

**D.V. Dobryanskyi<sup>1</sup>, G.L. Gymeniuk<sup>2</sup>, P.F. Dudka<sup>1</sup>, R.I. Ilnytskyi<sup>1</sup>, I.P. Tarchenko<sup>1</sup>, N.M. Kuzmenko<sup>1</sup>**

<sup>1</sup> Bogomolets National Medical University,

<sup>2</sup> Shupyk National Medical Academy of Postgraduate Education

# Nebulized therapy – practical aspects

**Key words:** *nebulizer, nebula (nebulizing solution), nebulized therapy, pulmonology.*

**Abstract.** Recently, nebulized therapy has become increasingly popular in practical medicine due to the effectiveness, accessibility and appearance of a wide range of nebulized dosage forms.

Today the basis of nebulized therapy is modern technology, which is successfully applied worldwide and increases the effectiveness of treatment and in some aspects has become indispensable in various fields of medicine, especially in emergency care, as well as in pulmonology and phthisiology, pediatrics and geriatrics.

The article describes the types of nebulizers, the principle of their work, the main drawbacks and advantages in detail. The main indications and contraindications to nebulized therapy are listed. Practical recommendations about techniques and rules for providing nebulized therapy and typical errors as well as a list of basic medications recommended for use in nebulizers are given.

**Key words:** nebulizer, nebula (nebulizing solution), nebulized therapy, pulmonology.

Inhalation therapy is one of the oldest methods of treatment. Aerosols were widely used in the form of vapors of various substances and medicinal plants, as well as smoke from the combustion of solids for the treatment of many diseases but mainly respiratory organs in medicine.

Aerosols are dispersed systems consisting of a gas that contains solid or liquid particles. There are natural aerosols in nature such as the air of seaside resorts, phytoncides and terpenes, they are emitted by plants, etc.

The nebulizer (from the Latin *nebulo* – fog, cloud) is a device for generating an aerosol which containing fine particles. Today, the basis of nebulizer therapy is modern technology, which is successfully applied worldwide and increases the effectiveness of the treatment of many diseases [3, 14, 15].

Nebulizers can be stationary, which is used in hospitals, and individual for the treatment of individual patients. In connection with accessibility and convenience, more

and more patients in our country apply individual nebulizers [2, 6, 13].

Only those devices may be called nebulizers that meet the requirements of the European standard of nebulizer therapy EN13544–1 [1, 18], namely:

- 50% or more of the aerosol particles should have a size less than 5 microns;
- The residual volume of the medicinal substance after inhalation is not more than 1.0 ml;
- Time of inhalation – no more than 15 minutes at a volume of solution 5,0 ml;
- Recommended flow – no more than 10 l / min, pressure – 2–7 bar;
- Productivity – not less than 0,2 ml / min.

Choosing the type of nebulizer and the correct technique of its application has a great influence on the effectiveness of therapy.

## The main types of nebulizers:

- Compressor (jet, pneumatic);
- Ultrasound;
- Mesh (MESH, membrane).

Jet nebulizers obtained more widespread clinical application today, the nebulizer system in which is a device consisting of a reservoir for a medicinal product – a nebulizer chamber, a mouthpiece or a mask, a nasal cannula, thin silicone tubes and a source of a «working» gas – a compressor (a device that produces a stream of air).

The principle of operation of a compressor nebulizer is based on the Bernoulli effect (Fig. 1). The energy of the compressed gas (air or oxygen) is used, which comes under high pressure from a built in compressor through a narrow hole – a diffuser in a nebulizer chamber. At the exit from this opening the pressure drops and the gas velocity increases significantly, that leads to entering of fluid from the nebulizer chamber in this area through the narrow channels. The liquid at the meeting with the air stream is divided into small particles of the size from 15 to 500 microns (forming a «primary» aerosol). Subsequently, these particles are in contact with the deflector,

resulting in the formation of a «secondary» aerosol – ultra-fine particles of a size preferably of 0.5 to 10 microns, which are inhaled, and a large proportion of particles of the primary aerosol is deposited on the inner walls of the nebulizer chamber and again takes part in the process of formation of an aerosol [8, 18].

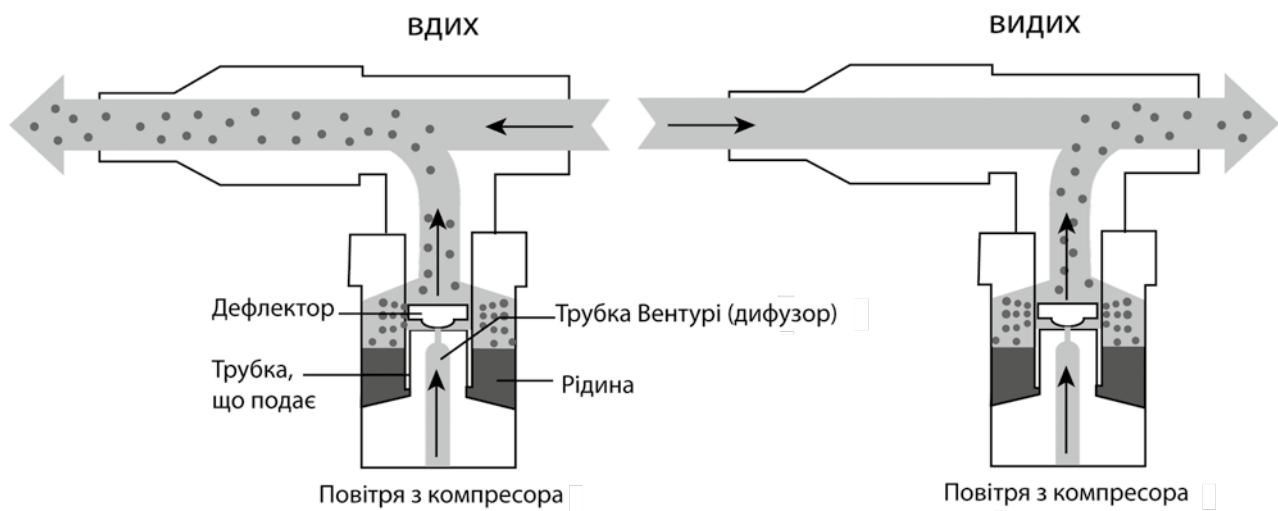
The mouthpiece helps to send a high dose of the drug to the lower respiratory tract (LRT), because inhalations through the mouth are much more effective than inhalations through the nose in the treatment of diseases LRT. A significant amount of the drug is lost with daily application of the drug through the mask and the risk of local undesirable reactions increases. For example, ipratropium

