50-60% in developing countries and 10-20% in developed countries [8, 9 , ten]. A study of the prevalence of anemia in Uzbekistan showed similar results among young children [7, 17].

The development of pneumonia against the background of iron deficiency anemia in conditions of pronounced metabolic imbalance aggravates the course of the pneumonic process and contributes to even greater stress on adaptive mechanisms [12, 14, 15, 16, 17, 18, 19]. Naturally, in such a situation, the role of erythron in iron deficiency anemia in association with acute pneumonia can be of great clinical importance, indicating both the severity of metabolic disorders and the prognosis of the disease as a whole.

The Purpose of the Study

To identify the features of changes in erythron parameters in acute pneumonia in infants.

Material and Research Methods

The article contains the results of clinical and hematological studies of 138 children aged from 2 months to 1 year, 86 of them with acute pneumonia against the background of iron deficiency anemia, who were treated at the Regional Children's Multidisciplinary Medical Center of Samarkand. The research methodology consisted in studying the morphological state of the peripheral erythron using phase contrast microscopy (PCM), erythrocyte lifespan (EL), mean erythrocyte diameter (MED), mean erythrocyte volume (MEV), hematocrit, reticulocytes, and the functional state of erythrocytes.

Research results. In 20 children aged 2 months to 1 year with clinical and radiologically confirmed acute pneumonia, the disease proceeded against the background of IDA of the 1st degree. According to the classification of pneumonia, focal-uncomplicated acute pneumonia was detected in 14 children (70.0%), in 5

patients (25%) segmental and segmental-confluent, only 1 patient (5%) had a complicated course of the disease.

When collecting anamnestic data, it turned out that the disease began with catarrhal phenomena from the upper respiratory tract in more than 1/3 (n=7) children. In most patients, upon admission to the hospital, the condition was assessed as moderate. Along with symptoms such as dry cough 8 (40%), shortness of breath 5 (25%), general lethargy 7 (35%), the majority of children (80%) had subfebrile temperature. An objective study drew attention to the pallor of the skin, moderate excitability and irritability, sleep disturbance, some disorders of the vasomotor system were clearly manifested (lability of vascular tone, cyanosis of the nasolabial triangle, swelling of the wings of the nose). The proportion of symptoms characteristic of IDA was slightly different from the IDA group without OP, when grade I IDA was not accompanied by acute pneumonia. The study of quantitative indicators of red blood compared with a group of children with IDA without pneumonia is shown in Table 1.

Table 1. Quantitative indicators of red blood in acute pneumonia against the background of IDA of the 1degree (M±m)

Indicators	IDA I degree (n=20)	IDA I degree + AP (n=20)	P *
Erythrocytes, 10^{12}/l	3,85±0,45	3,76±0,26	>0,1
Hemoglobin, g/l	98,12±2,05	96,26±1,18	>0,1
Fetal hemoglobin, %	8,08±0,27	11,47±1,23	<0,02
hematocrit,	0,31±0,03	0,34±0,05	>0,1
Reticulocytes, ‰	8,02±0,27	7,24±0,25	<0,05
MED, μm	7,54±0,03	7,61±0,03	<0,001
PZhE, days	72,56±2,11	70,24±2,11	>0,1

Note: P - reliability in relation to IDA of the 1 degree.

As follows from the table, in case of pneumonia against the background of IDA of the 1st degree, the quantitative indicators of red blood, although they differed from those of healthy children, remained the same as in the case of IDA of the 1st degree without association with pneumonia. The study of individual deviations showed that in half of the patients the number of erythrocytes fluctuated within 3.85×10^{12}/l, in 6 patients (30%) within 3.6×10^{12}/l, the content of erythrocytes was less than 3.51×10^{12}/l in 1 μl of blood was observed in 4 (20%) children. Thus, we found that in acute pneumonia with IDA of the I degree of severity, the content of hemoglobin in the erythrocyte in relation to patients with IDA without pneumonia does not change significantly, and the concentration of hemoglobin in erythrocytes slightly increases, although it corresponds to the age norm.

However, the level of serum iron in mild IDA associated with pneumonia, compared with healthy children, is reduced by more than 25%. Apparently, in acute pneumonia, the concentration of hemoglobin in the erythrocyte increases compensatory.

In acute pneumonia at the height of respiratory hypoxia, significant changes occur in the morphological structure of erythrocytes, which were revealed in their native study. Our data indicate that the number of main functioning discocyte cells decreased by 17%, the number of stomacytes, echinocytes, spherocytes and deformed erythrocytes increased (Table 2.).

