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Effects of inhalation of decamethoxin antiseptic solution on respiratory function in patients with infectious exacerbation of asthma

Key words: *asthma, respiratory function, decamethoxin, nebuliser therapy.*

According to current national and international consensus, elimination of trigger factors and intensification of basic therapy (bronchodilating and anti-inflammatory agents) remain the fundamental principles to manage exacerbations of asthma. The therapy of asthma exacerbations presents a number of clinical challenges, including:

- decreasing bronchial inflammation and prevention of recurrent exacerbations;
- maintaining adequate oxygen saturation;
- improving respiratory function [3].

As for the trigger factors, multiple epidemiological and pathophysiological evidence suggests upper respiratory infection (URI) as the commonest cause of exacerbation (responsible for 80–85 % paediatric cases and 75 % of adult cases). The connection between URI and asthma exacerbations has been proven by multiple authors [17, 19, 20, 23, 24]. Moreover, one of the components of the adverse impact of viral respiratory infection is creating the preconditions for bacterial superinfection and formation of viral-bacterial associations [18], which leads to severe exacerbations, changes in clinical presentation of the disease and enhanced sensitization [16].

It is expected that timely eradication of trigger pathogens for infectious exacerbation would lead to improved treatment outcomes and quality of life in patients with infectious exacerbations of asthma. At the same time, there is currently no consensus concerning the strategy of antibacterial treatment for infectious exacerbations of asthma and administration routes.

In recent years, there have been reports of clinical efficacy of decamethoxin antiseptic in management

of lower respiratory infections, pneumonia and bronchial asthma. Decamethoxin has been effectively used as a part of multimodality treatment of patients with exacerbations of chronic obstructive pulmonary disease and in purulent-destructive processes in the lungs [2, 4, 7, 11, 12, 15]. In vitro decamethoxin was found to have a virucidal action against complex viruses, in part, against respiratory viruses, such as influenza A (H1N1) and A (H3N2), thereby fully inactivating them in virus-containing fluids [13]. There is evidence in literature the effective use of inhalation decamethoxin in management of patients with pneumonia [10]. The option of inhalation decamethoxin via a nebuliser as also a promising therapeutic application. The inhalation route has the following advantages: maximum speed of antibacterial effect, local action of the medication within the focus of inflammation and the absence of adverse systemic effects when used in therapeutic doses [1, 5, 9].

On the one hand, inhalation use could contribute to better patient outcomes in infectious exacerbations of asthma; however, it is generally known that these patients are at high risk for acute bronchoconstriction, triggered by various stimuli, which are safe for otherwise healthy subjects, inhalation of decamethoxin being one of them. Since there are no prior studies of the ability of decamethoxin inhalations to affect respiratory function (RF) in patients with asthma, and since safety/absence of adverse effects is an important characteristic of any treatment modality, the **aim of this study** was to investigate the impact of inhalations with 0.02 % solution of decamethoxin

antiseptic upon respiratory function parameters in patients with infectious exacerbation of asthma.

Materials and Methods

To assess the RF impact of 0.02 % solution of decamethoxin and the reference product (0.9 % solution of NaCl), 35 patients with infectious exacerbation of asthma have been assessed, including 19 (54 %) males and 16 (46 %) females age 19 to 76 years, mean age (42.8 ± 6.8) years, FEV1 (66.8 ± 2.4) %. The diagnosis of infectious exacerbation of asthma was established according to the guidelines specified in the Order of the Ministry of Health of Ukraine 'Concerning the approval and implementation of medical and technological documents for standardization of care in bronchial asthma' No. 868, dated 08.10.2013. [14]. All patients were treated at the Department of Treatment Technologies in Non-specific Lung Disease of the State Institution 'The National Institute for Tuberculosis and Pulmonology named after F.G.Yanovsky of the National Academy of Medical Sciences of Ukraine'

Study design included 3 visits. At each visit, the patients had RF assessments before and 15 minutes after each inhalation with a respective drug; comparative evaluations have been performed at the end of study.

At Visit 1 (Day 1), the patients had a broncholytic test (with short-acting β_2 -agonist salbutamol). The tests were conducted in the morning, after 12–14 hours of interruption of broncholytic therapy. The RF findings obtained 15 minutes after 2 inhalations of salbutamol were observed and documented in the patient's Case Report Form (CRF).

