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# EFFICACY OF DECAMETHOXINE IN THE COMBINED TREATMENT OF INFECTIOUS EXACERBATION OF ASTHMA

**Key words:** *asthma, decamethoxine, infectious exacerbation.*

In recent years, a permanent increase in asthma morbidity has been observed in the most countries of the world. According to literature data, from 1 to 10 % of people all over the world suffer from asthma. On the average, about 5 - 7 % of the population has asthma [8]. According to the official statistics, in Ukraine in 2011 asthma morbidity amounted to 515.9 patients per 100 thousands of adult population and this number continues growing year by year [7]. Exacerbations of asthma, particularly severe exacerbations, lead to a long-term lung function decline after which the lung function is not always restored to the initial level and worsens the disease prognosis [9, 11].

It has been proved that respiratory viral infections top the list of causes of asthma exacerbations [12]. One of the components of pathogenic effect of respiratory viral infection is a secondary bacterial infection and formation of viral-bacterial associations [10]. Thus, success of treatment of asthma exacerbations largely depends on provision of adequate antibacterial therapy. However, there is no unified approach concerning drug products for antibacterial treatment and methods of their delivery into patient's organism.

In recent years, it has been reported about the efficacy of decamethoxine-based antiseptic products in the therapy of purulent and destructive pulmonary conditions, pneumonia and infectious exacerbations of chronic obstructive pulmonary disease [1, 2, 4]. *In vitro* studies have demonstrated high sensitivity of viral and bacterial agents of infectious exacerbations of bronchial asthma to decamethoxine [5, 6]; and it has been proven that inhalations of 0.02 % solution of decamethoxine do not affect indices of respiratory function (RF) in patients with infectious exacerbation of asthma [3]. However, the efficacy of nebulizer antimicrobial therapy with decamethoxine in patients with infectious exacerbation of asthma has not been studied sufficiently.



**Aim of the study:** to study clinical efficacy and to justify appropriateness of inclusion of 0.02 % solution of decamethoxine administered as inhalations into the combined therapy of infectious exacerbation of asthma.

**Materials and methods of the study**

To address the aims of the study, 64 patients were selected with virus-induced exacerbation of asthma who were hospitalized in the Department of technologies of treatment of non-specific lung diseases of SO 'The National Institute of Phthisiology and Pulmonology named after F. G. Yanoskyi of the NAMS of Ukraine' in 2012-2014. The diagnosis of infectious exacerbation of asthma was established according to the requirements specified in the Order of the Ministry of Health of Ukraine "On the approval and implementation of medical and technological documents for standardization of medical care in bronchial asthma" No. 868 dated 08.10.2013[7].

The course of therapy was adjusted for those patients who did not receive adequate treatment for their asthma exacerbation. Depending on the severity of the exacerbation, the patients received anti-inflammatory drugs (inhalations and/or systemic glucocorticosteroids) in combination with bronchodilators ($ß_2$-agonists and anticholinergic drugs of short and prolonged action). The scope of therapeutic interventions and routes of administration of the drug products (inhaled, oral or parenteral) were determined depending on the severity of the exacerbation and on the response to the initial stage of therapy according to the recommendations given in the Order of the MoH of Ukraine No.868 dated 08.10.2013 [7]. Mucolytics and antihistamines were concomitantly administered when indicated.

It should be emphasized that all patients with asthma received their basic therapy depending on the severity of their disease and according to the current standards of treatment; the therapy lasted for at least 4 weeks prior to the occurrence of a virus-induced asthma exacerbation and inclusion of patients into the study. When confirming the diagnosis of virus-induced asthma exacerbation, the

