Treatment and Management of Elderly Bronchial Asthma

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Abstract: There are certain characteristics of elderly bronchial asthma that are associated with aging, which must be considered during diagnosis and treatment. From the physiological viewpoint, a decrease in the forced expiratory volume per 1 sec (FEV1), an increase in the incidence of complications, such as chronic obstructive pulmonary disease and chronic heart failure, and a decrease in ventilatory response to hypoxemia must be considered. From the viewpoint of allergic reaction, the incidence of atopy-type asthma is not always low among elderly asthmatic patients, and their positive reaction to allergens is almost the same as that in young patients. In elderly asthmatic patients, obstruction of respiratory tracts tends to be severe, thus there is a high incidence of severe asthma. Because of the high incidence of death caused by asthma, introduction of inhaled steroids in the early stages for long-term control is important. Taking those characteristics in the elderly such as complications, drug interaction, and patients' drug compliance into consideration, the patients must be repeatedly educated, through which a partnership between doctors and patients needs to be established. This is a basic requirement for the treatment and management of bronchial asthma in elderly patients.

Key words: Elderly bronchial asthma; Chronic obstructive pulmonary disease; Drug interaction; Compliance

Introduction

Since the majority of our society will consist of elderly people in the very near future, patient-oriented treatment will be reexamined primarily to improve the quality of life (QOL) of the patients. In actual diagnosis and treatment of elderly bronchial asthma, many factors must be considered; not only decreases in physiological functions such as respiratory function, but also complications associated with chronic cardiopulmonary diseases, and drug metabolism and compliance. The purpose of this review is to clarify the characteristics of elderly bronchial asthma in order to properly diagnose it in the early stages and to treat the patients appropriately.
Pathophysiology

In elderly bronchial asthma, chronic airway inflammation is the main pathophysiological characteristic, the same as that in younger asthmatic patients. However, it is important to note that elderly patients with bronchial asthma exhibit physiological changes and allergic characteristics associated with aging that result in the intractability of their asthma.

1. Physiological changes with aging

Aging and smoking are the main risk factors that influence pulmonary function. In the lungs of elderly patients, the airway space distal from the respiratory bronchiole to the alveolar duct and alveolus is dilated, causing age-related changes, such as an increase in residual volume and decrease in forced expiratory volume per sec (FEV1) by 25 to 30 ml/year. In asthmatic patients, the decrease in FEV1 is larger compared to that of healthy controls (Fig. 2). Furthermore, the amount of cigarettes smoked and sensibility to smoking are also causes of a decrease in FEV1, which should also be considered in the treatment of chronic obstructive pulmonary diseases (COPD) including emphysema and chronic bronchitis. Indeed, the incidence of the complication of COPD in asthmatic patients 70 years or older is high; chronic bronchitis was observed in 16.3% and emphysema in 19.0%. In addition, it was reported that unlike in the case of young asthmatic patients, smoking was an independent risk factor for the development of steroid-dependent asthma in the elderly. Accordingly, education of elderly patients regarding the dangers of smoking must be thoroughly carried out not only to reverse the decrease in FEV1 so that it will be equivalent to that of nonsmokers by abstaining from smoking, but also to eliminate factors that contributed to the exacerbation of asthma.

The next important point is that ventilatory response to carbon dioxide is not likely to be influenced by aging, whereas ventilatory response to hypoxia deteriorates with aging.
In particular, patients with senile depression and dementia lack subjective symptoms such as dyspnea, thereby requiring more attention. Ischemic heart disease and congestive heart failure due to arrhythmia, namely cardiac asthma, must always be considered in treating elderly asthmatic patients. In cases of complication of pulmonary tuberculosis sequelae, increased chest wall resistance due to thoracic deformity should be considered.

