

THE ROLE OF HALOAEROSOL THERAPY IN IMMUNOREHABILITATION OF CONVALESCENTS AFTER COMMUNITY ACQUIRED PNEUMONIA

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Abstract

Aim: Investigation of the peculiarities of different haloaerosoltherapy regimes influence (treatment with different intensity of haloaerosol load) upon non-specific defense and cellular immunity at convalescents after community acquired pneumonia.

Objectives: patients with community acquired pneumonia in the early convalescence period (after completing antibiotic therapy), who received treatment in conditions of artificial rock salt aerosol medium (haloaerosoltherapy).

Material and Methods. 42 patients with non-severe community acquired pneumonia were examined in the early convalescence period before and after the course of haloaerosoltherapy, which was prescribed after antibacterial therapy. Immunological studies included: evaluation of phagocytic activity of neutrophils (PhAN - the percentage of phagocytic neutrophils), phagocytic number (PhN - average number of latex particles absorbed by a neutrophil); metabolism of neutrophils in the test with nitroblue tetrasolium (NBT-test) spontaneous and induced, which allowed to assess the functional reserve of neutrophils (FR); calculation of cytochemical coefficient (CCC) for lysosomal cationic proteins (LCP) and for myeloperoxidase (MPO) of neutrophils; number of T- and B-lymphocytes and their subpopulations (CD3⁺, CD4⁺, CD8⁺, CD22⁺-lymphocytes), calculation the number of 0- lymphocytes and the ratio of CD4⁺/CD8⁺ lymphocytes. Laboratory examinations were also conducted in 21 practically healthy individuals (control group).

Two regimes of haloaerosoltherapy were used in recovery treatment of patients with community acquired pneumonia: treating complex №1 (TC-1) with standard haloaerosol load and with increased haloaerosol load (TC-2).

Results. After completion the antibiotic therapy at patients with community acquired pneumonia the moderate inhibition of phagocytic activity of neutrophils (47,6±0,58% to 55,5±1,14% in control group) remained and was accompanied with a decrease in neutrophil bactericidal capacity, mainly oxygen-dependent. However, the disturbances of cellular immunity was observed which manifested by reduced number of T-lymphocytes, mainly on account of T-helper cells and decrease of the CD4⁺/CD8⁺ ratio and was accompanied by the elevation of 0-lymphocytes percentage.

Under the influence of recovery treatment on the base of haloaerosoltherapy usage the positive dynamics of studied parameters was observed and it was more expressed when using treatment procedures with increased haloaerosol load.

Conclusions.

1. The patients with non-severe community acquired pneumonia have moderate disturbances of neutrophils phagocytosis, associated with secondary T-cell dysfunction, which are accompanied with the increasing in the number of undifferentiated 0-lymphocytes and B lymphocytes, which remained after of completing of antibiotic therapy. These changes determine the necessity of recovery treatment in this stage of the disease.

2. Haloaerosoltherapy usage in the recovery treatment of convalescents after community acquired pneumonia improves the functioning of nonspecific defense and T-immunity, with more expressed effect while using more intensive haloaerosol load (TC-2).

3. After recovery treatment based on haloaerosoltherapy usage most of the studied parameters were not improved up to normal values that determine the necessity of new treating complexes elaboration, perhaps with additional prescription of immunomodulators.

Keywords: community acquired pneumonia, haloaerosoltherapy, immune disturbances.

Introduction

Community acquired pneumonia occupy a leading position among the diseases of bronchopulmonary system, is widespread, is characterized by a high frequency of prolonged torpid duration with complications that may barrier in full functional recovery of the patients in convalescence period after completing antibiotic therapy [1, 2]. The standard protocols of treatment regulate the basic principles of antibacterial drugs prescription, which, however, do not always provide full recovery [3-5]. According to computer tomography of high resolution, full recovery is observed only in 28.5% of patients [6].

It should be noted that the disturbances of immune system are of great significance in the pneumonia development and its' further duration [7-9]. However, most of antibacterial drugs have , rock salt has a bactericidal effect, which, in complex with the previous mentioned factors provides sanitation of bronchi and promotes decrease of infectious inflammatory processes in the bronchopulmonary system as a whole [16,17]. However, peculiarities of haloaerosol usage at convalescents after community acquired pneumonia and effectiveness of its' different regimes were not studied yet.