bromide can cause eye irritation when it is inhaled through a mask [8].

It is also possible to use the facial mask and to provide nasal inhalation using the nasal cannula. The mask is mainly used in children under 5 years old and in patients who cannot use a mouthpiece.

Dry powder inhalers may be used in children over 6 years old, but only if the child is well trained in inhalation technique and may correctly perform the respiratory maneuver.

Inhale and exhale need to be done through the nose (nasal inhalation) in diseases of the nose, the nasopharynx it is recommended to use special nasal nozzles (nasal cannula).



### Конструкція небулайзера

### Принципова схема небулайзерної камери

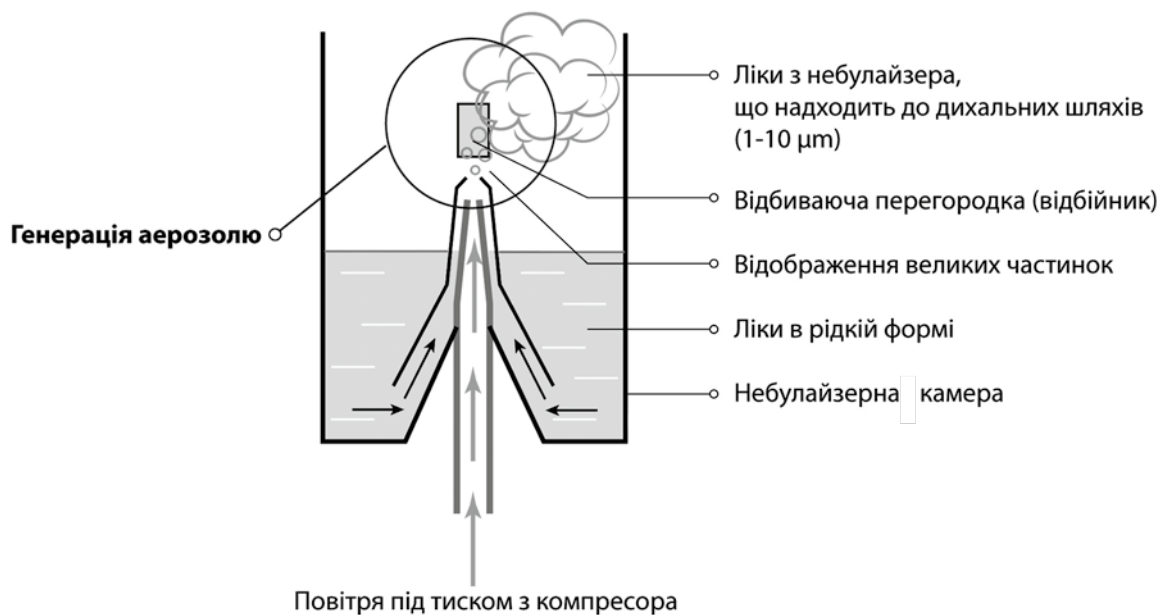


Fig. 1. Scheme of aerosol production.

### The main types of compressor (jet) nebulizers:

1) Convective nebulizers produce an aerosol at a constant rate both in the inhalation and exhalation phase; the drug gets into the respiratory tract only during inhalation, and during exhalation it enters the environment. The main disadvantage of this type of nebulizers is that the generation of aerosols proceeds into the inhalation and exhalation phase, so big part of the drug gets into the atmosphere, which increases the cost of treatment.

2) A nebulizer, which works in steady state and manages manually. The patient is able to stop aerosol discharges in the exhalation phase, thereby reducing its release into the atmosphere. Manual breath-operated devices do not apply to children, elderly and severely ill.

3) Breath actuated nebulizers are constantly producing aerosol. However, the release of aerosol increases during inspiration and weakens during exhalation; this is achieved due to the presence of an additional special valve in the aerosol formation area (in some models due to the special design a so-called «virtual» valve is created). These models significantly reduce the loss of aerosol during exhalation and increase the entrance of drug in the lungs when it is inhaled.

4) Synchronized with breathing (dosimetric nebulizers) generate an aerosol only in the inhalation phase due to a special valve which is operated by an electronic sensor. Thus, practically 100% of the use of the active substance is achieved. The disadvantage of this device is the duration of one inhalation and a significant cost of the device.

