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# EFFECTIVENESS OF COMPLEX THERAPEUTIC MEASURES IN PATIENTS WITH COMMUNITY-ACCOMBINE PNEUMONIA ASSOCIATED WITH MIXED INFECTION

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**Annotation.** The object of the study were 97 patients, children with community-acquired pneumonia associated with mycoplasma and chlamydial infection aged from 1 to 7 years. Dynamic analysis has proven the benefit of differentiated treatment. In group II, during therapy on the 6th day from the start of treatment, a pronounced positive dynamics of physical data was observed. Analysis of the effect of differentiated treatment on the parameters of biochemical data of the examined patients revealed a positive effect on the studied parameters. There was a significant decrease in the content of $NO_2(NO_3)$, HP, ONOO- and a significant increase in eNOS compared with the data of group I. After treatment, the concentration of MDA was 1.8 times higher than in practically healthy children and 1.4 times lower than in children who received basic therapy. A decrease in the level of MDA in the blood in patients with CAP associated with MI and CI during treatment states a decrease in free radicals and an increase in the intensity of AOS.

**Key words:** children, community-acquired pneumonia, mycoplasma, chlamydia, mixed infection

**Relevance.** The interest of scientists in community-acquired pneumonia (CAP) associated with mixed infection in childhood in the modern world remains high due to its high prevalence, severe course and frequent complications, which leads to significant social and material damage. Thanks to the active implementation of modern diagnostic methods, numerous new strains of mycoplasmal, chlamydial and herpesvirus infections, as well as a number of patterns of immunopathological changes, have been discovered and characterized, the significance of nitric oxide, prooxidant and antioxidant systems is still insufficiently studied [1,3,4,7,9 ,11,12].

Recently, research has been carried out to improve modern methods of diagnosis, treatment, rehabilitation and prevention of community-acquired pneumonia associated with mixed infection in the following priority areas: including the rationale for the development of pathogenetic mechanisms in the development of community-acquired pneumonia; identification of the frequency of occurrence and risk factors, identification of clinical and biochemical features; determination of the features of indicators of nitric oxide and pro- and antioxidant systems; assessment of immune and cytokine status; improvement of methods of differential

treatment of CAP associated with mixed infection in children through the use of antiviral, membrane stabilizing and immunocorrective drugs [2,5,6,8,10,14,15].

All these statements reflect the complexity of the multifaceted problem of CAP and determine the need to find ways to optimize both the diagnosis and treatment of this disease.

**The aim of the study** is to study the clinical and laboratory data of patients with community-acquired pneumonia associated with mycoplasma and chlamydial infection after differentiated therapy.

**Material and research methods.** The object of the study were 97 patients, children with community-acquired pneumonia associated with mycoplasma and chlamydial infection aged 1 to 7 years, who were hospitalized in the pulmonology department of the Republican Scientific and Practical Center of Pediatrics. When distributing children by gender, boys predominated - 60.7%, than girls - 39.3% (P<0.001).

We analyzed the dynamics of clinical symptoms, as well as biochemical and immunological data in patients with CAP associated with MI and CI, depending on the use of differentiated treatment regimens.

To determine the effectiveness of differentiated treatment regimens in patients with CAP associated with MI and CI, clinical symptoms were assessed in the course of the disease.

**Results.** We stated the dependence of the frequency of the main clinical manifestations of the disease on the treatment option (table 1).

Dynamic analysis has proven the benefit of differentiated treatment. In group II, on the background of therapy, 13 (25.0%) children had a decrease in shortness of breath on the 6th day from the start of treatment, and in children of group I, the number of children increased by 1.6 times. The cough became softer, the amount of sputum decreased, and physical data had a more pronounced positive trend.

In group II, on the 3rd-4th day of therapy, in 34 (65.4%) children, severe intoxication was not detected, decreasing by 1.6 times compared with group I, normalization of body temperature was fixed 2 times faster (in 22 (42.3%) %), p<0.01) than in children of the first group (34 (75.6%, p<0.01). In children 40 (76.9%) of group II who received differentiated treatment, on days 3-4 appetite improved, whereas in group I, during these periods, an improvement in appetite was observed only in 25 (55.5%) children.Catarrhal phenomena stopped, the number and prevalence of crepitus and finely bubbling wet rales decreased after the use of complex treatment.