With deterioration of immunoprotective ability in elderly patients, chronic respiratory infec-
Table 1 Allergy Characteristics of Elderly Patients with Bronchial Asthma14–18

1) Ability to produce IgE decreases with aging.14,15
2) The total IgE level in the serum and RAST positivity rate decrease in the elderly.16,17
3) With respect to age, the positivity rate for immediate intradermal skin reaction to major allergens, such as house dust, mites and Japanese cedar pollen, decreases with aging reaching 30% or less among patients in their 60’s and 70’s. On the other hand, the positivity rate for Candida ranges from 40% to 50%, and Candida is the allergen that elicits positive reaction at a highest rate among patients in their 50’s or older (Fig. 3).16
4) Positivity rate in the bronchial provocation test of patients with positive intradermal reaction to dust is 70% to 80% for age groups. Bronchial hypersensitivity and intradermal skin reaction to histamine are not influenced by aging.19

Fig. 3 Immediate intradermal skin reaction to major allergens at various ages19 (quoted from Ref. 18)
Horizontal axis indicates year.
Number in parentheses indicates the number of patients in a specific age group.

2. Characteristics of allergy associated with aging

The longer the duration of a disease, the more severe and irreversible the airway obstruction becomes, thus predisposing an individual to greater hypersensitivity; due to airway remodeling phenomena. Those are the reason that asthma in elderly patients tends to be chronic and intractable.13 Table 1 and Fig. 3 show characteristics of elderly patients with respect to IgE production in response to allergens, indicating that the incidence of atopy-type asthma decreases in elderly patients, whereas positive reaction to allergens is almost the same as that in young asthmatic patients.14–18 A study of the total IgE level in patients 60 years or older in our hospital revealed that the percentage of patients with high levels of total IgE, that is, 400 IU/ml or more, was 35.2%, which is almost the same as that in young patients with asthma (Fig. 4). As stated above, since COPD is often observed as a complication in elderly patients, it is often difficult to accurately determine the presence or absence of bronchial asthma. To confirm this, the following examinations should be performed: determination of whether or not bronchial hypersensitivity, airway reversibility by inhaled β-stimulants and the eosinophil ratio in sputum increased; these tests are clinically easily performed and effective.
Treatment and Management

Treatment of elderly bronchial asthma must not deviate from the principles of treatment stated in the guideline. However, in general, with deterioration of physiological functions due to aging, drug concentrations in the plasma tend to increase and the degree of response to drugs increases, thereby adverse reactions are likely to develop. In addition, due to complication of multiple diseases, adverse reactions due to multiple-drug interactions sometimes develop. The actual state of drug treatment including compliance, which needs to be studied, is discussed below.

1. Steroid inhalation

In the guideline, inhalation of steroids is the main strategy for long-term control of asthma. To promote inhalation of beclomethasone dipropionate (BDP) using a metered dose inhaler (MDI), use of a spacer and repetitive inhalation need to be strongly recommended to the elderly patients. The frequency of inhaling fluticasone (Diskheller is used), using a dry powder inhaler (DPI), is twice daily. Moreover, DPI is easier for the patients to use; therefore, from the aspect of compliance, the use of fluticasone is advantageous. It is also frequently used recently due to its effect of inhibiting airway inflammation. On the other hand, to prevent regional adverse reactions such as hoarseness and oral candidiasis, patients need to be repeatedly educated; for example, they should be encouraged to gargle after inhalation. A recent report indicates that significant differences were observed in the improvement of pulmonary functions and bronchial hypersensitivity depending on the stage of asthma at which inhaled steroids were introduced. Based on this finding, early intervention with inhaled corticosteroid to prevent the development of airway remodeling is being tested. Moreover, in elderly patients, osteoporosis and cataracts, which are complications occurring with high incidence, cannot be ignored. To determine the long-term efficacy of high doses of inhaled steroids, large-scale clinical trials were carried out in subjects that included the elderly. These trials provide evidence of a negative relationship
between total cumulative dose of inhaled corticosteroid and bone-mineral density; however, the risk of developing cataracts did not increase following the use of inhaled steroids. According to latest findings, inhaled corticosteroids lead to a dose-related loss of hip bone-mineral density in premenopausal women. Further studies are required in order to accumulate more relevant data.

