ASTHMA, ALLERGIC RHINITIS AND ATOPIC ECZEMA IN THE ELDERLY

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ABSTRACT

This article briefly reviews the anatomical, physiological and immunological changes which occur with age in relation to the presentation, diagnosis and management of asthma, rhinitis and eczema in the elderly. Although new onset of asthma is much less common in the elderly, the prevalence is up to 17%. Because the classic symptoms of asthma have a poor predictive value in the elderly and breathlessness is underestimated by the patient due to a combination of altered sensory perception and multiple pathologies leading to reduced function and activity, the diagnosis is often missed. Because of physiological and immunological changes with age there is an increase in lower respiratory tract infections and chronic bronchitis, or aspiration often coexists with bronchospasm. In addition changes in respiratory physiology make the interpretation of pulmonary function tests difficult and the differential diagnosis is wide. In the elderly management is not only complicated by a higher incidence of adverse drug effects but the problems of multiple pathologies, polypharmacy and drug-drug interactions. The article explores the efficacy and problems associated with medications used to manage asthma in the elderly. Similarly it is unusual for a new diagnosis of allergic rhinitis or eczema to be made in the elderly and the clinician should focus on the wide spectrum of possible pathologies which form the differential diagnosis of these conditions. The article discusses the investigation and diagnosis of rhinitis and eczema in the elderly and highlights the potential problems of therapy and which drugs are preferred.

ASTHMA IN THE ELDERLY

The prevalence of asthma in older people is estimated to be between 6.5% and 17%.[1] In clinical practice asthma in the elderly is often underdiagnosed, misdiagnosed and undertreated.[2,3] There are many contributing factors. Frail elderly people often have multiple pathologies leading to reduced function and activity. This in turn leads to an underestimation of the degree of breathlessness, and up to 30% of people 70 years and older become breathless walking on the flat with their peers.[4] The typical symptoms of asthma, i.e. wheeze, breathlessness, chest tightness and cough, have a poor predictive value in the elderly.[5] Apart from chronic obstructive pulmonary disease and cardiac fail-

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ure, the differential diagnosis includes aspiration, vocal chord paralysis, respiratory tract tumours, bronchiectasis, foreign bodies, pulmonary emboli, interstitial lung disease and hyperventilation.

Structure and function of the lungs in elderly patients with asthma

Factors responsible for the development of asthma in the elderly are poorly understood. Family history of atopy is unusual and common environmental antigens are thought to be less important.[6] With ageing and immunosenescence there are changes in the structure and function of the lung as well as the immune system. Asthma is caused by a complex interaction of inflammatory cells such as mast cells, eosinophils, activated T cells and the production of IgE, prostaglandin E, histamine, proteases and cytokines such as leukotriene(LT)-C_4, LTD_4, LTE_4, platelet-activating factor and bradykinin which lead to airways inflammation. There are characteristic cellular changes of the constitutive cells, such as epithelial cells, mucous glands, endothelial cells and myofibroblasts, as well as the resident cells, such as mast cells and macrophages, which are accompanied by infiltrating cells, such as eosinophils, CD4 T cells, basophils, neutrophils and activated platelets. Bronchoconstriction results from a wide variety of inflammatory and other mediators.

Some differences in both the structure and function of the lungs as well as the immune activation associated with asthma have been observed in the elderly. Firstly with ageing there is impaired mucociliary clearance and ciliary function with an increased frequency of ciliary ultrastructural abnormalities. This might help to explain the increase in respiratory infections in the elderly, especially the frequent overlap between chronic bronchitis and new onset of reversible airways obstruction.[7] FEV_1 and FVC decline with age, independently of smoking and environmental or other factors, but concurrent illnesses and deconditioning also play a role.[8] Alterations in the cross-linkage of collagen and decreased elasticity of the extracellular matrix lead to reduced small airways calibre in the elderly which, coupled with a loss of diaphragmatic continuity,[7] contributes to a decrease in respiratory power.