The main advantages of the compressor (jet) nebulizers are inhalation of practically all liquids that have a small residual volume (the amount of solution remaining at the bottom of the chamber at the end of inhalation and cannot be converted into aerosol), easily undergoing purification and sterilization [8, 18]

The main disadvantages of most of the compressor nebulizers are considerable size and high noise during work [8]. Although today the Ukrainian market also presents budget, compact and portable models of compressor nebulizers that can be recharged in the car and convenient to take it in a trip [2].

There is a large choice of budget models among the compressor nebulizers, but it must be borne in mind that the increment of the technical characteristics of the device significantly increases its value and accessibility in the population.

### Ultrasonic nebulizer

In ultrasonic nebulizers the aerosol is created by ultrasonic vibrations generated by the piezoelectric element (Fig. 2).

The main advantages of ultrasonic nebulizers are compact and almost silent in operation.

The main disadvantages are limited clinical use because they cannot create a viscous liquid aerosol and have a larger amount of residual fluid. Under the influence of ultrasound, including through the heating of the drug, some substances that have large molecules (eg antibiotics, corticoids) are destroyed [5, 8, 18].

Ultrasonic nebulizers cannot be processed with thermal methods of disinfection.

### MESH nebulizers

The principle of the work is that ultrasound does not shred the drug, but pushes it through a very small mesh (Fig. 3), the so-called MESH-technology (MESH – the number of holes made in one inch length – 2.5 cm).

The use of MESH technology is essential in the formation of a monodisperse aerosol with certain particle sizes that are not destroyed by ultrasound.

The main advantages are compact size, silent work. One of the additional advantages of this type of nebulizers is that it operates effectively in almost any position relative to the horizon and has a very small ( $\approx 0.1$  ml) residual volume [5, 9].

The main disadvantage is the high cost of the device.

### Advantages of nebulizer therapy:

- In the case of oral administration of the drug during passage through the intestinal tract and the liver it undergoes active metabolism and the drug is already in the altered form, a lower concentration and begins to act later in its place of action.

- Inhalation rate of delivery of drugs makes it possible to create a high concentration directly at the site of the lesion and allows to minimize systemic effects (including minimizing of systemic side effects), which is especially important for the treatment of respiratory diseases that have a long or chronic course (cystic fibrosis, chronic bronchitis,

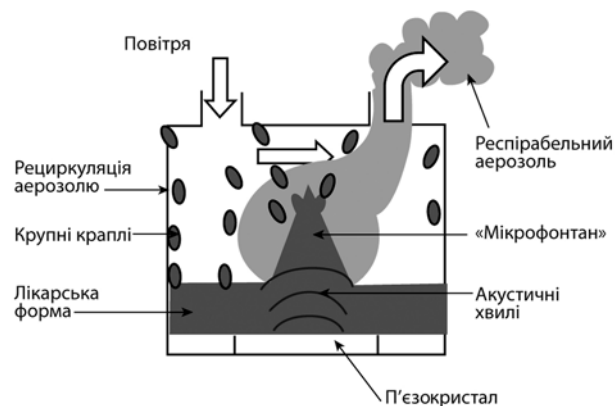


Fig. 2. Device of US-nebulizer

### Пристрій небулайзера з «активною» вібрацією мембрани

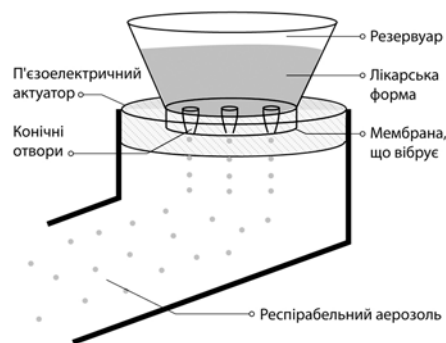


Fig. 3. Scheme of work of MESH nebulizer.

bronchial asthma (BA), chronic obstructive pulmonary disease (COPD)).

- The therapeutic concentration of medicines in the blood after inhalation lasts longer than when it is administered intramuscularly.

- A painless way of administering of drugs.
- Provides rapid action of the drug.
- Provides the ability to apply multiple drugs at the same time.

- Allows to reduce the systemic dose of drugs (corticosteroids, antibiotics) or do not apply them at all (for example, for treatment of exacerbation of asthma or COPD).

- Ability to use at all stages of medical care (at home, «emergency» help, clinic, hospital, emergency department).

- Possibility of humidifying the airways simultaneously with the delivery of the drug.

- Possibility of inhalation and simultaneous supply of oxygen.

- Significant reduction of expenses for provision of emergency medical care.

- Reduces the risk of hospitalization and reduces the number of visits to a doctor.

#### **Advantages of nebulizer therapy compared with other delivery devices:**

- Large lung bioavailability. To achieve maximum pharmaceutical activity of the active substance by influencing on the large area of the surface of the respiratory tract and the possibility of getting into weakly ventilated lung departments.

- When there is a need to inhale large doses of the drug (exacerbation of asthma or COPD when pulmonary bioavailability is significantly reduced due to narrowing of the bronchi, mucosal edema and sputum).

- Simple inhalation technique and ease of use – no need to coordinate breathing with aerosol delivery.

- Possibility of long exposure to drugs.

- Opportunity to achieve optimal dispersion of the aerosol.

- Does not contain propellants that irritate the respiratory tract.

- Insignificant precipitation of the drug in the mouth and the pharynx.

- Possibility to use it when the condition of the patients or their capacity restricts or prevents the prescription of other routes of the administration of drugs (in the postoperative period, in unconscious patients, patients who are on artificial ventilation of lungs, in severe conditions (asthmatic status), in the elderly, children).