Aim: Investigation of the peculiarities of different haloaerosoltherapy regimes influence (treatment with different intensity of haloaerosol load) upon non-specific defense and cellular immunity at convalescents after community acquired pneumonia.

Objectives: patients with community acquired pneumonia in the early convalescence period (after completing antibiotic therapy), who received treatment in conditions of artificial rock salt aerosol medium (haloaerosoltherapy).

Material and Methods. 42 patients with non-severe community acquired pneumonia were examined in the early convalescence period before and after the course of haloaerosoltherapy, which was

immunosuppressive properties that can intensify the immune dysfunction [10] and promote recurrent infectious inflammatory processes in the convalescence period after acute stage of pneumonia. Therefore, a rehabilitation treatment that provides recovery of normal functioning of the immune system is very important.

One of these methods is the usage of artificial rock salt aerosol medium (haloaerosoltherapy), which perform sanative influence and improves the mucociliary clearance [11,12]. It is known that rock salt aerosol medium provides an expressed hiperosmolar stimulation upon bronchial mucosa that leads to the improvement of rheological properties of bronchial secretions, stimulation of ciliary epithelium and elimination of biologically active substances, which promote the improvement of bronchi drainage function [13-15]. In addition

prescribed after antibacterial therapy. Immunological studies included: evaluation of phagocytic activity of neutrophils (PhAN - the percentage of phagocytic neutrophils), phagocytic number (PhN - average number of latex particles absorbed by a neutrophil); metabolism of neutrophils in the test with nitroblue tetrasolium (NBT-test)spontaneous and induced, which allowed to assess the functional reserve of neutrophils (FR); calculation of cytochemical coefficient (CCC) for lysosomal cationic proteins (LCP) and for myeloperoxidase (MPO) of neutrophils; number of T- and B-lymphocytes and their subpopulations (CD3⁺-, CD4⁺-, CD8⁺-, CD22⁺-lymphocytes), calculation the number of 0- lymphocytes and the ratio of CD4⁺/CD8⁺ lymphocytes.

Laboratory examinations were also conducted in 21 practically healthy individuals (control group).

Two regimes of haloaerosoltherapy were used in recovery treatment of patients with community acquired pneumonia: treating complex №1 (TC-1) with standard haloaerosol load and with increased haloaerosol load (TC-2).

According to the standard regime (TC-1) haloaerosoltherapy includes adaptation period - 1-2 days, during which patients undergo functional and laboratory examinations; adaptation period to the haloaerosol treatment - 3-4 days, during which the duration of haloaerosol procedures gradually increases from 15 to 60 minutes (15 min., 30 min., 45 min. and 60 min.); central (basic) therapeutic period, including daily (except Sundays) haloaerosoltherapy sessions lasting 60 minutes each (17-19 procedures). In general, treatment consisted of 20-22 sessions of haloaerosoltherapy.

Treatment according to the TC-2 included 2 stages of haloaerosoltherapy sessions for 30 minutes each with interval between them 3-4 hours in freshly- prepared rock salt aerosol medium. This provides the total increasing of aerosol concentration, especially particles of 4-10 microns. The course of treatment included 20-22 haloaerosoltherapy sessions also.

Results. In early convalescence period (after completing the antibiotic therapy) of patients with community acquired pneumonia the inhibition of nonspecific antibacterial defense remained, which was manifested by significant decrease of PhAN and PhN in both groups (tabl.1). The percentage of positive cells in spontaneous and induced NBT-test was also significantly reduced, which resulted in decreasing of neutrophils' functional reserve (FR).

The oxygen-dependent and oxygen-independent mechanisms of microorganisms' elimination were suppressed also, which was testified by the reduction CCC MPO and CCC LCP. This condition of phagocytic defense indicated a significant risk for any recurrent infectious inflammatory processes occurrence immediately after pneumonia and is dangerous for the development of chronic inflammatory processes in the broncho-pulmonary system.