Table 1

Dynamics of the main clinical symptoms in patients with CAP associated with MI and CI

| Clinical symptoms | Before treatment n=97 (I) | | I group n=45 (II) | | II group n=52 (III) | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Lethargy | 83 | 85,6 | 27 | 60,0** | 19 | 36,5***/** |
| Intoxication | 69 | 100,0 | 31 | 68,9** | 18 | 34,6***/** |
| Temperature | 69 | 100,0 | 34 | 75,6** | 22 | 42,3***/** |
| Dyspnea | 74 | 64,3 | 18 | 40,0** | 13 | 25,0***/** |
| Decreased appetite | 76 | 78,4 | 20 | 44,5** | 12 | 23,1***/** |

| | | | | | | |
|---|---|---|---|---|---|---|
| Cough | 69 | 100,0 | 39 | 86,7* | 25 | 48,1***/** |
| Wheezing | 69 | 100,0 | 35 | 77,8* | 21 | 40,4***/** |
| SW. lymph nodes | 69 | 71,1 | 22 | 48,9** | 16 | 30,8***/** |
| Hepatomegaly | 53 | 54,6 | 20 | 44,5* | 11 | 21,2***/** |

Note: differences relative to the data of groups I and II of patients are significant (*P<0.05, ** P<0.01), differences relative to the data of groups I and III of patients are significant (***P<0.001),
differences relative to the data of II and III groups of patients are significant (**P<0.001).

A decrease in the size of enlarged peripheral lymph nodes occurred on the 5th-6th day of treatment, but their size was completely restored to normal within 1 month. None of the children experienced side effects during the complex treatment.

Analysis of the effect of differentiated treatment on the parameters of biochemical data in patients with CAP associated with MI and CI revealed a positive effect on the studied parameters. The results of studies of the effect of differentiated treatment on the level of end products of nitric oxide are presented in table 2.

As follows from the presented data, in children of group II, there was a significant decrease in the content of NO2 (NO3) to 11.4±0.5 μmol/l compared with the data of group I (13.2±0.4 μmol/l, p<0 .05).

There was a significant increase in eNOS to 14.2±0.7 μmol/min*mg of protein compared with the data of group I (12.0±0.6 μmol/min*mg of protein, P<0.05).

table 2

Dynamics of indicators of the nitric oxide system in patients with CAP associated with MI and CI, (M±m)

| Indicators | Practically healthy children (n=24) (I) | Before treatment n= 97 (II) | I gr. after treatment n=45 (III) | II gr. after treatment n=52 (IV) | P | $P_1$ | $P_2$ |
|---|---|---|---|---|---|---|---|
| NO, mmol/l | 9,67±0,4 | 13,8±0,5 | 13,2±0,4 | 11,4±0,5 | >0,05 | <0,05 | <0,01 |
| eNOS, mmol/min•mg of protein | 16,88±0,9 | 11,2±0,4 | 12,0±0,6 | 14,2±0,7 | >0,05 | <0,05 | <0,01 |
| HP, mmol/min•mg of protein | 0,22±0,005 | 0,29±0,009 | 0,27±0,012 | 0,23±0,007 | >0,05 | <0,05 | <0,01 |
| ONOO, mmol/l | 0,08±0,003 | 0,15±0,008 | 0,14±0,005 | 0,11±0,006 | >0,05 | <0,01 | <0,01 |

Note: P - reliability of differences between indicators of II and III groups;
P1 - reliability of differences between indicators of groups III and IV after treatment;
P2 - reliability of differences between indicators of IV and V groups after treatment.

The activity of HP in the blood of patients with CAP associated with MI and CI after the use of differentiated therapy decreased by 1.2 times compared with the data of group I (0.27±0.012 mmol/min*mg of protein, $p<0.05$). There was a decrease in ONOO- in the blood to 0.11±0.006 μmol/l, i.e. 1.3 ($p<0.01$) times lower than the values of children of group I. As can be seen from the data presented, the indicators of the nitric oxide system in the blood of CAP patients associated with MI and CI during treatment approached those of practically healthy children.

Thus, the use of differentiated treatment leads to an improvement in the indicators of nitric oxide in the blood in children with CAP associated with MI and CI.

To assess the effectiveness of the treatment in the examined children, we analyzed the dynamics of the indicators of the prooxidant and antioxidant systems. The results of studies of the effect of differentiated treatment on the processes of prooxidants are presented in Table 3.

Table 3

Dynamics of indicators of prooxidants in the membrane of lymphocytes in patients with CAP associated with MI and CI, (M±m)

| Indicators | Practically healthy children (n=24) (I) | Before treatment n= 97 (II) | I gr. after treatment n=45 (III) | II gr. after treatment n=52 (IV) | P | $P_1$ | $P_2$ |
|---|---|---|---|---|---|---|---|
| MDA, nmol/ml | 2,3±0,1 | 6,7±0,5 | 5,9±0,4 | 4,1±0,3 | >0,05 | <0,01 | <0,01 |

Note: P - reliability of differences between indicators of II and III groups;
P1 - reliability of differences between indicators of groups III and IV after treatment;
P2 - reliability of differences between indicators of groups II and IV after treatment.