#### **Absolute indications for nebulizer therapy:**

1. The drug is only available in a form for nebulizer and cannot be delivered to the respiratory tract with other inhalers.

2. The need for delivery of the drug in the alveoli (for example, pentamidine in pneumocystis pneumonia in patients with AIDS, drugs of surfactant).

3. Significant severity of illness of the patient (inspiratory flow less than 30 liters per minute; decrease in inspiratory vital capacity less than 10.5 ml / kg (for example, < 735 ml in a patient, 70 kg), inability to hold breath for more than 4 seconds) and / or his inability use other inhalers [5, 8].

#### **Relative indications for nebulizer therapy:**

- 1) Insufficient effectiveness of basic therapy and the need for the applying of high doses of drugs that have bronchodilator effect.

- 2) Planned therapy of moderate or severe BA, moderate or severe COPD when it is difficult to achieve control of the disease with basic therapy in standard doses.

- 3) Inability to coordinate the inspiration and puffs on the cartridge of the metered dose inhaler.

- 4) As the first choice in the treatment of moderate and severe exacerbation of asthma, severe protracted attack and asthmatic status.

- 5) As the first choice in the complex therapy of exacerbation of COPD (moderate and severe).

- 6) The value of FEV1 is less than 35% of the relevant values in patients with severe chronic bronchoconstriction.

- 7) Receiving the extended clinical effect and increase of FEV1 by 12% in a week during the trial course of nebulizer therapy in inpatient or outpatient regime.

- 8) The need for moisturizing the airway simultaneously with the inhalation of the drug.

- 9) The appearance of signs of respiratory irritation with the use of usual inhalers (MDI and DPI).

- 10) Advantage for patients (many patients during exacerbation want to use therapy and techniques different from those they use at home).

- 11) Practical convenience (a simple method that does not require the control of a doctor) [5, 8, 18].

#### **Contraindications for providing nebulizer therapy are:**

- Pulmonary hemorrhage and hemoptysis;

- Traumatic and spontaneous pneumothorax;

- Arrhythmia and severe heart failure;

- Individual intolerance to solutions for inhalation.

#### **Practical guidelines for use of nebulizer therapy**

- 1) Solvent (diluent). If you want to add solvent unless otherwise specified only isotonic (0.9%) solution of sodium chloride should be used just before inhalation.

- 2) The volume of filling. The residual volume in the chamber is from 0.5 to 1.0 ml in almost all nebulizers. An increased amount of filling when diluent is added to the can reduce the amount of unused medication.

It is necessary to fill the nebulizer chamber by the drug substance specified by the manufacturer in the instructions for the use of the nebulizer or in the calculation for nebulizer therapy:

- Minimum volume – 2 ml.

- Maximum – 6 ml.

To measure the amount of drug which is required, it is desirable to use drugs for nebulizer (including saline) or sterile syringes and needles.

The volume of filling affects the output of an aerosol, for example, with a residual volume of 1 ml and a volume of 2 ml can be converted into aerosol no more than 50% of the medicine (because 1 ml of the solution remains in the chamber), and with the same residual volume and volume of filling to 4 ml 75% of the drug can be delivered to the respiratory tract.

However, it should be borne in mind that with a residual volume of 0.5 ml increase in filling volume from 2.5 to 4 ml leads to an increase in the yield of the drug only by 12%, and the duration of inhalation increases by 70%. The higher the initial volume of the solution, the greater the proportion of the drug can be inhaled. However, at the same time, the time of nebulizer therapy also increases, which can significantly reduce the compliance.

### 3) The size of the particles of the drug.

It is known that the main factor determining the deposition of particles in the respiratory tract is the size of the aerosol particles. The smaller the size of the particles in the aerosol, the longer they remain in the stream and the deeper penetrate the respiratory tract (Fig. 4).

Particles with a diameter in 8–10 microns deposit in the oral cavity and nose, from 5 to 8 microns – in the upper respiratory tract and trachea, from 3 to 5 microns – in the lower respiratory tract, from 1 to 3 microns – in bronchioles, from 0.5 to 2  $\mu\text{m}$  – in the alveoli. Particles with a diameter less than 0.5 microns do not precipitate at all.

For the effective delivery of drugs to the respiratory organs the size of particles in the aerosol should be about 5 microns or less, the so-called «respirable particles».

The homogeneity of the delivered dose and the amount of fine particles in the range of flow velocity are the main indicators that characterize the work of the nebulizer. One of the main parameters of a nebulizer is the value of the median aerodynamic diameter of the mass – MMA (determined by the fact that half the mass of aerosol is contained in particles of greater diameter, and half – in particles of smaller diameter) [5, 8].

«Respiratory fraction» is the amount of respirable particles in aerosol expressed in a percentage. The amount of fine particles (fine particle mass) characterizes by the amount of medicinal substance in the solution for inhalation which is usually enter the lower respiratory tract

and provide effective therapy for bronchopulmonary diseases [8, 18].

As a rule, it is more than 50% of the total aerosol power of the device. Other factors that influence on the effectiveness of nebulizer therapy and the choice of a nebulizer include: the stability of the aerosol, the flow rate at the outlet of the aerosol from the nebulized chamber and the reliability of its work.

An important parameter for inhalation therapy is a dosing interval – a recommended interval between doses of drugs that is indicated in information for patients and healthcare professionals (instructions for medical use).

4) Deposition of aerosol. The aerosol deposition occurs under the influence of two physiological phenomena: inertial hit and gravity.