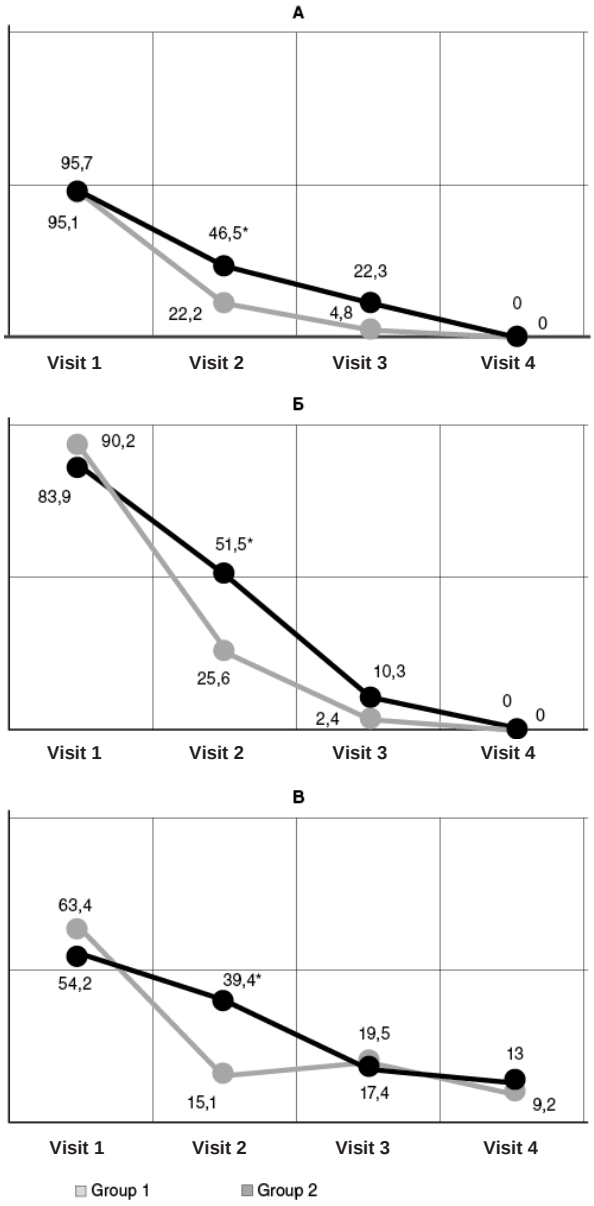


***Fig. 1.*** **Dynamics concerning the main clinical manifestations of toxic syndrome: a - body temperature, b - sweating, c - headache.**
* The difference of indices compared to Group 1 is statistically significant ($p < 0.05$).

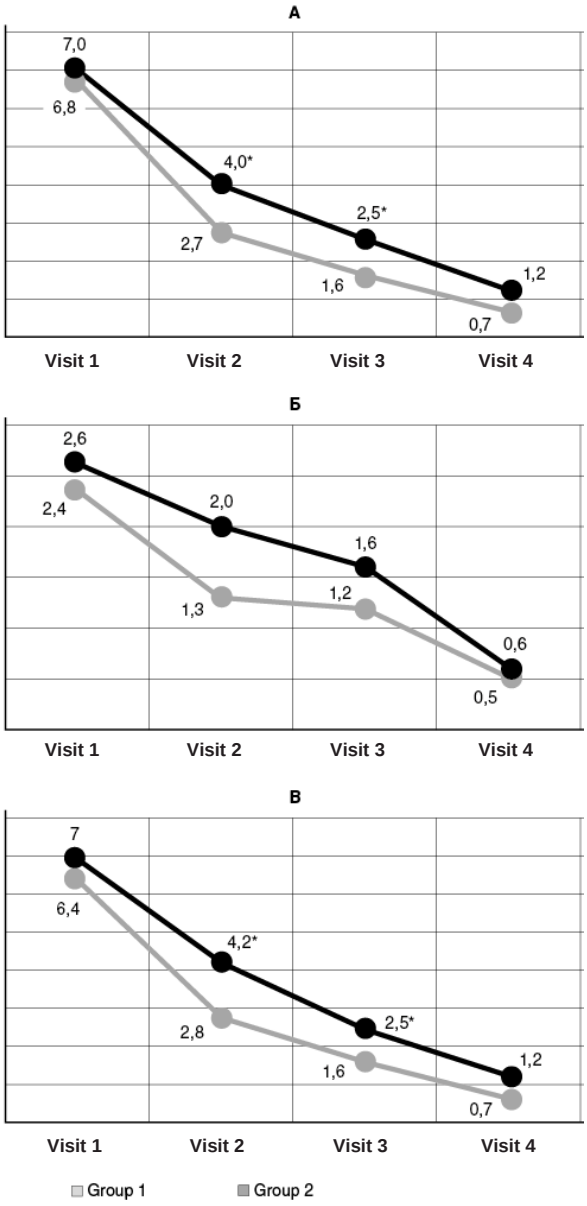


***Fig. 2.*** **Behavior of clinical symptoms of virus-induced exacerbation of asthma a - day-time symptoms, b - night-time symptoms, c - need for a bronchodilator.**
* The difference of indices compared to Group 1 is statistically significant ($p < 0.05$).

following factors were taken into account: history of the disease, clinical symptoms of asthma exacerbation, Asthma Control Test and toxic syndrome test, parameters of respiratory function (spirometry and peak expiratory flow, PEF) and the reversibility of bronchial obstruction in a bronchodilator test.