Table 2. Morphological and functional features of erythrocytes in acute pneumonia against the background of IDA of the 1 degree (M±m).

Indicators	IDA I degree (n=20)	IDA I degree + AP (n=20)	P *
Discocytes, %	77.31±1.37	65.35±1.64	<0 001
Spheroids, %	8,54±1,42	9,36±1,52	>0 1
Echinocytes, %	1,84±0,22	4,82±0,44	<0,001
Stomacytes, %	5,86±0,18	6,46±0,63	>0,1
Spherocytes, %	1,63±0,09	2,53±0,36	<0,02
deformed cells	4,82±0,26	11,42±1,24	<0,001
Erythrocyte pulsation 1 min	42,87±1,39	41,54±1,43	>0,1

Note: P - reliability in relation to IDA of the 1 degree.

Thus, IDA of the 1st degree is an unfavorable premorbid background of acute pneumonia in infants, it expands the clinical manifestations of the disease, and changes in the quantitative and qualitative indicators of peripheral erythron in the FCM study of the morphofunctional features of erythrocytes are not clearly expressed, only minor changes are noted.

In acute pneumonia against the background of IDA II degree in 47 children, among which focal pneumonia was diagnosed in 10 (21.3%), segmental - in 30 (63.8%), segmental-confluent - in 4 (8.5%) and in 3 patients (6.4%) clinical and radiographically the disease was characteristic of the interstitial form of OP. Acute pneumonia was observed in 89 (94.7%) patients, of which 4 (8.4%) children had complicated pneumonia.

Therefore, the clinical symptoms of acute pneumonia, its severity and severity depend on an unfavorable premorbid background, in particular, on IDA. Depending on the degree of IDA, the severity of the condition of the patients differed significantly:

severe and extremely severe general condition of the child with IDA II degree increased tenfold. Such children are more adynamic than when pneumonia developed in the absence of IDA.

Along with adynamia and the severe condition of the child, characteristic of acute pneumonia, high temperature in IDA of the II degree was much less common. Unstable febrile fever was more often observed in patients with pneumonia without IDA. Since fever is one of the important clinical signs of acute pneumonia and characterizes the reactivity of the body, the relatively low subfebrile temperature in children with acute pneumonia against the background of II degree IDA indicates the participation of IDA in the immunological reactivity of the child's body.

Neurological changes in acute pneumonia against the background of IDA and II degree are a combination of impaired consciousness, changes in the functional state of the nervous system, thermoregulation disorders and convulsions. The genesis of neurological disorders is complex, apparently, they are due to a complex of causes - hypercapnia, hemic hypoxia, toxicosis, etc.

We were of particular interest to compare the clinical data of the two examined groups of patients on the part of other organs and systems, since IDA undoubtedly affects their function. First of all, we noted that in patients with pneumonia against the background of IDA I and II degrees of severity, a significant increase in the liver and spleen, mainly in children with a complicated form of pneumonia. Compared with uncomplicated pneumonia, with complicated pneumonia against the background of II degree IDA, re- and superinfections developed 2 and 3 times more often. The reasons for this fact, undoubtedly, lie in the change in the immunological reactivity of the body in infants with IDA, which was taken into account in the treatment of the disease.

Summarizing the data, it can be argued that the quantitative indicators of red blood in the acute period of pneumonia against the background of IDA of II degree from I degree of severity were insignificant, there were no significant significant statistical differences. However, when comparing these parameters in acute complicated pneumonia, we found significant differences in the number of reticulocytes, hematocrit levels, which were statistically significantly changed ($P<0.05$). Thus, the number of reticulocytes was almost doubled, and the hematocrit was reduced to 0.29. In acute complicated pneumonia against the background of II degree IDA, the life span of erythrocytes decreased. The degree of change in the quantitative indicators of red blood depends not only on the severity of IDA, but also on extrapulmonary complications of acute pneumonia.

Therefore, with a relative stability of changes in the quantitative indicators of red blood in IDA of the II degree, the qualitative blood indices significantly (statistically significantly) undergo changes. The level of content and concentration of hemoglobin in the erythrocyte with pneumonia approaches the norm. At the same time, the volume of the erythrocyte increases by almost 7-8 µm3 than in patients with IDA of the II degree without the manifestation of acute pneumonia.