In elderly patients with asthma airway walls and smooth muscle are thickened compared with younger patients, leading to reduction in airway lumen. This results in a greater proportion of 'fixed' or irreversible airway obstruction.[9] As in younger patients there is prominent eosinophilia and CD4+ lymphocytosis on bronchoalveolar lavage but there are differences in eosinophil function, predominantly reduced superoxide anion production, which influence responsiveness to some medications.[10] The autonomic nervous system plays an important role in modulating bronchoconstriction and inflammation in asthma. It is known that parasympathetic nervous system functions decline with age but the cholinergically mediated cough reflex appears to be unaffected.[11,12]

In elderly asthmatics, even in the absence of structural changes of emphysema, only 20% have normal pulmonary function (FEV_1 >80% predicted) and 20% have moderate to severe airflow obstruction (FEV_1 <50%

predicted) after the administration of bronchodilators.[13] Older patients with late-onset asthma have reduced β-adrenergic receptor affinity, while maintaining the same receptor density as younger patients and also impaired post receptor cyclic adenosine monophosphate (AMP) production.[14]

Although allergy and atopy are less important in the pathogenesis of asthma in the elderly, where only 20% are atopic, elevated IgE levels are still strongly predictive of a subsequent diagnosis of asthma in the elderly[15] whether or not the patient smokes. 'Intrinsic asthma,' where there is no evidence of positive immediate hypersensitivity reactions to skin-prick testing or elevated IgE, is more common in the elderly and the severity of the bronchial mucosal inflammatory cell infiltrate is greater than that for atopic or 'extrinsic asthma' of comparable clinical severity.[16] Of note is that most people who develop asthma after the age of 65 have their first asthmatic symptoms during an upper respiratory tract infection.[17]

Diagnosing asthma in the elderly

Asthma is primarily a clinical diagnosis and the classic symptoms of wheeze, chest tightness, cough and breathlessness may be absent as the perception of bronchoconstriction is less in the elderly[18] and they may accept their symptoms as part of ageing. In frail elderly patients comorbidities such as dementia can make the diagnosis difficult, and elderly patients often present with a geriatric syndrome, such as decline in function. Distinguishing asthma from chronic bronchitis and emphysema, especially if there is a history of smoking, can be difficult and the demonstration of reversible airways obstruction is important. The differential diagnosis of asthma in the elderly includes left ventricular failure. In systolic failure B-type naturetic peptide (BNP) is useful; however levels increase in normal elderly and it is less sensitive for diastolic failure which is common in the elderly.[19]

The differential diagnosis also includes viral tracheobronchitis, gastro-oesophageal reflux disease, aspiration, bronchial carcinoma or mediastinal lymphadenopathy, pulmonary embolism, bronchiectasis and, although rare, bronchopulmonary aspergillosis and Churg-Strauss syndrome. Polypharmacy is common in the elderly and bronchospasm can be induced by β-adrenoreceptor antagonists (including eye drops for glaucoma), non-steroidal anti-inflammatory drugs (NSAIDs), aspirin and cholinergic drugs. Angiotensin-converting enzyme (ACE) inhibitors can cause cough. The minimum investigations required in the diagnosis of asthma in the elderly should include spirometry, chest radiograph and an ECG. Although allergy testing is more likely to be positive in those who have a history of rhinosinusitis, nasal polyps or childhood allergies, radioallergosorbent testing (RAST) for specific IgE levels to common indoor allergens associated with asthma (mites, cockroaches, moulds, cats and dogs) should be done.[20]

Managing asthma in the elderly

Evidence-based guidelines for the stepwise management of asthma have been developed by many bodies and are widely available. The problem is that they refer to the management of asthma in children and young adults and several adaptations are required for the elderly. In the non-pharmacological management of asthma stopping smoking is the most important as not only will this reduce the rate of decline in lung function but it will also improve the response to bronchodilators.