Changes of nonspecific resistance were accompanied with a significant decreasing of total T-lymphocytes (CD3⁺-cells) mainly by reducing the number of T-

helper cells (CD4⁺-lymphocytes), although the content of CD8⁺-lymphocytes was also significantly reduced in comparison with the control group (tabl.2). This was accompanied by a decrease in the value CD4⁺/CD8⁺ ratio, which confirmed the presence of immune disturbances.

At the same time, the number of 0-lymphocytes increased in 1,4-1,5 times (tabl.2), which indicates a presence of significant intensity of inflammation, accompanied by intensified migration of highly differentiated cells into the inflammation focus, while the percentage of undifferentiated functionally defective lymphocytes increased in the peripheral blood. This phenomenon was accompanied by disturbances in the receptors' ability of T lymphocytes, which is a manifestation of their potential biological activity. This, in turn, leads to the development of negative changes in the immune response because the receptors of T-lymphocytes are important in its realization.

The reduced number of CD3⁺-, CD4⁺-cells and changes of the ratio CD4⁺/CD8⁺ indicate the comparative depletion of the immune system capabilities or its inability to generate adequate response to antigenic stimulus, which may contribute in the further chronic inflammation.

The level of B-lymphocytes (tabl.2) also have a tendency to increase in comparison with the control group, which indicates some activation of humoral immunity due to the necessity for intensified antibody production.

After the recovery treatment positive dynamics of the nonspecific defense parameters was observed, but its manifestation depended on the TC, which was prescribed (tabl.1). Under the influence of TC-1 the PhAN had a tendency to increase and significant growth of PhN, but both of them remained significantly lower than in control group, indicating residual insufficiency of neutrophils absorbance insufficiency.

The usage of TC-2 led to more expressed positive dynamics of phagocytosis and the level of PhAN and PhN after TC-2 were significantly higher than those after treatment according to the TC-1.

Values of spontaneous and induced NBT-test reached the levels of those in the control group after both TC, but changes in

the functional reserve weren't noted and its value remained slightly below normal.

The CCC MPO and CCC LCP were significantly increased. The oxygen-independent mechanisms of bacteria elimination (CCC LCP) were normalized under the influence of both TC, but oxygen-dependent one (CCC MPO) - only when using the TC-2 (tabl.1).

Table 1. – Changes in some non-specific defense indices at convalescents after community acquired pneumonia under the influence of different regimes of haloaerosoltherapy

| Data, units | Control group (n=21) | TC-1 (n=25) | | TC-2 (n=17) | |
|-------------------------------------|----------------------|------------------|--------------------------|------------------|--|
| | | before treatment | after treatment | before treatment | after treatment |
| PhAN, % p p ₁₋₂ | 55, 5±1,14 | 46,3±1,17** | 49,1± 1,32** <0,2 | 49,2±0,76** | 53,5± 0,81* <0,00 1 p ₁₋₂ <0,01 |
| PhN p p ₁₋₂ | 3,7 6±0,08 | 2,98± 0,06** | 3,29± 0,05** <0,01 | 3,19± 0,04** | 3,45± 0,07** <0,01 p ₁₋₂ <0,05 |
| NBT-test spontaneous, % p | 25, 0±0,75 | 21,9±0,89** | 24,9± 0,77 <0,02 | 22,3±0,61** | 24,6± 0,50 <0,01 |
| NBT-test induced, % p | 32, 8±0,84 | 28,8±0,87** | 31,6± 0,87 <0,05 | 29,4±0,58** | 31,8± 0,56 <0,01 |
| FR p | 7,8 4±0,34 | 6,85±0,40* | 6,73± 0,55* | 6,20± 0,45** | 7,00± 0,56* <0,3 |
| CCC MPO p | 2,1 2±0,04 | 1,70±0,05** | 1,99±0,07* <0,01 | 1,88±0,06** | 2,06±0,04 <0,02 |
| CCC LCP p p ₁₋₂ | 1,5 2±0,05 | 1,39±0,04* | 1,50±0,03 <0,05 | 1,46±0,03* | 1,59±0,03* <0,01 p ₁₋₂ <0,05 |

Notes:

1. * - the tendency to significant changes at patients in comparison with the control group;

2. ** - significant changes in rates at patients in comparison with control group;

3. p - statistical validity of patients' indices before and after treatment;

4. p₁₋₂ - statistical validity of difference in patients' indices after treatment between TC-1 and TC-2.