2. \( \beta_2 \) stimulants

\( \beta_2 \) stimulants must be carefully administered because these are contraindicated for patients with hyperthyroidism, hypertension, chronic cardiac disease, and diabetes mellitus; further consideration is required in the case of elderly patients who develop complications at a high incidence. The American Thoracic Society (ATS) encourages careful attention be paid to the occurrence of adverse reactions in elderly asthmatic patients, such as tremor, restlessness, palpitation, and tachycardia. On the other hand, it is reported that the affinity between catecholamine and \( \beta \)-adrenoreceptors decreases with aging, whereas another report indicates a decrease in drug response that is proportional to the duration of the disease rather than age. Recently, since the efficacy of increasing the dose of inhaled steroids has been limited and frequent use of short-acting inhaled \( \beta_2 \)-stimulants causes the wearing-off phenomenon, regular use of inhaled steroids in combination with long-acting \( \beta_2 \) stimulants (salmeterol and formoterol) is recommended to control moderate and persistent chronic asthma in Europe and United States. It is reported that concomitant use of formoterol is effective to improve and avert acute deterioration of pulmonary functions for patients with intractable asthma and whose conditions were insufficiently controlled by merely inhaling steroids, leading to an improvement of QOL. Similar efficacy of concomitant use is expected in elderly patients.

3. Theophylline

Theophylline is widely used in Japan, but it is believed to be inferior to long-acting \( \beta_2 \) stimulants with respect to capability of mitigating nocturnal dyspnea and improving pulmonary functions. Since theophylline has many interactions with other drugs and its effective and toxic concentrations are close, its concentration in plasma needs to be monitored. Table 2 shows a list of drugs which influence plasma theophylline concentration. In addition, clearance of theophylline decreases in cases of severe liver damage and congestive heart failure. On the other hand, smoking decreases plasma theophylline concentration. These are clinically significant points.

4. Anticholinergic drugs

Anticholinergic drugs have a great bronchodilating property for central airways but less bronchodilating ability for peripheral airways, and the onset of its efficacy is slowly developed compared to inhaled \( \beta_2 \)-stimulants. Rather, anticholinergics are effective for asthmatic patients complicated with mild to moderate pulmonary emphysema. The duration of effectivity is long.

<table>
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<tr>
<th>Table 2 Drugs that Influence Plasma Theophylline Concentration</th>
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<td><strong>1. Drugs that increase plasma theophylline concentration:</strong></td>
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<td>Cimetidine, mexiletine hydrochloride, amiodarone hydrochloride, enoxacin, pipemidic acid trihydrate, ciprofloxacin hydrochloride, norfloxacin, tosufloxacin tosylate, erythromycin, clarithromycin, roxithromycin, tiabendazole, ticlopidine hydrochloride, verapamil hydrochloride, diltiazem hydrochloride, fluvoxamine maleate, fluconazole, aciclovir, interferon, iriprilavone, cyclosporin, allopurinol and halothane</td>
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<td><strong>2. Drugs that decrease plasma theophylline concentration:</strong></td>
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<tr>
<td>Riphampicin, phenobarbital, lansoprazole, ritonavir, phenytoin and carbamazepine</td>
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and its efficacy is not reduced by long-term use. The amount of sputum and its viscosity are negligibly influenced by anticholinergic drugs; however, attention must be paid to the possible adverse reaction of ischuria in male patients with benign prostatic hyperplasia, which rarely occurs. The synergistic effect between a β₂ stimulant and an inhaled anticholinergic drug has been reported, based on which a MDI containing both types of drugs, Combivent, is used in United States.

Conclusions

The disease state and treatment of elderly bronchial asthma were outlined in this paper. The purpose of treatment in the clinical field is to prevent death from asthma and improve QOL. The necessity of administering appropriate treatment in the early stages is important to build an established partnership between physicians and patients, and is the same for both the young and elderly asthmatic patients.

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