During the recovery period, after the elimination of clinical signs of acute pneumonia, we found an improvement in the quantitative and qualitative indicators of red blood. In this period, there was a slight decrease in the number of erythrocytes, hemoglobin and hematocrit. With an increase in hematocrit in these patients, the average hemoglobin content in one erythrocyte (SSHE) decreased to 28.28±1.07 ng. This indicated plasmatic hypotension in IDA of the II degree, the proof of the above was the acceleration of MEV to 119.01±2.56 µm3, which was taken into account during infusion therapy.

In acute pneumonia, which developed against the background of II degree IDA, the level of serum iron increased slightly compared to IDA of the same degree without pneumonia, however, compared with healthy children, this indicator decreased by more than 38%. This may be due to the limited intake of iron in the body due to loss of appetite, impaired absorption in the intestine, and also with the depletion of iron reserves during infection.

With this pathology, significant changes occur in the morphofunctional parameters of erythrocytes (Table 3.).

Table 3 Morphofunctional features of erythrocytes in acute pneumonia against the background of II degree IDA (M±m).

Indicators	IDA II degree (n=26)	IDA II degree + AP (n=47)	P *
Discocytes, %	71,27±1,52	56,37±1,73	<0,001
Spheroids, %	9,21±0,59	10,96±1,39	<0,1
Echinocytes, %	2,36±0,07	7,42±0,27	<0,001
Stomacytes, %	5,62±0,14	8,37±0,19	<0,001
Spherocytes, %	3,13±0,09	4,83±0,39	<0,001
deformed cells	8,41±0,15	12,05±0,21	<0,001
Erythrocyte pulsation 1 min	41,67±1,22	37,74±1,37	<0,05

Note: P - reliability in relation to IDA of the II degree.

As follows from Table 3, in acute pneumonia against the background of IDA of II severity in the peripheral blood, the number of erythrocytes-discocytes decreases by half, echinocytes and spherocytes increase almost 3 times.

Although the erythrocyte pulsation remains low, it is somewhat reduced compared to grade II IDA without acute pneumonia. Probably, in the acute period of pneumonia, the association of respiratory and hemic hypoxia leads to a compensatory increase in erythrocyte pulsation, although erythrocytes newly entering the vascular bed rapidly lose their resistance.

In acute pneumonia on the background of III degree IDA, 19 patients were under observation, in whom acute pneumonia proceeded in the form of segmental and polysegmental forms.

Analysis of the obtained data on the number of erythrocytes in IDA in the acute period of pneumonia showed their insignificant ($P>0.1$) decrease (2.42 ± 0.36) in 1 µl of blood. The study of individual deviations showed that in 10 patients the number of erythrocytes varied within 3.01-3.22 per 1 µl, in 4 children 2.9-2.5 per 1 µl; the content of erythrocytes less than 2.3 was observed in 10 patients (54.05%).

The content of total hemoglobin decreased in the acute period, and in the recovery period (5-7 days) was 98.76 ± 1.5 g/l. The shortening of the life span of erythrocytes was accompanied by low hematocrit values (although a significant increase was observed during the recovery period), remained at low levels from the norm, which indicated continued tissue hypoxia, the evidence for this was a statistically unreliable increase in reticulocytes in fetal hemoglobin ($P> 0.1$). According to the data obtained, in the acute period there was an increase in fetal hemoglobin (18.46 ± 1.73). In the dynamics of the disease, a significant decrease was also observed in the recovery period, i.e. on days 20-25 remained at a high level, which can be attributed to the protective and adaptive reaction of the body in the fight against not only respiratory, but also hemic hypoxia, observed in IDA of the III degree. These data show that the development of acute pneumonia against the background of III degree IDA in infants is accompanied by severe disorders of metabolic processes in erythrocytes and hemoglobin-synthetic function of the bone marrow, which persist throughout the recovery period.

When studying the qualitative indicators of red blood, it was revealed that a decrease in the average concentration of hemoglobin and attention to changes was accompanied by a decrease in the average hemoglobin content in one erythrocyte.

In all groups of IDA with the association of acute pneumonia, the hematocrit was significantly lower than in healthy children ($P>0.1$).

Changes in hematocrit are primarily due to the number of erythrocytes in the peripheral blood and MEV. This is confirmed by the presence of a high degree of correlation between these indicators, the pair correlation coefficient was r=0.55 and r=0.74, respectively. This connection is well traced in some cases of the disease.