At Visit 2 (next day), all patients had an inhalation with 0.9 % solution of NaCl (4 mL via a nebuliser for 10–15 minutes). At Visit 3 (Day 3), the patients had an inhalation with 0.02 % solution of decamethoxin (4 mL via a nebuliser for 10–15 minutes).

Normal saline (0.9 % solution of NaCl) has been used a reference product to detect bronchoconstriction in response to a neutral stimulus). In addition, another rationale for the choice of the reference drug was also the fact that 0.02 % solution of decamethoxin (Decasan by Yuria-Pharm Ltd.) contains 0.9 % NaCl as an excipient (solvent), which allowed assessing both the active ingredient and an excipient concerning their potential influence on bronchial obstruction. To eliminate potential adverse effects in tracheal and bronchial thermal receptors, the solutions were warmed to body temperature prior to inhalations.

Fasting spirometry was performed using the spirometric system MS PFT (s/n 675122, by Jaeger, Germany) in the morning, allowing the patient to have a 30-minute rest prior to the test. All parameters were presented as absolute values and percentage to their respective normal reference values (calculated after Knudson, 1983) [21, 22]. The following requirements were to be met for the RF test: the patient refrained from broncholytics (short-acting β_2 -agonists for 4 hours, long-acting β_2 -agonists for 12 hours, short-acting

Table 1
Changes of RF parameters with time in patients with asthma (n = 35) before and after the test with 0.9 % solution of NaCl, (M \pm m)

Parameters, % of the normal values	Before the test	After the test
VC	84.2 \pm 2.3	86.0 \pm 2.5
FVC	82.2 \pm 2.1	84.2 \pm 2.4 *
FEV1	76.4 \pm 2.2	76.2 \pm 2.1
FEV1/FVC	77.3 \pm 1.5	76.3 \pm 1.6
MEF75 %	72.9 \pm 3.1	74.6 \pm 3.3
MEF50 %	50.6 \pm 3.6	51.3 \pm 3.5
MEF25 %	45.6 \pm 3.3	42.4 \pm 3.3
PEF	74.7 \pm 2.4	75.4 \pm 2.6
MMEF25–75 %	49.9 \pm 3.3	48.7 \pm 3.2

Note: * The difference of parameters before and after the test is statistically significant ($p < 0.05$).

Table 2
Changes of RF parameters with time in patients with asthma (n = 35) before and after the test with 0.02 % solution of decamethoxin (M \pm m)

Parameters, % of the normal values	Before the test	After the test
VC	83.9 \pm 2.7	84.6 \pm 2.5
FVC	82.4 \pm 2.5	83.3 \pm 2.4
FEV1	74.6 \pm 2.6	74.8 \pm 2.1
FEV1/FVC	77.4 \pm 1.7	75.8 \pm 1.4
MEF75 %	72.8 \pm 3.3	73.0 \pm 3.3
MEF50 %	49.6 \pm 3.4	48.4 \pm 3.3
MEF25 %	44.4 \pm 3.0	39.5 \pm 2.6 *
PEF	75.2 \pm 2.4	75.0 \pm 2.4
MMEF25–75 %	48.8 \pm 3.0	46.1 \pm 2.8

Note: * The difference of parameters before and after the test is statistically significant ($p < 0.05$).

cholinolytics for 8 hours, long-acting cholinolytics and theophylline for 24 hours).

The following RF parameters were assessed (in % to normal values): vital capacity (VC), forced vital capacity (FVC), forced expiratory volume per 1 sec (FEV1), maximum expiratory flow at 25, 50 and 75 % vital capacity (MEF25 %, MEF50 %, MEF75 %), peak expiratory flow (PEF) and maximum midexpiratory flow, at 25–75 % vital capacity (MEF25–75 %) [6, 8, 21, 22].

