Application of Acetyl Cysteine in Clinical Pulmonology

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ABSTRACT

New possibilities for the use of acetylcysteine, known as a mucolytic agent in clinical pulmonology, are being considered. Particular attention is paid to its antioxidant and antitoxic effects. The possibilities of using acetylcysteine for bronchiolitis and cystic fibrosis are described.

Keywords: acetylcysteine, mucolytics, treatment, chronic obstructive pulmonary disease, antioxidants, bronchiolitis, cystic fibrosis.

Introduction

Respiratory diseases occupy a leading position in the structure of morbidity in both adults and children. The high prevalence is explained by the variety of etiological factors, the ease of transmission of pathogens and their ability to change. One of the most common complaints when visiting a doctor is cough. In general, coughing is a normal reaction of the respiratory tract to various irritants; it serves as a protective mechanism that helps cleanse the respiratory tract of foreign particles and excess secretions. A large number of different particles contained in the air, including bacteria, viruses, and pollutants, enter the respiratory tract. In this case, only relatively large particles (>50 μm) are retained on the mucous membrane of the nasal cavity. About 60% of foreign particles penetrate into the lower sections of the respiratory tract. Thus, particles with a diameter of 30–50 μm enter the trachea, particles with a diameter of 10–30 μm settle in the bronchi, 3–10 μm in the bronchioles, and <3 μm in the alveoli [1]

Materials And Methods

Clearing the respiratory tract of foreign particles and excess secretions and removing them along with tracheobronchial mucus is carried out using a complex protective mechanism - mucociliary clearance (MMC). It is ensured by the well-coordinated activity of ciliated epithelial cells and the secretory apparatus, represented in the respiratory tract by goblet cells and protein-mucosal glands of the submucosal layer. The secretion they produce lines the surface of the respiratory tract in a thin layer. Its movement in the proximal direction is carried out under the influence of vibrations of the cilia on the apical part of the respiratory epithelium, which form a kind of “running wave” of mucus from the bottom up [2].

Results And Discussion

In inflammatory diseases of the respiratory tract, hyperproduction of sputum occurs, which at the initial stages is protective in nature and helps to enhance bronchial drainage. As the disease progresses, not only quantitative, but also qualitative changes in the bronchial secretion occur: its viscosity and adhesiveness increase significantly, and the speed of movement slows down or stops altogether, which paralyzes the MMC and activates coughing - the leading protective reflex aimed

at removing from the respiratory tract of sputum and foreign particles. Cough clearance does not depend on the activity of the ciliated epithelium of the bronchi, but its effectiveness is largely determined by the volume and viscosity of the bronchial secretion. Cough with difficult to separate sputum is a common clinical symptom of both acute and chronic respiratory diseases. Therefore, mucoactive therapy is one of the most important components of treatment.

There are several options for systematizing mucoactive drugs, but dividing them into groups according to their mechanism of action is very arbitrary: the same drug can have a number of effects on the bronchi and their contents. According to the classification developed by P. Braga et al. [5], mucolytic agents are divided into groups depending on their effect (direct or indirect) on bronchial secretion (Table 1).

Table 1
Classification of mucolytic agents

Group	Mechanism of action	Medications	
Indirect mucolytics	Changes in biochemical composition and mucus production	S-carboxymethylcysteine, sobrerol	
	Change in adhesion of the gel layer	Ambroxol, sodium bicarbonate	
	Effect on sol layer and hydration	Water, sodium salts, potassium salts	
	Volatiles and balms	Terpenes	
Direct acting mucolytics	Destruction of mucus polymers	Thiols	Cysteine, acetylcysteine, tiopronin, mesna
		Enzymes	Trypsin, α-chymotrypsin
		Other	Hypertonic solution, inorganic iodides, etc.

According to another classification [3], mucoactive drugs can be divided into 3 groups, but this division is largely arbitrary: the classification is based on identifying the leading (predominant) mechanism of influence on MMC, but most drugs have a complex effect.

The first drugs from the group of mucolytics were proteolytic enzymes (trypsin, ribonuclease, deoxyribonuclease). Due to possible complications (allergic reactions, destructive processes in the lung tissue), these drugs are used extremely rarely - for special indications. Of much greater practical importance is the group of non-enzymatic mucolytics, which depolymerize sputum macromolecules by cleaving disulfide bonds. One of the most widely used drugs in this group, acetylcysteine, a derivative of the natural amino acid L-cysteine, belongs to the group of thiols. The sulfhydryl groups (-SH) contained in its molecule break intra- and intermolecular disulfide bonds of acidic mucopolysaccharides of sputum, exerting a direct mucolytic effect. As a result of depolymerization of macromolecules, sputum, including purulent one, becomes less viscous and adhesive, which facilitates its discharge. The MMC rate also increases, which gives grounds to consider acetylcysteine not only a mucolytic, but also a mucokinetic. In addition, the drug has a mucoregulatory effect, since it increases the secretion of less viscous sialomucins by goblet cells.

When taken orally, acetylcysteine is well absorbed from the gastrointestinal tract (GIT), and its therapeutic concentration is created in the lungs. The level of absorption of acetylcysteine from the gastrointestinal tract is comparable to its entry into the blood after intramuscular administration. The effect of the drug begins within 30–90 minutes after administration. The maximum concentration in

blood plasma (2 μmol/l) is achieved 2–3 hours after administration. A study in adults with chronic bronchitis and pneumonia determined that the mucolytic effect of acetylcysteine (thinning and increasing the volume of expectorated sputum) manifests itself already from the 1st day of use and becomes maximum by the 3rd day [2].

To a large extent, acetylcysteine undergoes a "first pass" effect through the liver. There the drug is metabolized, transforming through hydrolysis into the active metabolite cysteine. Subsequently, cysteine serves as the basis necessary for the synthesis of glutathione. The half-life of acetylcysteine is 1 hour, increasing to 8 hours in liver cirrhosis; the elimination route is predominantly hepatic (70%).

The safety of the use of acetylcysteine in pediatric practice has been confirmed by 34 international studies involving 2064 children aged 2 months to 17 years [4].

Acetylcysteine is well tolerated in oral and injection forms, but in some cases its inhalation can cause bronchial obstruction in patients with asthma. Rare adverse events include dyspeptic disorders, headache, and tachycardia. Oral intake of acetylcysteine may inactivate the effect of antibiotics taken orally. The possibility of a single dose of both drugs allows you to separate the time of their administration by 2 hours.

Traditionally, mucolytics are used for respiratory diseases characterized by the formation of very viscous, difficult to separate sputum. Often these drugs are also prescribed to prevent complications during operations on the respiratory organs, upper respiratory tract, and after intratracheal anesthesia. In addition, in vitro studies have proven that acetylcysteine can reduce the adhesion of pathogenic bacteria to epithelial cells and the colonization of the respiratory tract by pathogenic microbes [2].

Conclusion

Thus, not only the pronounced mucolytic activity of acetylcysteine has been established, but also its antioxidant and detoxifying effects, which confirms the wide therapeutic potential of the drug. The effectiveness and safety of the use of acetylcysteine has been confirmed by many years of clinical experience and numerous studies.

References

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