Because breathlessness and bronchoconstriction may be poorly perceived or reported, especially if there is cognitive impairment, spirometry should be used to monitor severity and response to treatment.[18] For this reason mild intermittent symptoms in the elderly warrant regular inhaled corticosteroids (rather than intermittent inhaled β-adrenoreceptor antagonists) which should be started at the standard adult dose of 400 µg/day and reduced by 25-50% every 3 months to the lowest dose on which symptoms are controlled.[21] There is no significant reduction in bone mineral density with inhaled corticosteroids unless they are used at high doses (≥ 800 µg/day) for prolonged periods.[22] Inhaled bronchodilators should also be prescribed regularly for the same reason if they are required.

Inhaled β_2-agonists are the firstline bronchodilators. In the elderly, because of age-related β-adrenoreceptor changes, bronchodilator response may be reduced.[23,24] Consequently anticholinergic bronchodilators (e.g. inhaled ipratroprium bromide) may be required in combination with inhaled β_2-agonists in milder asthma than would be the case in young patients. Incorrect use of metered-dose inhalers (MDIs) is more common in the elderly (40% in one study),[25] especially if there is cognitive impairment, arthritis of the hand or reduced grip strength. Large volume spacer devices improve MDI technique in the elderly and are easier to use than larger breath-activated devices (Autohaler, Turbohaler) which are the alternative if there is poor MDI technique.[26,27]

When asthma is not controlled on inhaled bronchodilators and standard doses of inhaled corticosteroids, the options are to use high-dose corticosteroids, long-acting β_2-agonists or oral therapy. With high-dose inhaled corticosteroids cataracts and osteoporosis may result and comorbid diseases such as hypertension and diabetes may be exacerbated.[22] In women on high-dose inhaled corticosteroids osteoporosis prophylaxis should be considered. Long-acting β_2-agonists such as salmeterol appear to be effective and well tolerated in the elderly and may be useful if there are contraindications to high-dose inhaled corticosteroids.[28]

When optimal inhaled therapy is insufficient to control asthma, oral β_2-agonists or theophylline can be added but they are problematic in the elderly because of increased adverse effects due to multiple pathology and medications. Theophylline has a narrow therapeutic range which may be complicated by decreased clearance in the elderly. Cardiac stimulation with tachycardia caused by β_2-agonists and theophylline may be detrimental in elderly patients with ischaemic heart disease, cardiac arrhythmias or uncontrolled hypertension. Hypokalaemia may be precipitated by concomitant use of diuretics and oral corticosteroids. If used they should be started at low doses and plasma drug concentration monitoring for theophylline is mandatory. Plasma theophylline concentrations are increased if there is hepatic disease or congestion due to cardiac failure and by numerous drugs such as cimetidine, erythromycin, ciprofloxacin and some calcium channel blockers.

The adverse effects of long-term or frequent high-dose short courses of oral corticosteroids are well known. Leukotriene receptor antagonists (LTR) added to inhaled corticosteroids may improve symptoms and reduce the frequency of exacerbations but there is little evidence for a corticosteroid-sparing effect.[29] Although studies of LTR in the elderly are limited, they appear to be effective regardless of age and in the elderly the main improvement is in symptoms rather than pulmonary function.[30] LTR have a theoretical advantage in the elderly as they have fewer side-effects than

inhaled corticosteroids or β_2-agonists and oral formulation makes it easy to use. However, LTR should not be substituted for inhaled corticosteroids when the latter are clinically indicated since LTR are effective in the treatment of asthma but less effective than corticosteroids.[31] Several studies have demonstrated that LTR are less effective than long-acting inhaled β_2-agonists as add-on therapy.[32] Sodium cromoglycate and other 'mast cell stabilisers' are commonly used in children but it is difficult to predict the subgroup of patients who will respond, and the need for frequent doses makes them a less attractive option in the elderly.

