Research Progress of Atomizers and Drugs Used in Atomization Therapy

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Abstract At present, the commonly used treatment methods for chronic respiratory diseases are drug, oxygen, interventional and atomization therapy. Atomization therapy is the most widely used because of its characteristics of fast effect, high local drug concentration, less drug dosage, convenient application and few systemic adverse reactions. In this paper, the mechanism, characteristics, commonly used drugs and clinical application of atomization therapy are discussed.

Key words Ultrasonic atomizer, Atomized drugs, Atomization therapy

1 Introduction

Respiratory diseases are one of the four chronic diseases that seriously affect the health of Chinese residents, mainly affecting the trachea, bronchus, lungs and chest[1]. The total number of patients with chronic respiratory diseases in China has exceeded 300 million[2]. Atomization therapy has become a common method to treat respiratory diseases in clinic. Atomization inhalation, a direct drug delivery method with respiratory tract and lung as the target organs, has the advantages of rapid effect, high local drug concentration, less drug dosage, convenient application and fewer systemic adverse reactions[3]. In this paper, the mechanism, characteristics, commonly used drugs and clinical application of atomization therapy are reviewed.

2 Mechanism of ultrasonic atomizers

Medical ultrasonic atomizers have been widely used in clinic, and are composed of shell, base, power supply, transformer, fan motor, energy exchange sheet, medicine storage tank, plastic thread tube, mouth tube, *etc.* The atomizers can generate high-frequency oscillation through transducer coupling, and generate 1.7 M ultrasonic oscillation output from the wafer. The circuit mostly uses single tube output, and some use double tube output. With water as the medium, the water-soluble drug in a medicine cup is atomized into fine mist particles by ultrasonic wave through the resonant emission window at the bottom of the sink, and then the medicine mist is sent to the patient through a threaded pipe by a blower for inhalation treatment to achieve the effect of atomization[4].

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3 Characteristics of ultrasonic atomization inhalation

The characteristics of ultrasonic atomization inhalation technology reflect its advantages in the treatment of respiratory diseases. First of all, it can adjust the amount of fog produced by an atomizer flexibly according to the needs of patients, so as to maximize the therapeutic effect. In addition, the produced fog droplets have a uniform diameter of about 5 μm, so that the drug liquid is evenly distributed and effectively reach the terminal bronchus and alveoli, which improves the absorption and utilization of drugs[5]. Therefore, ultrasonic atomization inhalation has become an ideal choice for the treatment of upper respiratory tract infectious diseases such as colds, allergic rhinitis, and nasal congestion, and is especially suitable for elderly patients and people with mobility difficulties. Besides, because the electronic components of an ultrasonic atomizer produce heat, the temperature of the atomized gas increases slightly, and it provides a warm and comfortable treatment experience for patients. The cost of the treatment is low, and the noise is low, so it can not cause additional discomfort to patients.

Meanwhile, ultrasonic atomization inhalation also has certain limitations. For instance, when the atomizer works, it will affect the release ratio of atomized suspension (such as corticosteroid atomizing inhalation preparation), result in the temperature rise of the drug liquid in the container, and then affect the stability of protein or peptide compounds[6]. In addition, the amount of fog released by an ultrasonic atomizer is large, but due to the large capacity of drugs, the output efficiency of the drug fog particles is low, so it is not suitable for the treatment of asthma and other asthmatic diseases.

4 Clinical application of atomization therapy

The atomizers used in clinical practice is mainly divided into oral and mask atomizers.

4.1 Mode of use and applicable crowds Oral atomizers: patients inhale the atomized gas of drug through the mouth. Usually patients need to wear a mouth mask or tube. They are suitable for most patients who can inhale the atomized gas through the mouth,

including children and adults. Mask atomizers: patients inhale the atomized gas of drug through a mask, and they are suitable for patients who cannot effectively use oral atomizers, such as infants, patients with intellectual disabilities, or emergency patients in some special situations.

4.2 Method of drug delivery Oral atomizers: drugs are delivered directly to the mouth and respiratory tract, and can quickly reach the lungs through inhalation. Mask atomizers: drugs are delivered to the mouth and nose through a mask, and then inhaled into the respiratory tract.