Inertial hit absorbs aerosols with large particle size in the narrowing areas and bifurcations of the respiratory tract due to high flow velocity. Bronchial obstruction due to bronchospasm, swelling or hypersecretion of sputum leads to the deposition of aerosols by an inertial blow, even if the proportion of aerosol is small. Therefore, in patients with obstructive pulmonary disease special methods of delivery of aerosol in the lower respiratory tract are needed.

With the aid of gravity, aerosol deposits in the distal respiratory tract, where the flow rate of the air is low and the flow is predominantly laminar. Therefore, a slow, deep breath increases the amount of aerosol that stays distal, and breath stop at the end of the inspiration enhances this effect.

### 5) Flow rate.

The flow rate should be 6–10 liters per minute. It can be stable or change if there is a regulator of air supply on the nebulizers. Increasing of the flow leads to a linear reduction in the size of aerosol particles, as well as to increase the yield of aerosol and may shorten the inhalation time.

### 6) Delivery time of drugs.

The delivery time of the drug should not exceed 10 minutes, otherwise the compliance of the therapy will be reduced.

### 7) The body position of the patient.

The patient should feel comfortable and sit straight. Clothes should not clench the neck.

## Technique of nebulizer therapy

The procedure of inhalation is carried out in 1–1.5 hours after meals, physical activity. Smoking is prohibited before and after inhalations. Expectorants are not recommended before inhalation.

Solutions for inhalation should be prepared in accordance with the rules of antiseptic.

In order to prevent contamination of solutions, it is necessary to wash hands thoroughly.

Pour a drug for inhalation in a nebulizer chamber. It is advisable to use a drug that is manufactured in a special dosage form – nebula, which is primarily associated with convenience for the patient, and also reduces the risk of using non-sterile drugs that are used in large volumetric bottles and require special storage conditions for a short period of time.

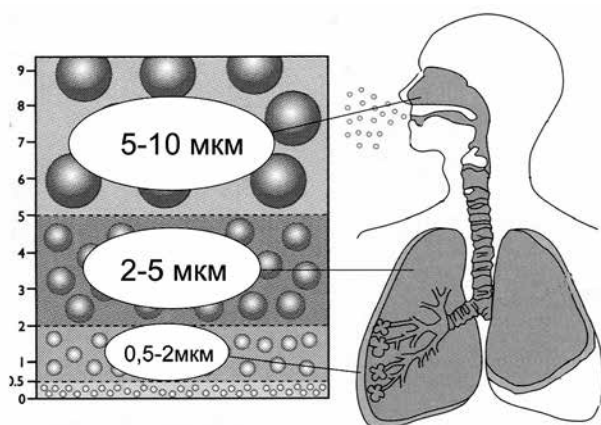


Fig. 4. Distribution of particles in the respiratory tract by the size.



Connect a compressor and nebulizer chamber by the tubes and a nebulizer chamber with a mouthpiece.

The required dose of the drug is, if necessary, diluted with a sterile physiological solution by adding it to the reservoir with a nebula or sterile needles and syringes into the nebulizer chamber to a final volume of about 4 ml (the content should preferably be from 2 to 5 ml). Do not use normal non-sterile water for these purposes because a hypotonic solution can cause bronchospasm in patients.

The solution should be comfortable (room) temperature. The temperature of the solution during inhalation with a jet nebulizer can be reduced by 10 °C or more which can increase the viscosity of the solution and reduce the yield of the aerosol. Some models of nebulizers use a heating system to increase the temperature of the solution to body temperature to optimize the conditions of nebulizer therapy.

Recommend the patient to sit straight and relax. Patient need to pinch the mouthpiece with his teeth and tightly hold his lips during nebulizer therapy.

When using a mask, make sure that it is properly worn, tightly attached to the face, comfortable, and helps the patient breathe constantly through the mouth (not through the nose) when it is possible.

It is important that the nebulizer chamber of the compressor nebulizer always remains in an upright position.

Proper inhalation is required depending on the type of nebulizer according to the manufacturer's instructions. Increase in power in those models where it is provided increases the proportion of fine dispersed aerosol.

It is desirable to breathe deeply and slowly during the inhalation (it is necessary to breathe through the mouth if patient uses mask), possibly keeping breath for 1–2 seconds before every exhale, but it is not possible in severely ill patients who are encouraged to have normal, calm breathing. Slow breath with respiratory delay in the end allows aerosol particles reach the distal parts of the respiratory tract. The faster the patient breathes, the greater part of the aerosol stays in the oral cavity and upper respiratory tract. It is desirable to exhale through the nose.

The patient should not talk because the effectiveness of taken drug in the respiratory tract decreases.

Deep breathing can cause dizziness so it is advisable to take short breaks in therapy as needed.

Exit of the drug at the end of inhalation is concentrated. Therefore, early termination of inhalation (for example, at the moment of «spattering» (the moment when the process of formation of an aerosol becomes intermittent) can significantly reduce the delivery dose of the drug. Therefore, it is necessary to continue the inhalation until the fluid remains in the nebulizer chamber (about 5–10 minutes) it is advisable to shake a little with a nebulizer chamber for more complete use of the drug before the end of inhalation.

It is necessary to wash your face and thoroughly rinse your mouth and throat with boiling water of room temperature after inhaling corticosteroids and antibiotics.

## Safety recommendations

Each patient should have an individual nebulizer chamber and a mouthpiece/mask that is associated with the risk of microbial contamination by pathogenic microorganisms that are not destroyed by normal disinfectant solutions in case of use of other nebulizer chambers, mouthpieces and masks. It is recommended to use disposable kits for inhalation therapy to inpatient care.