Annual vaccination against influenza prevents influenza and reduces hospitalisation for pneumonia in the elderly and is recommended for all people over 65 years of age. Although the evidence for pneumococcal polysaccharide vaccine is not as robust as that for influenza, because of the importance of pneumococcal pneumonia and bacteraemia in the elderly it is advocated for those over 65 years of age especially if there is respiratory disease such as asthma.[33,34]

ALLERGIC RHINITIS IN THE ELDERLY

Allergic rhinitis is an IgE-associated response to environmental allergens resulting in inflammation of the nasal mucosa which results in the characteristic symptoms of pruritus, sneezing, rhinorrhoea and nasal congestion. The condition is common with a prevalence estimated at 15-20% with 80% developing symptoms before the age of 20 years.[35] Onset of symptoms in the elderly should raise the suspicion that non-allergic rhinitis (NAR) is the primary diagnosis or contributes significantly to the symptoms. Many forms of NAR are non-inflammatory in nature and should more correctly be termed rhinopathies.

Differential diagnosis of allergic rhinitis in adults

Table I lists the differential diagnosis of allergic rhinitis in adults.

Managing allergic rhinitis in the elderly

When elderly patients present with new onset rhinorrhoea or nasal congestion a thorough history and examination should be done to exclude the conditions listed in Table I. In atopic individuals specific allergen sensitivities should be identified using skin-prick tests or serum specific IgE antibodies as allergen avoidance is the first step in management. The management in the elderly is no different to that in younger patients but topical therapy is preferable to minimise side-effects and drug interactions.

Antihistamines remain the mainstay of the symptomatic treatment of allergic rhinitis.[36] The non-selective receptor-binding properties of the first-generation antihistamines limits their use because of unfavourable side-effects.[37] The most common adverse effects are sedation and psychomotor impairment that can lead to increased falls and morbidity in the elderly. Other side-effects owing to the antimuscarinic actions include dryness of the mouth and respiratory passages, urinary retention, constipation and blurred vision. They should be avoided in elderly patients with symptomatic prostatic hypertrophy and narrow-angle glaucoma.The increased specificity for histamine receptors and lipophobic properties of second-generation antihistamines makes the side-effect profile more favourable but at higher than recommended doses second-generation antihistamines may also cause drowsiness, psychomotor retardation and anticholinergic effects. Of

Table I. Differential diagnosis of allergic rhinitis in adults

Mechanical obstruction
- Septal deviation
- Foreign body (unilateral purulent discharge)
- Hypertrophic turbinates
- Nasal tumours (benign, e.g. polyp, or malignant, e.g. squamous cell carcinoma)

Infectious rhinitis/rhinosinusitis
- Viral, bacterial or fungal

Perennial (vasomotor, idiopathic). Constant profuse, clear rhinorrhoea and nasal congestion without atopy or specific allergen exposure often triggered by environmental factors such as cold air, odours, barometric pressure

Non-allergic rhinitis with eosinophilia syndrome. Most often seen in adults; characterised by eosinophilia on nasal smears with negative testing for specific allergens

Reflex-induced
- Gustatory rhinitis: vagally mediated copious watery rhinorrhoea occurring immediately after ingesting food, especially if hot and spicy
- Chemical or irritant induced
- Postural reflexes: many different reflexes exist. A commonly encountered reflex involves ipsilateral nasal congestion when supine or prone with head turned to one side
- Nasal cycle: refers to unilateral nasal congestion that cycles from one side to the other over time in normal individuals.

Drug-induced rhinitis
- Antihypertensives: hydralazine, β-adrenergic blockers
- Aspirin and other non-steroidal anti-inflammatory drugs (with or without the aspirin triad/Samter's syndrome of rhinosinusitis, nasal polyps and asthma)
- Topical decongestants (rhinitis medicamentosa)

Hormonally induced rhinitis
- Hypothyroidism
- Exercise
- Atrophic

Granulomatous rhinitis
- Sarcoidosis
- Wegener's granulomatosis

the second-generation antihistamines cetirazine has the greatest propensity to cause sedation while fexofenadine and loratadine cause no sedation even at higher doses.[38] Among the medicines available on the South African market, cardiotoxicity is most likely with with the first-generation antihistamines although the absolute risk is small. The elderly have a decline in hepatic and renal function and often cardiac disease. These conditions place them at risk for the development of side-effects and therefore a second-generation antihistamine is preferred.