All 64 patients with virus-induced exacerbation of asthma included into an open-label randomized study, were divided into two groups. The treatment group (Group 1): 41 patients ((17 males and 24 females); mean age 48.2 ± 11.7 years, FEV1 - 66.8 ± 2.4 %, the increase in a bronchodilator test - 15.7 ± 2.0 %)) who were administered 0.2 % solution of decamethoxine in the course of combined treatment: 4 ml by inhalation (via a nebulizer) twice daily for 10 days. The control group (Group 2): 23 patients ((9 males and 14 females); mean age 47.4 ± 13.9 years, FEV1 - 64.9 ± 2.7 %, the increase in a bronchodilator test - 16.4 ± 2.8 %)) who received only conventional therapy required for the level of severity of bronchial asthma exacerbation. According to the results of clinical and instrumental examination, patients with moderate exacerbation of asthma prevailed both in the treatment and in the control groups (81.3 ± 4.9 % of all patients).

At the enrolment stage of the study, the patients filled in the Asthma Control Test questionnaire. The results of this test demonstrated that most patients in the treatment group and in the control group had uncontrolled disease development: 13.4 ± 0.4 and 13.7 ± 0.5 points, respectively. Concerning the main parameters (severity of virus-induced exacerbation of asthma, age, anthropometric measurements and concomitant disease), there were no difference between the patients of Group 1 and Group 2 ($p > 0.05$). The patients had complete examinations at the following stages of the study: enrolment stage, when group-appropriate therapy schedules were assigned - Visit 1, on day 3 of treatment - Visit 2, on day 7 – day 10 of treatment - Visit 3 and on day 18 – day 20 from the beginning of observation - Visit 4.

*Table.*

**Dynamics of RF parameters in patients of study groups (M ± m)**

| Parameters | Visit 1 | | Visit 2 | | Visit 3 | |
|---|---|---|---|---|---|---|
| | Treatment group (n=41) | Control group (n=23) | Treatment group (n=41) | Control group (n=23) | Treatment group (n=41) | Control group (n=23) |
| $FEV_1$, % of normal | 66,8 ± 2,4 | 64,9 ± 2,7 | 74,6 ± 2,6# | 76,4 ± 2,2# | 81,6 ± 2,5# | 77,9 ± 2,3# |
| Morning PEF, l/min | 236,6 ± 13,2 | 230,9 ± 14,5 | 254,0 ± 14,1 | 249,0 ± 15,3 | 302,7 ± 13,8# | 293,5 ± 15,1# |
| Evening PEF, l/min | 265,4 ± 14,9 | 266,4 ± 15,4 | 268,6 ± 16,8 | 270,6 ± 13,8 | 289,3 ± 13,6 | 290 ± 15,1 |
| Daily PEF variability, % | 32,9 ± 4,9 | 33,1 ± 2,7 | 26,1 ± 2,0 | 27,6 ± 2,4 | 18,0 ± 1,8 | 20,3 ± 2,0 |
| Increase in a bronchodilator test, % | 15,7 ± 2,0 | 16,4 ± 2,8 | 13,5 ± 2,4 | 14,1 ± 2,6 | 10, 2 ± 1,8# | 11,5 ± 2,7 |

Note. # The difference of parameters in the group (compared to Visit 1) is statistically significant ($p < 0.05$).

Efficacy assessment of a 10-day inhalation course of 0.02 % solution of decamethoxine as a part of combined therapy of exacerbation of asthma was conducted on the basis of dynamics in the following indicators: toxic syndrome, clinical symptoms of asthma, RF parameters, PEF and the number (%) of patients who required systemic antibiotic therapy during or after the treatment. The obtained results were processed and analyzed using the methodology of analysis of variance. Student's t-test was used to compare the populations which corresponded to the normal distribution law. When distributing data that contradicted the normal distribution law, non-parametric analogues of Student's t-test were used, namely Wilcoxon signed-rank test and Wilcoxon rank-sum test for linked samples and independent samples, respectively. The null hypothesis of the absence of significant differences between the comparable populations was rejected at $p \leq 0.05$. The study was sponsored from the state budget.

**Results and discussion**

Addition to the therapy of asthma exacerbation of 0.02 % solution of decamethoxine had a positive effect on the course of virus-induced exacerbations of asthma. Thus, the improvement of the main clinical manifestations of toxic syndrome was already recorded on day 3 of treatment (Visit 2) in both groups (Fig. 1).

