

## Asthma in the elderly

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As the population increases in age, the diseases of older age will have increasing prevalence and place a greater burden on the health system. Despite asthma being usually considered a disease of younger people, asthma mortality is currently greatest in the over 55 age-group. Symptoms and emergency presentations for health care due to asthma place a great burden on the quality of life of those over age 55 with asthma. Asthma in older people is under-diagnosed due to patient and physiological factors. Medication strategies for asthma have been dominantly derived from younger cohorts so that effective medication strategies have usually not been explored in older people. Older people with asthma are very concerned regarding side effects of medication so that adherence to therapeutic regimes is often poor. In addition physical disability can lead to difficulty in accessing treatment and using inhaler devices. Practical strategies to improve asthma outcomes in older people have been studied infrequently and the goals of self-management suitable for younger age-groups may not be applicable in this group. Consequently, asthma in older people is deserving of further attention both to basic mechanisms of disease, precision in diagnosis and effective therapeutic strategies, including those that involve self-management and device use.

**Key words:** Aged; Asthma; Health education; Middle aged; Respiratory function

### INTRODUCTION

As the population ages, the prevalence of diseases of older age will rise. Whilst asthma is often considered a disease of younger people, the high prevalence of asthma in the community indicates that many older people suffer from asthma with its associated impact on morbidity and mortality. Moreover, mortality and morbidity statistics suggest that older people suffer disproportionately from the burden of asthma and airways

disease with the majority of those dying from asthma aged over 55 years. The reasons for this are multi-faceted and relate to the pulmonary changes of ageing, perceptions of dyspnoea and its meaning to older people, difficulties in asthma diagnosis, and the burden of medication and co-morbidities which render asthma in older age-groups a unique problem deserving of specific examination and therapeutic intervention.

Older people are generally defined as being 65 years old or greater. In this age-group asthma is a common disease

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affecting greater than 10% of the population [1, 2]. Characteristic of asthma are symptoms of wheeze, cough and/or shortness of breath together with detection of variable airflow obstruction. Key to the definition of asthma is evidence of airway inflammation and characteristic airway wall remodelling involving a thickened airway basement membrane and smooth muscle hypertrophy. Examination of airway inflammatory changes, often through examination of induced sputum, has indicated the importance of eosinophils in a majority of those with asthma, however in older age neutrophilic airway inflammation is more common [3]. By contrast, chronic obstructive airways disease is associated with airflow obstruction which is only partly reversible with inflammatory airway changes are dominantly neutrophilic. In addition, a history of cigarette smoking is common in older people and therefore diagnostic uncertainty frequently exists in obstructive airways diseases in older age-groups with subsequent confusion regarding correct treatments [4, 5]. Importantly, asthma demonstrates airflow obstruction which is variable and reversible.

Clinical evidence suggests that asthma older age-groups has different characteristics from that in younger groups with a lower lung function and greater symptom severity [6]. Asthma in the elderly population is commonly classified according to the age of asthma diagnosis. "Late onset" asthma is first diagnosed after the age of 65 while "early onset" persists into older age. Late onset asthma is often a more severe phenotype, with less symptom free days, and a higher requirement for oral corticosteroids [6].

Late onset asthma patients tend to be less atopic with lower levels of serum IgE and both serum and sputum eosinophils. That is, they are likely to be non-atopic or have "intrinsic" asthma with evidence of sputum neutrophilia [6, 7]. Late onset atopic asthma is predicted by high levels of IgE and previous allergen sensitisation. However, allergen sensitisation can occur at any age. The Normative Ageing Study demonstrated that previous cat sensitisation was associated with late onset asthma as confirmed by methacholine bronchoprovocation testing [8].

### Normal ageing and the lung

Ageing is associated with a restricted chest wall as thoracic skeletal components become stiffer and less compliant [9]. Age related deterioration and calcification in the rib articulations appear to explain these findings. There is additional evidence that the contractile properties of the diaphragm deteriorate with ageing [10]. In addition, normal aging is associated with a reduction in elastic recoil of the lung due to loss of elastic fibres. In

expiration the loss of elastic recoil leads to small airways collapse with associated air trapping and an increase in the residual volume, a normal finding in ageing. There is also a decrease in the vital capacity as a result of a stiffer chest wall and muscle weakness. As a result, the ageing lung is put at a mechanical disadvantage.