Systemic nasal decongestant preparations commonly contain sympathomimetics such as pseudoephedrine, phenylpropanolamine and phenylephrine. Many contraindications and adverse effects should be considered when prescribing these medicines in the elderly. Central nervous system stimulation leads to anxiety, insomnia, palpitations and restlessness, and vasoconstriction may cause hypertension and possible cerebral haemorrhage. In November 2000 the FDA issued a public warning about the possible risk of haemorrhagic stroke when using phenylpropanolamine. A literature review concluded that it causes a small but significant

increase in blood pressure that is more pronounced when using short-course, high-dose immediate-release preparations.[39] Extreme caution should be taken when prescribing these drugs for the elderly who have an increased prevalence of cardiovascular and cerebrovascular disease. Concomitant cardiovascular and antidepression medication may further aggravate these side-effects.

ATOPIC ECZEMA IN THE ELDERLY

Itching with or without a rash is the commonest dermatological complaint in the elderly. The prevalence of dry skin and itching increases from the young elderly, in their sixties, to the very elderly in their nineties.[40] Xerosis is the commonest cause of itching in the elderly. Other common causes include contact dermatitis, seborrhoeic dermatitis, stasis dermatitis (with or without autoeczematisation) and reactions to medications. Allergic non-eczematous dermatitis in the elderly is most commonly due to drugs. If there is no cutaneous rash, systemic causes such as biliary or renal disease, malignancy, thyroid disease or HIV infection should be considered.

Atopic dermatitis is less common in the elderly, as is allergy to foods.[41] Atopic dermatitis goes through several phases starting with erythema and oedema leading to vesiculation, crusting, excoriation, scaling and lichenification. Non-eczematous diseases with a similar appearance include scabies (especially in institutionalised elderly), mycosis fungoides, seborrhoeic dermatitis, stasis dermatitis, psoriasis, drug reactions and Darier's disease. Atopic dermatitis usually affects the flexural surfaces while psoriasis has a predilection for extensor surfaces, the genital area and above the anal sphincter. Stasis dermatitis affects the lower legs and intertrigo the breast fold, axilla and groin. Cutaneous T-cell lymphoma (mycosis fungoides) involves the entire lymphoreticular system and presents like nummular eczema, but there may be a history of improvement with sunlight exposure, lymphadenopathy and elevated white blood cell count. These three findings along with hair loss and pruritus should raise the suspicion of Sézary syndrome. Contact dermatitis is common in the elderly and usually has a specific distribution such as the hands, face or area treated with topical medication. Where the diagnosis is in doubt skin biopsies should be taken and where eczema is confirmed skin-patch testing for common allergens is advised.

Because dry skin contributes to pruritus associated with eczema in the elderly, patients should be advised to avoid frequent washing, use tepid water, avoid harsh or astringent cosmetics such as deodorant soaps and apply bland emollients containing only water, petroleum jelly or mineral oil. In dry climates humidifiers can improve itching as can soft water treatment devices where water quality is poor. The mainstays of treatment are lubrication, topical steroids (with or without occlusion) and antihistamines for pruritus. Short-course oral, intramuscular or intralesional steroids can be used at the initiation of treatment. Where long-term use of potent topical steroids or oral steroids becomes necessary, the prevention and treatment of osteoporosis is necessary and alternative immune modulators such as pimecrolimus or tacrolimus should be considered.[42]

Declaration of conflict of interest

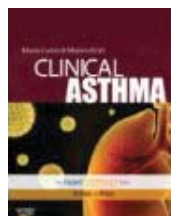The authors declare no conflict of interest.

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