Patients who receive long-term nebulizer therapy should replace the nebulizer chamber and the mouthpiece / mask every 3 months.

The liquid should not enter to the compressor in all models of nebulizers and it is prohibited to cover the compressor during work.

It is necessary to rinse thoroughly all the parts of the nebulizer with clean warm tap water after inhalation (you can immerse the parts for 5 minutes in water), dry (frequent washing of the nebulizer is necessary to prevent the crystallization of preparations and bacterial contamination of the device). If a single nebulizer is used by several people, after each use it is necessary to carry out the recommended cleaning instructions and disinfect the nebulizer with the utmost care.

Always pay attention to the rules of cleaning and storage specified in the manufacturer's instructions. To prevent damage to the aerosol generator do not use a microwave oven or dishwasher when cleaning the nebulizer chamber. Mechanical brushing may also adversely affect the working capacity of the device.

Terms of service of the nebulizer chamber vary from manufacturer to manufacturer (from 3 months to 3 years).

As a rule, it is recommended to store the nebulizer in a disassembled form for better preservation of the connection nodes.

It is necessary to check regularly the components of the nebulizer and replace it in the event of a defect.

Check the air filter and replace it timely.

Check the working capacity of the compressor.

## The use of nebulizer therapy is possible for the treatment of acute and chronic respiratory diseases such as:

- diseases of the upper respiratory tract: acute respiratory infections, rhinitis, pharyngitis, tonsillitis, tracheitis, laryngitis;
- diseases of the lower respiratory tract: acute and chronic bronchitis; bronchial asthma; chronic obstructive pulmonary disease; cystic fibrosis; pneumonia, especially caused by atypical pathogens; allergic pulmonitis; viral bronchitis in children; respiratory distress syndrome; bronchiectasis; tuberculosis of the lungs and bronchi.

## The use of nebulizer therapy is possible for the treatment other diseases and procedures (manipulations):

- Other diseases in which inhalation therapy is used in the complex intensive therapy.
- Postoperative respiratory failure in patients with artificial ventilation of the lungs.
- For conducting anesthesia with bronchoscopy;
- To receive induced sputum for sputum analysis.

The main groups of drugs used in clinical practice are bronchodilators, mucolytics, antibiotics, antiseptics, antifungal and antiviral agents, enzymes, hormones, antihistamines, biostimulants and immunomodulators.

#### Basic drugs:

##### *Antibacterial and antiseptic agents.*

Antibacterial agents (amikacin, tobramycin), including anti-tuberculosis (isoniazid), antifungal drugs with wide spectrum of action (amphotericin B), and antiseptics (deccasan) [7, 16, 17, 19] can be used for nebulizer therapy in clinical practice.

**Bronchodilators** are used for nebulizer therapy and represented by  $\beta_2$ -adrenergic agents (salbutamol, phenoterol, terbutaline), cholinolytics (ipratropium bromide) and combination of drugs [4, 6, 12, 20].

**Mucolytics and mucoregulators** are drugs for sputum dilution and improvement of expectoration (acetylcysteine, ambroxol), mucolytic (dornaza alpha). Physiological solution (0.9% solution of sodium chloride) and hypertonic solutions of sodium chloride, including the addition of hyaluronic acid which are presented in the Ukrainian market under the name of Lorde Hyal increase the mucosal component of sputum (provide direct mucolytic action), and moisturize the mucous membrane of respiratory tract and promote reparative mucosal processes [3, 21]. A soda-buffer (a solution of sodium bicarbonate 4.2%) has the similar mechanism of action.

**Anti-inflammatory** drugs. Corticoids (budesonide, fluticasone, beclamethasone, flunisolide) and non-steroidal anti-inflammatory drugs (sodium cromoglycate) are widely used in nebulizer therapy.

The following drugs are used for both prophylactic purposes and for the treatment of acute respiratory diseases, recurrent and chronic bronchopulmonary diseases:

Pentamidine for pneumocystis pneumonia in patients with AIDS.

Inhaled ribavirin which is prescribed for viral bronchiolitis.

Preparations of surfactant.

Proteolytic enzymes.

Adrenaline for acute stenotic laryngitis.

Iloprost for the treatment of pulmonary hypertension.

Inhalation nebulizer therapy is also used in palliative medicine to reduce refractory cough (lidocaine) and incurable shortness of breath (morphine, fentanyl).

Popular immunomodulators (eg. interferon), as well as proteolytic inhibitors ACA (aminocaproic acid) are used for the treatment of acute respiratory infections, especially

in ENT practice. But it should be noted that the size of the particles for inhalation should be greater than 6 microns and inhalation of the drug should be through the nose with using mask or nasal cannula.

It is desirable to adhere a certain sequence with simultaneous prescription of several drugs. The bronchodilator is used first, after 10–15 minutes – expectorant, anti-inflammatory or antimicrobial drug is applied later.

At the same time, it is necessary to use medical devices with caution due to possible chemical and biological incompatibility. It is acceptable to mix bronchodilators and mucolytics in one inhalation.

What cannot be inhaled through a nebulizer?

- oil solutions are strictly prohibited because they increase the risk of developing «oil pneumonitis». For inhalation of such solutions, steam inhalers that are not intended to deliver drugs to the distal airways should be used;

- systemic hormones (dexamethasone, hydrocortisone, prednisolone) – inhalation is technically possible, but the action will not become local and will remain systemic;

- suspensions (they include decoctions of herbs) – the particles of the suspension are larger than the aerosol particles in the nebulizer, in addition, the plants themselves can cause an attack of broncho-obstruction, especially in patients with increased respiratory reactivity.