In some (6%) children, low hematocrit was observed with a simultaneous decrease in MEV and hematocrit. An example is the changes in D.V., 9 months old. (case history No. 19550/487 dated February 29, 2021.) and Kh.Kh., 6 months. (case history No. 2523/119 dated March 11, 2021). In both children, a decrease in hematocrit to 0.219 and 0.32 was characterized by a decrease in the number of erythrocytes 3×10^{12} and 3.5×10^{12} per µl/l of blood and a decrease in MEV - 81.2 and 82.3 μm^3. These data allow us to conclude that it is impossible to focus only on the content of erythrocytes and hemoglobin in IDA in children, it is necessary to determine the hematocrit value, which allows one to judge not only the mass of erythrocytes, but also the average volume of erythrocytes. Therefore, it must be assumed that the MEV, reflecting the morphological features of erythrocytes, gives an idea of the qualitative characteristics of erythropoiesis.

In the acute period of the disease, there is a decrease in the level of plasma iron and the saturation coefficient of transferrin with iron, which can be considered as a protective reaction of the body, which accelerates the metabolism of iron in the body. In the dynamics of the disease, during the period of clinical improvement in the child's condition with a significant increase in ἀ-1 and γ globulins (P <0.001), an increase in serum iron (6.23±0.53 µmol/l) and transferrin saturation coefficient with iron (6,36±0.29%). In the recovery period, the red blood values approached those of the group of patients with IDA, the only sign of insufficient reserves of deposited iron requiring continued treatment is the level of plasma iron and a low saturation of transferrin with iron.

To determine the causes of violations in the life span of erythrocytes, iron metabolism in the body of patients with acute pneumonia against the background of severe IDA, it is of great importance to study the morphofunctional properties of native erythrocytes. The data of these studies, which were conducted in the acute period of pneumonia, are shown in Table 4.

Table 4 Morphological and functional features of erythrocytes in acute pneumonia against the background of III degree IDA (M±m)

Indicators	IDA III degree (n=6)	IDA III degree + AP (n=19)	P *
Discocytes, %	71,27±1,52	56,37±1,73	<0,001
Spheroids, %	9,21±0,59	10,96±1,39	<0,1
Echinocytes, %	2,36±0,07	7,42±0,27	<0,001
Stomacytes, %	5,62±0,14	8,37±0,19	<0,001
Spherocytes, %	3,13±0,09	4,83±0,39	<0,001
Deformed cells	8,41±0,15	12,05±0,21	<0,001
Erythrocyte pulsation 1 min	41,67±1,22	37,74±1,37	<0,05

Note: P - reliability in relation to IDA of the III degree.

A comparative evaluation of the data presented in Table 4 allows us to conclude that respiratory hemic hypoxia has a pronounced effect on the morphological structure of peripheral blood erythrocytes compared to hemic hypoxia caused by IDA without the manifestation of pneumonia. Strengthening of the spheroid reaction in the acute period of pneumonia is regarded as a consequence of the action of pathological agents (toxins, biologically active substances), leading to faster aging and a reduction in the life of erythrocytes.

Summarizing the above data, it can be stated that the results of a comprehensive study of acute pneumonia against the background of IDA in young children showed changes in the red blood - a decrease in erythropoiesis, high hemolysis of erythrocytes, a reduction in their life expectancy, significant changes in the morphostructure of native peripheral blood erythrocytes, which can be explained by a decrease in the content of protein fractions of serum iron. The degree of disturbance in the erythron system in patients with acute pneumonia depends on the severity of anemia.

The results of the study of the morphofunctional features of the erythrocyte system indicate that in the acute period of the disease, the number of the main functioning cells of discocytes decreased to 40.09 ± 1.46%, in parallel with the severity of IDA, echinocytes, stomatocytes, spherocytes increased (2.1 times) and deformed cells (up to 10.99±0.26%). During the height of the disease, one of the main clinical signs of the disease - tachypnea was accompanied by a parallel acceleration of erythrocyte pulsation (P<0.001).

Conclusion

In acute pneumonia against the background of IDA, the appearance of rare forms of erythrocytes, depending on the severity of the pathological process, is apparently associated with a pronounced change in the qualitative composition of membranes

and their surface ultrastructure, which leads to functional inferiority of mature cells of the erythrocyte system, impaired hemoglobin synthesis, a reduction in the life span of erythrocytes, which ultimately exacerbates the severity of hypoxia, which can be considered as a damaging phase of the modular type of the compensatory-adaptive reaction of the erythrocyte system.

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