### Diagnostic challenges

The diagnosis of late onset asthma can be difficult and delayed. There are both patient and physician factors underlying the problem. Connolly et al. [11] demonstrated that elderly asthmatics have a reduced awareness of acute bronchoconstriction following a methacholine challenge compared to younger asthmatics patients. Further, Ekici et al. [12] performed an airway challenge on an asthmatic population. Elderly asthmatics reported less breathlessness on Borg dyspnoea score compared to the young asthmatics for a comparable level of bronchoconstriction. Furthermore, even when dyspnoea is recognised, older patients may regard their symptoms as a consequence of old age and therefore not report their dyspnoea to doctors [13]. Low socio-economic status may result in lack of access to health care, contributing to such under-reporting in an elderly population [1, 13].

Studies in older populations confirm substantial under-diagnosis by as much as 50%. In a community sample, 3.9% of patients had been diagnosed with asthma by a physician, however, a further 4.1% of patients had undiagnosed yet probable asthma [14]. Furthermore, Dow and co-workers [15], in a cross sectional survey of 6,000 residents of Bristol over the age of 65, not taking asthma treatments, reported an estimated population prevalence for untreated asthma of 1.7%. The majority of these patients (84%) had moderate or severe disease as defined by spirometric parameters. A history of wheeze and breathlessness or a past history of doctor diagnosed asthma were most likely to indicate untreated asthma [15].

The diagnostic challenge is exacerbated by the reduced reliability of normal predicted spirometry values in the elderly population which are frequently extrapolated from younger age-groups [16]. Further, old age (71-73 years) was an independent predictor for unsuccessful spirometry as defined by American Thoracic Society testing criteria amongst a Norwegian randomly selected population [17].

### Prevalence

The over-all prevalence of asthma over the life-span indicates

that the prevalence of current asthma peaks in the 10 to 24 year old age-group with a reported prevalence of between 3 and 18% [18]. Whilst many children do grow out of asthma recent longitudinal cohorts suggest that asthma may remit in as many as 65% of children with asthma, but asthma that occurs in adulthood is less likely to remit [19]. The prevalence of current asthma in those over 65 years has been documented in Australia as between 7.5 and 12.5%, with a predominance of females [1]. Data from the USA suggests a prevalence between 4 and 10%, again with a predominance of females [2]. One of the controversies in the diagnosis of asthma in older people is the overlap with chronic obstructive airways disease so that a diagnosis of asthma is often considered less certain in this age-group. However Abramson and co-workers undertook a careful examination of airways disease by complex spirometry in people over age 50 and showed that asthma was evident in 55% of those with obstructive lung disease with syndromes overlapping with asthma evident in only 8% of subjects [20].

### Morbidity and mortality

Asthma in the elderly is responsible for a significant and increasing mortality in the elderly population. Asthma deaths are highly over-represented by the elderly population. In Australia between 2003 and 2007 sixty-nine percent of all asthma deaths were in those 65 years and above [1]. In 2009, 259/411 asthma related deaths in Australia were over the age of seventy [21]. The pattern of mortality in older people with asthma also differs from younger age-groups with the peak time of death occurring over winter months, in contrast to the more even spread of mortality throughout the year in the 5 to 64 year old age groups, suggesting a potential infective cause of death [1, 2].

Asthma in older age-groups has been observed to impact on survival. Bellia et al. [22] assessed the mortality rate amongst 210 elderly asthmatic patients and 1,023 controls with a chronic non-respiratory condition. The five year mortality rate was 24% in the asthmatics and 16% in the controls, however the difference in mortality was not attributable to respiratory disease. A population-based study in Rochester, Minnesota reported an incidence of 95/100,000 for the diagnosis of late onset asthma. Forty-two percent of these patients had at least one hospital admission. In this study, the observed survival was not significantly different from the expected survival [23], an observation confirmed by Australian data [1].