- common misconception is the inhalation of a solution of theophylline that does not have a topical effect, so such inhalations will be ineffective.

- mineral water due to the impossibility to maintain their sterility, as well as the presence of foreign impurities in the solution (carbon dioxide, heavy metal salts, etc.).

#### Conclusions

1) Nebulizer therapy is a modern way for delivering drugs to the respiratory tract, the effectiveness and safety of which is scientifically substantiated, including patients with severe somatic pathology, the elderly and children.

2) In some cases, the use of nebulizers is the only way to ensure that the medicinal product enters directly to the respiratory system.

3) Successful inhalation therapy depends not only on the choice of the drug, but also on the choice of method of delivery of drugs to the respiratory tract and the correct technique of inhalation.

4) For nebulizer therapy, it is better to use drugs that are produced for nebulizer. They are manufactured sterile, ready for use and easy to use, does not present a risk of infection to the patient in contrast to large multi-dose vials.

## Список літератури

1. Сухий кашель: сучасний підхід до лікування / І.В. Баранова, І.А. Ілюк, С.І. Лещенко, О.В. Солейко, К.П. Постовітенко, О.В. Долинна. Астма та алергія. 2018. № 1. С. 20–26.
2. Вплив інгаляції розчину антисептика декаметоксину на показники функції зовнішнього дихання у пацієнтів з інфекційним загостренням бронхіальної астми / М.І. Гуменюк, С.І. Панчук, В.І. Ігнат'єва, О.В. Денисова. Астма та алергія. 2015. № 3. С. 23–27.
3. Кузьменко Н.М., Яременко О.Б. Небулайзерна терапія у хворих на хронічне обструктивне захворювання легень. Астма та алергія. 2018. № 1. С. 40–47.
4. Лещенко С.І. Небулайзерная терапия – современная технология лечения заболеваний дыхательных путей. Український пульмонологічний журнал. 2009. № 2. С. 13.
5. Небулайзерна терапія в клінічній практиці: методичні рекомендації. Державний вищий навчальний заклад «Ужгородський національний університет», факультет післядипломної освіти, кафедра курортології, медичної реабілітації та фізіотерапії. Ужгород, 2010. 40 с.
6. Перцева Т.А., Гашинова Е.Ю. Небулайзерная терапия при обострении бронхиальной астмы. Астма та алергія. 2010. № 1/2. С. 55–58.
7. Сухан В.С. Небулайзерна терапія як метод інгаляційної аерозольної терапії у лікуванні хворих на бронхіальну астму. Науковий Вісник Ужгородського Університету. 2015. Випуск 1 (51). С. 279–283.
8. Фещенко Ю.І., Яшина Л.А., Туманов А.Н. Применение небулайзеров в клинической практике (методическое пособие для врачей). К.: НИФП, 2006. 32 с.
9. Хронічне обструктивне захворювання легень: етіологія, патогенез, класифікація, діагностика, терапія / Ю.І. Фещенко, Л.О. Яшина, О.Я. Дзюблик, В.К. Гаврисюк та ін. Укр. пульмонолог. журнал. 2013. № 3. С. 7–12.
10. Balsamo R., Lanata L., Egan C.G. Mucoactive drugs. Eur Respir Rev. 2010. Vol. 19. P. 127–133.
11. European Respiratory Society Guidelines on the use of nebulizers / J.J. Boe, H. Dennis, B.R. O'Driscoll et al. European Respiratory Journal. 2001. Vol. 18. P. 228–242.
12. Drug delivery: principles and applications. Edited by B. Wang, L. Hu, T.J. Siahaan. USA: John Wiley & Sons, Inc., 2016. 59 p.
13. Dhand R. The role of nebulized therapy in the management of COPD: evidence and recommendations / R. Dhand, M. Dolovich, B. Chipps et al. International Journal of Chronic Obstructive Pulmonary Disease. 2012. Vol. 9 (1). P. 58–72.
14. Global initiative for chronic obstructive lung disease, 2017: Pocket guide to COPD diagnosis, management and prevention. A Guide for Health Care Professionals 2017 Report. 2017. 42 p.
15. Global Initiative for asthma – Global Strategy for asthma management and prevention: updated 2017. Режим доступу: <http://www.ginasthma.org>
16. Gumenuk M., Panchuk S. Decamethoxine efficiency in the treatment of infectious exacerbation of asthma. ERS: annual Congress. Munich, 2014. P. 315.
17. Inhalation Aerosols: Physical and Biological Basis for Therapy. Second Edition. Edited by A.J. Hickey. USA: Informa Healthcare, 2007. 504 p.
18. European Respiratory Society Guidelines on the use of nebulisers / J. Boe et al. Eur. Respir. J. 2001. Vol. 18. P. 228–242.
19. Esposito S. Inhaled Antibiotic Therapy for the Treatment of Upper Respiratory Tract Infections / S. Esposito, C. Rosazza, C.S. Sciarabba, N. Principi. J Aerosol Med Pulm Drug Deliv. 2017. Vol. 30 (1). P. 14–19.
20. Pulmonary Drug Delivery Advances and Challenges. Edited by A. Nokhodchi and G.P. Martin. John Wiley & Sons, Ltd., 2015. 323 p.
21. Nebulized hypertonic saline containing hyaluronic acid improves tolerability in patients with cystic fibrosis and lung disease compared with nebulized hypertonic saline alone: a prospective, randomized, double-blind, controlled study / M.L. Furnari et al. Ther Adv Respir Dis. 2012. Vol. 6. P. 315–322.