A similar regularity revealed to be characteristic for the most parameters of cellular immunity (tabl.2). The usage of both TC led to the significant growth of T-lymphocytes number and their main subpopulations (T-helper and T-suppressor), but the ratio of CD4⁺/CD8⁺ was increasing only after TC-2, approaching their level in the control group. The difference between values of CD4⁺/CD8⁺ ratio and between the

numbers of CD3⁺-lymphocytes after TC-1 and TC-2 is significant.

At the same time, the number of 0-lymphocytes decreased more distinctly after TC-2, reaching their level in the control group. These changes are the result of the reduction of residual manifestations of inflammation under the influence of haloaerosoltherapy and indicate normalization of cell differentiation's direction and further immune response of the organism.

Table 2 – Changes in some cellular immune indices at convalescents after community acquired pneumonia under the influence of different regimes of haloaerosoltherapy

| Data, units | Control group (n=26) | TC-1 (n=25) | | TC-2 (n=17) | |
|---|----------------------|------------------|--------------------------|------------------|---|
| | | before treatment | after treatment | before treatment | after treatment |
| CD3 ⁺ , % p p ₁₋₂ | 65, 8±0,49 | 54,8± 1,15** | 58,9± 1,62** <0,05 | 55,6± 0,79** | 62,6± 0,67** <0,00 1 p ₁₋₂ <0,05 |
| CD22 ⁺ , % p | 14, 2±0,39 | 16,5± 0,59** | 15,1± 0,58* <0,1 | 16,5± 0,59** | 15,5± 0,45** <0,2 |
| 0-lymphocytes % p p ₁₋₂ | 20, 0±0,78 | 29,7± 1,48** | 24,7± 1,32** <0,02 | 28,1± 1,28** | 20,7± 0,84 <0,001 p ₁₋₂ <0,02 |
| CD4 ⁺ , % p p ₁₋₂ | 37, 3±0,43 | 29,6± 0,66** | 32,2± 1,15** <0,05 | 29,3± 0,65** | 34,1± 0,71** <0,00 1 p ₁₋₂ <0,2 |
| CD8 ⁺ , % p | 27, 2±0,39 | 24,1± 0,93** | 26,4± 0,61* <0,05 | 25,3± 0,72** | 26,8± 0,27 <0,05 |
| CD4 ⁺ /CD8 ⁺ p p ₁₋₂ | 1,3 6±0,02 | 1,21± 0,04** | 1,24± 0,03** | 1,18± 0,04** | 1,32± 0,028* <0,01 p ₁₋₂ <0,05 |

Notes:

- * - the tendency to significant changes at patients in comparison with the control group;
- ** - significant changes in rates at patients in comparison with control group;
- p - statistical validity of patients' indices before and after treatment;

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More pronounced changes in the studied parameters, especially in the ratio of CD4⁺/CD8⁺ under the influence of TC-2 indicate a more efficient and complete elimination of residual inflammatory manifestations when using TC-2. Probably, it was due to more expressed sanative and anti-inflammatory influence of haloaerosoltherapy while using two daily procedures with more intensive aerosol load.

The number of B-lymphocytes changed insignificantly, which probably indicates a presence of some antigenic load and requires further improvement of treatment.

Thus, the usage of the different regimes of haloaerosoltherapy in the recovery treatment of convalescents after community acquired pneumonia leads to the significant improvement of the function of nonspecific defense and cellular immunity, but complete normalization of the most of studied parameters was not reached. This confirms the depth and seriousness of the immunity disturbances at patients with community acquired pneumonia, which remained after completing antibacterial therapy and determines the necessity of additional correction of phagocytosis and T-immunity in the early convalescence period

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in order to achieve their full recovery, prevention of recurrent infectious inflammatory processes and their chronization.

Conclusions:

1. The patients with non-severe community acquired pneumonia have moderate disturbances of neutrophils phagocytosis, associated with secondary T-cell dysfunction, which are accompanied with the increasing in the number of undifferentiated 0-lymphocytes and B lymphocytes, which remained after of completing of antibiotic therapy. These changes determine the necessity of recovery treatment in this stage of the disease.

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