Mathematical data processing was performed with licensed software products, included into the package of Microsoft Office Professional 2007, License Russian Academic OPEN No Level No.17016297. Statistical

Table 3
The relative increase of RF parameters in patients with asthma (n = 35) in pharmacological testing Δ , % (M \pm m)

Parameters	Salbutamol test (Visit 1)	Test with 0.9 % NaCl (Visit 2)	Test with 0.02 % decamethoxin (Visit 3)
VC	6,1 \pm 1,6	2.2 \pm 0.9	1,1 \pm 0,8
FVC	7.7 \pm 1.6	2.3 \pm 1.0	1.3 \pm 0.9
FEV1	15.7 \pm 1.9	0.2 \pm 1.0	1.7 \pm 2.2
FEV1/FVC	7.7 \pm 1.8	-1.2 \pm 0.9	-1.6 \pm 1.1
MEF75 %	22.9 \pm 5.6	2.4 \pm 1.7	2.3 \pm 3.0
MEF50 %	40.8 \pm 6.5	4.0 \pm 4.4	-1.8 \pm 2.2
MEF25 %	59.1 \pm 9.8	-2.0 \pm 6.4	-8.0 \pm 4.5
PEF	10.1 \pm 3.2	1.0 \pm 1.2	0.0 \pm 1.2
MMEF25–75 %	40.9 \pm 5.4	0.1 \pm 3.7	-4.5 \pm 3.2

Note: No statistically significant differences between the test with 0.02 % decamethoxin and the test with 0.9 % NaCl solution were found ($p > 0.05$).

processing has been performed using the statistical capacities of MS Excel. The methods of descriptive statistics were used; to assess the statistical significance of differences, parametric (Student's t-test) and non-parametric (Wilcoxon T-test) tests were used.

Study results

Analysis of RF parameters at study baseline has demonstrated that all patients with infectious exacerbations of asthma had FEV1 and PEF 80 % below normal (66.8 ± 2.4 %) and (69.8 ± 2.9 %), respectively).

After a pharmacological test with short-acting β_2 -agonist (salbutamol at the dose of 400 μ g), the relative FEV1 increase in patients was 15.7 %, the increase of PEF was 10.1 %, which was consistent with exacerbation of asthma.

After inhalation of 0.9 % NaCl, the patients with infectious exacerbations of asthma were noted to have increased FVC levels, from (82.2 ± 2.1 %) to (84.2 ± 2.4 %), $p < 0.05$. No statistically significant changes of other RF parameters have been documented. 1).

After the test with 0.02 % decamethoxin, only a slight decrease in maximum expiratory flow at 25 % vital capacity (MEF25 %) was noted, from (44.4 ± 3.0 %) to (39.5 ± 2.6 %), $p < 0.05$; there were no significant changes in other RF parameters (see Table 2).

No statistically significant differences between decamethoxin and 0.9 % NaCl solution were found ($p > 0.05$), when comparing RF parameters before and after the tests with investigational products (see Table 3).

In course of study, there was a thorough analysis of potential adverse effects; patient-reported outcomes and objective changes in patients receiving inhalations of decamethoxin and 0.9 % NaCl were taken into account. As a result, we have obtained data indicating that the vast majority of patients with infectious exacerbations of asthma had good tolerance of nebulised investigational drugs. Adverse events, manifest as retrosternal burning sensation

and hypersalivation (after inhalation of decamethoxin) have both occurred in only one patients. These events reversed spontaneously after the inhalation and did not require discontinuation of the product. No cases of bronchoconstriction or hypersensitivity in response to inhalations with investigational drugs were observed during the study. Inhalations with 0.9 % NaCl solution provide an additional moisturising effect in the respiratory pathways and facilitate expectoration of sputum.

Conclusions

Inhalations of 0.02 % decamethoxin antiseptic have been demonstrated to have no adverse impact on respiratory function.

Nebuliser therapy with solution of decamethoxin is tolerated well by patients with exacerbations of asthma and is not accompanied by any adverse effects.

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ВЛИЯНИЕ ИНГАЛЯЦИИ РАСТВОРА АНТИСЕПТИКА ДЕКАМЕТОКСИНА НА ПОКАЗАТЕЛИ ФУНКЦИИ ВНЕШНЕГО ДЫХАНИЯ У ПАЦИЕНТОВ С ИНФЕКЦИОННЫМ ОБОСТРЕНИЕМ БРОНХИАЛЬНОЙ АСТМЫ

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Резюме

Многочисленные исследования свидетельствуют о том, что наиболее распространенной причиной обострения бронхиальной астмы (БА) являются острые респираторные вирусные инфекции. Кроме того, респираторная вирусная инфекция способствует созданию условий для присоединения бактериальной инфекции, что ведет к тяжелому течению обострений. В то же время, единого мнения относительно средств антибактериальной терапии инфекционного обострения БА и методов их доставки в организм больного нет.