As can be seen from the above data, a dynamic analysis of the effectiveness of differentiated therapy for CAP associated with MI and CI after treatment in children of group II showed a significant decrease in the high level of MDA to 4.1 ± 0.3 nmol/ml compared with the data of group 1 (5, 9±0.4 nmol/ml, $p<0.01$).

After treatment, the concentration of MDA was 1.8 times higher than in practically healthy children and 1.4 times lower than in children who received basic therapy. A decrease in the level of MDA in the blood in patients with CAP associated with MI and CI during treatment states a decrease in free radicals and an increase in the intensity of AOS.

Dynamics of the level of AOS against the background of the use of differentiated treatment in patients with CAP associated with MI and CI is presented in Table. 4.

Table 4

Dynamics of indicators of the antioxidant system in the membrane of lymphocytes in patients with CAP associated with MI and CI, (M±m)

| Indicators | Practically healthy children (n=24) (I) | Before treatment n= 97 (II) | I gr. after treatment n=45 (III) | II gr. after treatment n=52 (IV) | P | $P_1$ | $P_2$ |
|---|---|---|---|---|---|---|---|
| SOD, | 8,7±0,6 | 4,5±0,3 | 5,1±0,5 | 7,2±0,4 | >0,05 | <0,01 | <0,01 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| arb.u/min•mg of protein | | | | | | | |
| Catalase, mmol/mg protein | 0,16±0,006 | 0,10±0,005 | 0,09±0,007 | 0,13±0,005 | >0,05 | <0,01 | <0,01 |

Note: P - reliability of differences between indicators of II and III groups;
P1 - reliability of differences between indicators of groups III and IV after treatment;
P2 - reliability of differences between indicators of groups II and IV after treatment.

Analysis of the results of AOS activity in children of group II revealed a significant increase in the level of SOD to 7.2±0.4 conventional units/min•mg of protein compared with the indicators of group I 5.1±0.5 conventional units/min•mg of protein ($p<0.01$).

However, the studied indicator was still 1.2 times lower compared to practically healthy children. Analysis of the concentration of catalase in patients with CAP associated with MI and CI against the background of differentiated therapy significantly increased to 0.13±0.005 μmol/mg of protein compared with group I 0.09±0.007 μmol/mg of protein ($p<0.01$ ). At the same time, an increase in the concentration of catalase after treatment indicates the activation of AOS. The results of changes in POS and AOS parameters in children with CAP associated with MI and CI confirm the greater effectiveness of differentiated therapy compared to basic treatment.

**Discussions.** Thus, the results of the study will allow us to conclude that the use in differentiated therapy in patients with CAP associated with MI and CI contributes to the inhibition of the oxidative process, the effective functioning of the AOS and the reduction of inflammation.

After the treatment, in patients with CAP associated with MI and CI, who received differentiated therapy from the immune system, a positive effect of the drugs on the studied parameters was revealed.

In children of group II, under the influence of differentiated therapy, the content of CD3+- and CD4+- lymphocytes significantly increased to 53.6±1.4% and 34.2±0.8%, respectively, compared with group I ($p<0.05$). There was a decrease in the level of CD8+- lymphocytes to 23.1±0.5% in comparison with group I ($p<0.05$). There was a significant decrease in the level of CD16+- lymphocytes to 14.1±0.6% in comparison with group I ($p<0.05$). The index of immune regulation in the group of patients increased to 1.5±0.04, in contrast to the indices of IIR in group I, where it remained stably low (1.3±0.04, $p<0.01$). After treatment in children of group II, phagocytosis of neutrophils increased to 50.2±1.0% compared with group I ($p<0.05$).

There was a significant decrease in CD20+- lymphocytes to 31.4±0.8% in comparison with group I ($p<0.05$). There was also a significant increase in the level of IgG, IgA and a decrease in IgM in comparison with group I ($p<0.05$).

Their content in children of group II, more significantly approaches the normative indicators and amounts to 718.6±26.7 mg/%; 138.7±6.4 mg/%; 110.2±5.1 mg/%, respectively, in contrast to patients of group I ($p<0.05$).