However, in patients of Group 1, improvement of the study parameters was significantly more rapid than in the control group. Subfebrile body temperature persisted only in (22.2 ± 7.0) % patients of Group 1 and in (46.5 ± 10.6) % patients of Group 2 ($p < 0.05$), excessive sweating was observed in (25.6 ± 7.6) % patients of Group 1 and in (51.5 ± 10.6) % patients of Group 2 ($p < 0.05$); headache was observed in (15.1 ± 5.9) % patients of Group 1 and in (39.4 ± 9.8) % patients of Group 2 ($p < 0.05$). At the later stages of the study, there continued to be observed more rapid improvement of the main clinical manifestations of toxic syndrome in Group 1, which contributed to a faster (by an average of 1-2 days) resolution of the main clinical manifestations of toxic syndrome.

The analysis of clinical symptoms of virus-induced exacerbation of asthma also demonstrated improvement on day 3 of the therapy in both groups (Fig. 2). The aforementioned changes occurred significantly faster in patients of the treatment group than in the control group. Thus, day-time episodes of asthma on the average amounted to (2.7 ± 0.3) in the treatment group and to (4.0 ± 0.2) episodes per day ($p < 0.05$) in the control group. The administration of a bronchodilator when required was (2.8 ± 0.5) doses/day in Group 1 and (4.2 ± 0.3) doses/day in Group 2 ($p < 0.05$). At the subsequent stages of the study, the patients of the treatment group also had faster therapy responses.

On treatment day 4-5, 3 (7.3 ± 4.1 %) patients of the treatment group and 7 (30.4 ± 9.6 %) patients of the control group still had elevated body temperature (above 37°C), which either persisted for more than 3 days from the onset of symptoms of respiratory viral infection or was observed after a previous recovery of normal body temperature. Fever was accompanied by more intensive cough and increased expectoration, which gradually became mucopurulent or purulent. The specified symptoms indicated bacterial superinfection and required additional systemic antibacterial therapy. Taking into account that the non-specific inflammation developed in an in-patient setting, the patients received intravenous Levofloxacin 500 mg twice a day for 5 –7 days. The incidence of bacterial complications in the control group was 23.1 % higher than in the treatment group.

The improvement of clinical symptoms at all visits was confirmed by RF and PEF indices (see Table).

There was a significant improvement of RF on treatment day 3(Visit 2) in both groups. Compared with the initiation of treatment, there was an increase of $FEV_1$ from (66.8 ± 2.4) % to (74.6 ± 2.6) % in the treatment group ($p < 0.05$); the increase in a bronchodilator test reduced to (3.5 ± 2.4) %. In the control group, there was an increase of $FEV_1$ from (64.9 ± 2.7) % to (76.4 ± 2.2) % ($p < 0.05$), and the increase in a bronchodilator test reduced to (14.1 ± 2.6) %.

Compared with Visit 1, there was a significant increase of $FEV_1$ in the treatment group on treatment day 7 –10 (Visit 3), from (66.8 ± 2.4) % to (81.6 ± 2.5) %, $p < 0.05$; and the increase in a bronchodilator test reduced to (10.2 ± 1.8) %, $p < 0.05$. In the control group, there was also observed an increase of $FEV_1$ from (64.9 ± 2.7) % to (77.9 ± 2.3) % ($p < 0.05$), and the increase in a bronchodilator test reduced to (11.5 ± 2.7) %. Comparing Group 1 and

Group 2, it was observed that $FEV_1$ values tended to be higher in Group 1 - (81.6 ± 2.5) % and (77.9 ± 2.3) %, respectively.

Therefore, compared to the standard inhalation therapy alone, addition to the therapy of infectious exacerbation of asthma (according to the current standards of treatment) of inhaled antiseptic solution of decamethoxine contributed to a significantly faster elimination of toxicity and clinical symptoms of asthma exacerbations and improved indices of RF and PEF.

**Conclusions**

1. Inclusion of a 10-day inhalation course with the use of 0.02 % solution of decamethoxine to the combined treatment in patients with infectious exacerbation of bronchial asthma enables to establish control over the disease in 92.4 % of patients.
2. Using a 10-day inhalation course of 0.02 % solution of decamethoxine (as a part of combined therapy in infectious exacerbations of asthma) is 23.1 % more efficient as compared to the standard inhalation therapy.
3. Infectious exacerbation of bronchial asthma is an indication for a 10-day inhalation course of 0.02 % solution of decamethoxine.

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