## References

1. Baranova IV, et al. Sukhyy kashel : suchasnyy pidkhid do likuvannya (Dry cough: modern approach of treatment). Astma ta alerhiya. 2018;1:20–26.
2. Gumenyuk MI, et al. Vplyv inhalyatsiyi rozchynu antyseptyka dekametoksynu na pokaznyky funktsiyi zovnishn oho dykhannya u patsiyentiv z infektsiynym zahostrennyam bronkhial noyi astmy (Influence of inhalation of antiseptic solution of decamethoxin on indicators of respiration in patients with infectious exacerbation of bronchial asthma). Astma ta alerhiya. 2015;3:23–27.
3. Kuzmenko NM, Yaremenko OB. Nebulayzerna terapiya u khvorykh na khronichne obstruktyvne zakhvoryuvannya lehen (Nebulized therapy in patients with chronic obstructive pulmonary disease). Astma ta alerhiya. 2018;1:40–47.
4. Leshchenko SI. Nebulayzernaya terapiya – sovremennaya tekhnolohyya lechenyya zabo-levanny dykhatel nykh putey (Nebulized therapy – the modern technology of treatment of the respiratory tract diseases). Ukrainy kyy pul monolohichnyy zhurnal. 2009;2:13.
5. Nebulayzerna terapiya v klinichniy praktitsi (Nebulized therapy in clinical practice): metodychni rekomendatsiyi. Derzhavnyy vishchyy navchal nyy zaklad «Uzhhorodskyy natsional nyy universytet», fakul tet pislyadyplo mnoyi osvity, kafedra kurortolohiyi, medychnoyi reabilitatsiyi ta fizioterapiyi. Uzhgorod, 2010. 40 p.
6. Perceva TA, Gashinova EYu. Nebulayzernaya terapiya pry obostrenny bronkhial noy astmy (Nebulized therapy in the exacerbation of bronchial asthma). Astma ta alerhiya. 2010;1/2:55–58.
7. Sukhan VS. Nebulayzerna terapiya yak metod inhalyatsiynoyi aerezol terapiyi u likuvanni khvorykh na bronkhial nu astmu (Nebulized therapy as a method of inhalation aerosol therapy for treatment of patients with bronchial asthma). Naukovyy Visnyk Uzhhorodskoho Universytetu. 2015;1(51):279–283.
8. Feshchenko Yul, Yashina LA, Tumanov AN. Prymenenye nebulayzerov v klynycheskoy praktyke (metodycheskoe posobyie dlya vrachey) (The use of nebulizers in clinical practice). Kyiv: NIFP, 2006. 32 p.
9. Feshchenko Yul, et al. Khronichne obstruktyvne zakhvoryuvannya lehen : etiolojiya, pato-henez, klasyfikatsiya, diahnostyka, terapiya (Chronic Obstructive Pulmonary Disease: Etiology, Pathogenesis, Classification, Diagnosis, Therapy). Ukr. pul monol. zhurnal. 2013;3:7–12.
10. Balsamo R, Lanata L, Egan CG. Mucoactive drugs. Eur Respir Rev. 2010;19:127–133.
11. Boe JJ, et al. European Respiratory Society Guidelines on the use of nebulizers. European Respiratory Journal. 2001;18:228–242.
12. Drug delivery: principles and applications. Edited by B. Wang, L. Hu, T.J. Siahaan. USA: John Wiley & Sons, Inc., 2016. 59 p.
13. Dhand R, et al. The role of nebulized therapy in the management of COPD: evidence and recommendations. International Journal of Chronic Obstructive Pulmonary Disease. 2012;9(1):58–72.
14. Global initiative for chronic obstructive lung disease, 2017: Pocket guide to COPD diagnosis, management and prevention. A Guide for Health Care Professionals 2017 Report. 2017. 42 p.
15. Global Initiative for asthma – Global Strategy for asthma management and prevention: updated 2017. Available from: <http://www.ginasthma.org>
16. Gumenuk M, Panchuk S. Decamethoxine efficiency in the treatment of infectious exacerbation of asthma. ERS: annual Congress. Munich, 2014. P. 315.
17. Inhalation Aerosols: Physical and Biological Basis for Therapy. Second Edition. Edited by A.J. Hickey. USA: Informa Healthcare, 2007. 504 p.
18. Boe J, et al. European Respiratory Society Guidelines on the use of nebulisers. Eur. Respir. J. 2001;18:228–242.
19. Esposito S, et al. Inhaled Antibiotic Therapy for the Treatment of Upper Respiratory Tract Infections. J Aerosol Med Pulm Drug Deliv. 2017;30(1):14–19.
20. Pulmonary Drug Delivery Advances and Challenges. Edited by A. Nokhodchi and G.P. Martin. John Wiley & Sons, Ltd., 2015. 323 p.
21. Furnari ML, et al. Nebulized hypertonic saline containing hyaluronic acid improves tolerability in patients with cystic fibrosis and lung disease compared with nebulized hypertonic saline alone: a prospective, randomized, double-blind, controlled study. Ther Adv Respir Dis. 2012;6:315–322.

*Theoretical and practical J. «Asthma and allergy», 2018, 3*

*D.V. Dobrianskyi, Ph. D.*

*Bogomolets National Medical University*

*13, T. Shevchenko avenue, Kyiv, Ukraine, 01601;*

*tel.: +38 (093) 630-66-46; e-mail: ddoobr@meta.ua*