The dynamics of the level of CD25+- lymphocytes as a result of complex treatment (Table 5.2.6) significantly increased to 9.8±0.7% compared with group I ($p<0.05$). The level of CD25+- lymphocytes significantly increased by 1.3 times in comparison with group I, however, the studied indicator was still 1.4 times lower in comparison with practically healthy children. In group II, the content of CD95+-lymphocytes significantly decreased to 34.1±1.0% compared with group I ($p<0.05$). The level of CD95+ - lymphocytes significantly decreased by 1.1 times compared with the data of group I and 1.2 times higher than in practically healthy children.

Table 5

Dynamics of the levels of lymphocytes with a marker of activation and apoptosis in patients with CAP associated with MI and CI (M±m)

| Indicators | Practically healthy children (n=24) (I) | Before treatment n= 97 (II) | I gr. after treatment n=45 (III) | II gr. after treatment n=52 (IV) | P | $P_1$ | $P_2$ |
|---|---|---|---|---|---|---|---|
| CD25+, % | 13,9±0,6 | 7,1±0,5 | 7,4±0,8 | 9,8±0,7 | >0,05 | <0,05 | <0,01 |
| CD95+, % | 29,2±1,1 | 38,4±1,0 | 37,8±1,2 | 34,1±1,0 | >0,05 | <0,05 | <0,01 |

Note: P - reliability of differences between indicators of II and III groups; P1 - reliability of differences between indicators of groups III and IV after treatment; P2 - reliability of differences between indicators of groups II and IV after treatment.

The analysis of the cytokine profile indices of the II group states the positive dynamics of the studied parameters. The dynamics of cytokine production after various methods of treatment is presented in Table 6. As can be seen from the table, the level of IL-1β after treatment decreased in patients of both groups, averaging 112.2±3.9 pg/ml and 96.4±3.7 pg/ml compared with pre-treatment values ($p>0.05$ and $p<0.01$).

In group II, the level of IL-1β was reduced by 1.2 times compared with group I ($p<0.05$), but the studied indicator was still 3.5 times higher compared to practically healthy children. As a result of differentiated treatment, the level of IL-4 significantly decreased to 10.4±0.7 pg/ml in comparison with group I ($p<0.05$), 1.3 times lower than in group I and 2. 3 times more in comparison with practically healthy children. As a result of treatment in patients with CAP associated with MI and CI, the level of IL-8 significantly decreased to 60.4±3.2 pg/ml compared with group I ($p<0.05$), which is 1.2 times lower in in comparison with group I and 3.3 times more in comparison with practically healthy children.

Table 6

Dynamics of levels of cytokine status in patients with CAP associated with MI and CI, (M±m)

| Indicators | Practically healthy children (n=24) (I) | Before treatment n= 97 (II) | I gr. after treatment n=45 (III) | II gr. after treatment n=52 (IV) | P | $P_1$ | $P_2$ |
|---|---|---|---|---|---|---|---|
| IL-1β, pg/ml | 27,8±2,6 | 121,6±7,1 | 112,2±3,9 | 96,4±3,7 | >0,05 | <0,05 | <0,01 |
| IL-4, pg/ml | 4,6±0,6 | 14,8±1,0 | 13,1±0,8 | 10,4±0,7 | >0,05 | <0,05 | <0,01 |
| IL-8, pg/ml | 18,1±2,4 | 81,4±4,9 | 73,6±3,5 | 60,4±3,2 | >0,05 | <0,05 | <0,01 |
| TNFα, pg/ml | 28,4±1,5 | 65,7±4,2 | 59,4±3,8 | 47,8±3,1 | >0,05 | <0,05 | <0,01 |
| IFNγ, pg/ml | 34,3±2,7 | 17,2±1,4 | 19,6±1,2 | 24,5±1,8 | >0,05 | <0,05 | <0,01 |

Note: P - reliability of differences between indicators of II and III groups; P1 - reliability of differences between indicators of groups III and IV after treatment; P2 - reliability of differences between indicators of groups II and IV after treatment.

The level of TNFα decreased by 1.2 times in comparison with group I, which amounted to (47.8±3.1 pg/ml) versus 59.4±3.8 pg/ml ($p<0.05$). In children of group II, IFNγ increased by 1.3 times compared to group I, which amounted to (24.5±1.8 pg/ml) versus 19.6±1.2 pg/ml ($p<0.05$)

**Conclusions.** Our studies have shown that differentiated therapy in patients with CAP associated with mycoplasma and chlamydial infection contributes to the restoration of some studied parameters of cellular and humoral immunity, as well as cytokine status. It is shown that it is an integrated approach to treatment that reduces the likelihood of recurrence of the disease.

Thus, differentiated therapy for community-acquired pneumonia associated with mycoplasma and chlamydia has a good clinical effect, improves the biochemical and immunological parameters of children.

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