4.3 Application environment

4.3.1 Oral atomizers. (i) Treatment of asthma and chronic obstructive pulmonary disease (COPD). Oral atomizers can effectively deliver drugs to the lungs for the treatment of acute asthma or COPD[7]. The atomizers can provide fast and efficient drug delivery, making them suitable for palliative care for these diseases[8]. Commonly used drugs include bronchodilators such as salbutamol and inhaled steroids. The atomizers have been in use for more than a century, and they are the first choice for patients whose inhalation is difficult to control[9]. Guan Liping *et al.*[6] found that oral atomizers should be preferred by patients who can inhale drugs by the mouth, and patients who use a mask to inhale drugs should be advised to breathe with open mouth to increase the amount of orally inhaled drugs and thus improve the therapeutic effect.

(ii) Treatment of respiratory infection. Oral atomizers can be used to deliver antibiotics or other anti-infective drugs to the lungs to treat respiratory infection. Antibiotics are atomized to deliver higher concentrations of drugs directly to the site of infection, thereby minimizing systemic adverse reactions associated with oral or parenteral administration[10]. The atomizers are widely used in respiratory medicine department, and are effective for a variety of respiratory diseases, so they are preferred by special groups such as children and the elderly. Cen Xiuxian *et al.*[11] found that pacifier atomizers could effectively eliminate children's fear and greatly promote children's acceptance of treatment. Patients receiving a respirator can use the atomizers, such as those receiving non-invasive or invasive mechanical ventilation[12].

(iii) Atomization therapy by solid drugs. Atomization therapy by solid drugs can use an oral atomizer to atomize powder to treat certain respiratory diseases. Atomizer therapy is suitable for a variety of patient populations, including premature infants, elderly patients, and patients receiving a respirator[13]. Patients who have dysphagia can make it difficult to swallow solid drugs, so the use of liquid alternatives or proper disposal of solid drugs may be necessary. Atomization inhalation therapy offers the administration of multiple drugs, and can be easily used for tidal breathing, so it is suitable for children, the elderly, and severely ill patients.

4.3.2 Mask atomizers. (i) First aid and acute treatment. Mask atomizers are widely used in emergency rooms and emergency places to deliver drugs to patients suffering from acute asthma or severe breathing difficulties. Atomizer therapy is effective for many respiratory diseases and is preferred by special groups such as children and the elderly. Besides, it is suitable for severe worsening symptoms. The atomizers convert liquid drugs into inhalable aerosols that can be easily administered by tidal breathing[14].

(ii) Drug delivery to patients with difficulties. For patients who are unable to use traditional inhalers, such as infants, young children, people with intellectual disabilities or those who are unconscious, mask atomizers are convenient and suitable for them. The atomizers can deliver drugs through a face mask without patients' assistance in inhaling. Atomizer therapy is widely used in respiratory medicine department and is the first choice for special groups such as children and the elderly. It allows for spontaneous breathing and the use of drugs without the need for other inhalers. Chi Li[15] found in clinical observation that the use of mask atomizers could improve the symptoms of hypoxia, and the inhaled fog had less stimulation on the respiratory tract of patients, making them feel more comfortable.

5 Present situation of drugs in atomization therapy

5.1 Improvement of drug delivery technology Researchers have been working to improve the drug delivery technology of atomizers to enhance the absorption efficiency and treatment effect of drugs. They focus on optimizing atomizer design, improving drug formulation, and exploring new drug delivery systems, such as nanoparticle technology or carrier technology[16]. Microfluidic technology has become a reliable method for the synthesis of precise nanoparticles of uniform size, thereby improving the encapsulation efficiency and controlling the release of drug particles at the appropriate site[17].

5.2 Application of new drugs Researchers are studying the safety and effectiveness of oral atomizers for the delivery of new drugs such as biologics and gene therapy drugs[18]. Nanotechnology based drug delivery systems, including nanotherapeutics, have shown the potential to improve asthma treatment by reducing side effects and increasing drug bioavailability. The ability of self-emulsifying drug delivery systems (SEDDS) to improve the solubility and bioavailability of insoluble substances has also been studied[19]. In the field of orthopaedics, oral non-steroidal anti-inflammatory drugs have been found to be effective in pain management after total knee replacement[20]. In the treatment of multiple myeloma, new combinations of monoclonal antibodies and targeted drugs are being used to overcome resistance and improve prognosis.