Цель исследования — изучить влияние ингаляции 0,02 % раствора антисептика декаметоксина на показатели функции внешнего дыхания (ФВД) у пациентов с инфекционным обострением БА.

Объект исследования — 35 пациентов с инфекционным обострением БА: 19 (54 %) мужчин и 16 (46 %) женщин в возрасте от 19 до 76 лет, средний возраст — $(42,8 \pm 6,8)$ лет, FEV_1 — $(66,8 \pm 2,4)$ %. Дизайн исследования состоял из 3 визитов, на каждом из которых у больных исследовали ФВД до и через 15 минут после ингаляции отдельным препаратом, а по окончании исследования проводили сравнительную оценку. На 1-м визите (1-й день) проводили пробу с бронхолитиком (сальбутамол в дозе 400 мкг), на 2-м визите (2-й день) всем пациентам проводили ингаляцию 0,9 % раствором NaCl в дозе 4 мл через небулайзер на протяжении 10–15 минут, на 3-м визите (3-й день) — ингаляцию с 0,02 % раствором декаметоксина в дозе 4 мл через небулайзер на протяжении 10–15 минут.

Методы исследования: клинико-функциональные, статистические.

Результаты. Сравнивая динамику показателей ФВД до и после проб с исследуемыми препаратами, статистически значимого отличия между 0,02 % раствором декаметоксина и 0,9 % раствором NaCl не выявлено ($p > 0,05$). В большинстве случаев пациенты с инфекционным обострением БА удовлетворительно переносили ингаляции препаратов через небулайзер; нежелательных реакций, требующих отмены препаратов, не выявлено.

Выводы. Ингаляции 0,02 % раствора антисептика декаметоксина не оказывают негативного влияния на показатели ФВД. Небулайзерная терапия раствором декаметоксина хорошо переносится пациентами с инфекционным обострением БА и не сопровождается развитием побочных эффектов.

Ключевые слова: бронхиальная астма, функция внешнего дыхания, декаметоксин, небулайзерная терапия.

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EFFECTS OF INHALATION OF DECAMETHOXIN ANTISEPTIC SOLUTION ON LUNG FUNCTION IN PATIENTS WITH INFECTIOUS EXACERBATION OF ASTHMA

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Summary

Numerous studies indicate that the most common cause of exacerbation of bronchial asthma is acute respiratory viral infections. In addition, respiratory viral infection contributes to creating the conditions for joining of a bacterial infection that leads to severe course of exacerbations. At the same time, there is no common opinion about antibacterial therapy and its delivery in case of infectious exacerbation of asthma.

The purpose of the research is to study the effect of inhalation of decamethoxine antiseptic 0,02 % solution on lung function (LF) in patients with infectious exacerbation of asthma.

The object of the study: 35 patients with infectious exacerbation of asthma. 19 (54 %) of them were men and 16 (46 %) – women aged 19 to 76 years, the average age – $(42,8 \pm 6,8)$ years, FEV_1 – $(66,8 \pm 2,4)$ %. The study design consisted of 3 visits, on each of which LF studied before and after 15 minutes after inhalation of study drugs. At the end of the study we conducted a comparative evaluation. On the 1st visit (day 1) was carried out a probe with bronchodilator (salbutamol 400 mcg), on the 2nd visit (day 2) all patients underwent inhalation of 4 ml of 0,9 % NaCl nebulized for 10–15 minutes, on the 3rd visit

(day 3) – inhalation of 4 ml of 0,02 % solution of decamethoxine nebulized for 10–15 minutes.

Methods of research: clinical and functional, statistics.

Results. Comparing the dynamic of LF indicators before and after probes with study drugs, there were no significant difference between the 0,02 % decamethoxine solution and 0,9 % NaCl were found ($p > 0,05$). In most cases nebulized medications were satisfactorily tolerated by patients with infectious exacerbation of asthma, adverse reactions requiring drug withdrawal were not revealed.

Conclusions. Inhalations with 0,02 % solution of decamethoxine doesn't cause negative influence on LF. Nebulizer therapy with decamethoxine solution is well tolerated and not associated with the development of side effects in patients with infectious exacerbation of asthma.

Key words: asthma, lung function, decamethoxine, nebulizer therapy.

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