5.3 Commonly used drugs in ultrasonic atomization

5.3.1 Inhaled corticosteroids (ICS). Representative drugs: budesonide, and beclomethasone. Action characteristics: hormones can act on many links in the formation of airway inflammation, effectively inhibit airway inflammation, reduce airway hyperresponsiveness, and relieve bronchospasm. Adverse reactions: oropharyngeal candida infection, hoarseness, pharyngitis, and bronchospasm. Recommended dose: for budesonide (specifications: 0.5 and 1.0 mg/2 mL), the starting dose, or the dose in

the severe asthma or the case with reduced oral hormones is 1.0 – 2.0 mg for adults and 0.5 – 1.0 mg (bid) for children; the maintenance dose is 0.5 – 1.0 mg for adults and 0.25 – 0.50 mg for children (bid); according to patients' condition, the number and total dose of drugs per day can be increased as appropriate. Beclomethasone (specification: 0.8 mg/2 mL): the dose is 0.8 mg for adults and 0.4 mg (bid) for children.

5.3.2 Short-acting β2 receptor agonists (SABA). Representative drugs: salbutamol, and terbutaline (specification: 5 mg/2 mL). Action characteristics: they can stimulate β2 receptors on the surface of airway smooth muscle and mast cells, activate adenylate cyclase, increase the synthesis of cyclic adenosine phosphate in cells, stabilize the hypertrophic cell membrane, and relax airway smooth muscle. Adverse reactions: headache, tremor, hypokalemia, and palpitation. Recommended dose: for salbutamol (specifications: 50 mg/10 mL, and 100 mg/20 mL), when it is used in adults, 0.5 mL of the stock solution is diluted with normal saline to 2.0 mL, or 1.0 mL of the stock solution is diluted to 2.5 mL, and 2.0 mL of the stock solution is directly used for atomization in the case of intermittent use. For children under 12 years old: 0.5 mL of the stock solution is diluted to 2.0 – 2.5 mL, and intermittent therapy can be repeated 4 times a day. Terbutaline (specification: 5 mg/2 mL): for adults and children over 20 kg, the dose is 5 mg (tid); for children under 20 kg: it is 2.5 mg, up to 4 times a day at most.

5.3.3 Short-acting muscarinic antagonist (SAMA). Representative drug: ipratropium bromide. Action characteristics: it can antagonize M1 and M3 receptors, block postganglionic vagus pathway, reduce vagus tone and play a role in bronchial dilation and mucus secretion, but its bronchial dilation effect is weaker than β2 receptor agonists. Adverse reactions: dizziness, headache, dry mouth, and urinary retention. Recommended dose: ipratropium bromide (specification: 0.5 mg/2 mL) is used for adults and adolescents over 12 years of age, and the dose needs to be adjusted individually. Treatment of acute attacks: it is 0.5 mg; administration can be repeated before the condition is stable, and the interval of administration is determined by the doctor. Maintenance treatment: 0.5 mg, tid-qid.

5.3.4 Slime dissolving agent. Representative drug: N-acetylcysteine. Action characteristics: the sulfhydryl group in the molecular structure of acetylcysteine can break the disulfide bond between mucin molecular compounds, reduce the viscosity of sputum, and make sputum easy to cough up. Adverse reactions: nausea, vomiting, stomatitis, bronchospasm, and urticaria. Recommended dose: for N-acetylcysteine (specification: 0.3 mg/3 mL), the dose is 0.3 mg qd-bid, and the administration lasts for 5 – 10 d[3].

6 Summary and prospects

In this paper, the importance of atomization therapy in the treatment of respiratory diseases is introduced, and the mechanism and characteristics of ultrasonic atomizers are discussed. There are certain differences between the two types of atomizers in the way of use, suitable population and the method of drug delivery, and they are selected according to the specific situation of patients. These studies provide physicians with more treatment options and provide important reference for optimizing the treatment of respiratory diseases. It is believed that intelligent medicine is also the future trend in this field, such as connecting to mobile applications for remote monitoring and management, and monitoring patients' usage and treatment outcomes through sensors, thereby realizing more accurate treatment management and improving patients' care and treatment outcomes.

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come one of the development trends in the future cognitive field, which is helpful for further understanding the cognitive function of depression. Therefore, a lot of research and analysis work needs to be carried out.

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