Increased health service utilisation is also evident in the older

age-group with 36% of those interviewed in an Australian cohort of over 55 year olds with asthma claiming an emergency visit to a medical practitioner or hospital in the previous 12 months [13]. Hospital statistics also testify to the relatively high rate of hospital admission for asthma in older age-groups with the 65 and older group having slightly higher admission rates for asthma than the 15 to 34-year-old age-group [1, 2]. Once in hospital the older group had a significantly longer length of stay [1].

### Quality of life

Enright et al. [14] surveyed a community sample of 2,527 elderly patients with and without asthma. Asthma was associated with a reduced quality of life. Asthmatics also reported increased impairment in activities of daily living and were twice as likely to have symptoms of depression. Asthmatics were more likely to rate their general health as fair or poor.

Quality of life was also assessed in elderly (>70 years) asthmatics and non-asthmatic controls in a general practice population using the Short Form (SF)-36 and the St. George's Respiratory Questionnaire (SGRQ) [24]. Quality of life was significantly impaired in the asthmatic population. Asthmatics reported significantly impaired quality of life in the physical, social and general health domains of the SF-36 and in all domains of the SGRQ. Elderly asthmatics also reported more depressive symptoms than the controls [24].

Plaza et al. [25] performed a cross-sectional study in an asthmatic population in a county of Barcelona addressing both quality of life and direct economic impact of asthma in the elderly (>65 years) versus an adult (<65 years) population. Again, asthma in the elderly was associated with reduced quality of life across all domains of the SGRQ. Asthma was more severe in the elderly with significantly more patients (55% vs. 18%) classified as severe. Asthma derived direct costs in the elderly were double than the adult population. Most of this excess expense was explained by hospitalisation costs [25].

### Lung function

Weiner et al. [26] measured lung function and recorded asthma symptom scores in 30 consecutive elderly asthmatics, 15 diagnosed prior to (long-standing), and 15 after the age of 65 years (late-onset). Fifteen young asthmatics, aged under 65 were also included in this analysis. Elderly patients with longstanding asthma had the most severe airway obstruction and importantly, also complained of fewer asthma symptoms.

Asthma is a chronic inflammatory condition that has been shown to be correlated with a slow but progressive loss of lung function over time. Lange et al. [27] presented the results of a longitudinal epidemiological study of 17,506 Danish subjects of which 1,095 had asthma studied over a 15 year period. Asthmatics' rate of lung function/FEV1 decline was 38 mL/year which was significantly greater than the normals at 22 mL/year. These results stress the importance of good asthma control and the impact in the elderly asthmatic population where a prolonged duration of disease is evident.

### Treatment

Pharmacological treatment of asthma in the elderly needs to be administered with care as this population are more likely to experience medication side effects and are also more likely to suffer from drug-drug interactions [28, 29]. Beta-agonist therapy can cause tremor, a dose dependent reduction in serum potassium and tachycardia. Tremor is a common concern in the elderly asthmatic and it is caused by  $\beta_2$  stimulation of skeletal muscle. To minimise systemic absorption though oropharyngeal deposition a spacer device is recommended [28]. Older people particularly attribute side effects to reliever medication and are concerned by these, frequently being unfamiliar with an "as needed" approach to inhaled  $\beta$ -agonist therapy [13].

Theophylline is recommended in patients with uncontrolled asthma despite combination inhaler therapy – Global Initiative for Asthma (GINA - Step 3) [31]. Theophylline must be used carefully in the elderly population and is associated with a number of adverse effects particularly when drug levels are above the therapeutic range. Drug toxicity is most likely in those with established cardiac or liver disease and there are a number of described drug interactions eg. quinolones and allopurinol. Careful monitoring of drug levels is required to reduce the risk of very serious adverse events such as cardiac arrhythmias and seizures. However, side effects including nausea, insomnia and gastro-oesophageal reflux disease are not uncommon.

Inhaled steroids at moderate doses are generally not associated with systemic side effects in the elderly population. However, local side effects are not uncommon and include oral candidiasis and hoarseness of the voice. These effects are dose-dependent and can usually be managed with the addition of a spacer device. The fear of corticosteroid side effects are substantial in this age-group and are emphasised by the increasing frequency of cataracts and osteoporosis which are associated with "steroid" therapy in this

age-group [13, 30].

Systemic corticosteroids can cause or exacerbate significant systemic adverse effects in the elderly population including diabetes, cataracts, hypertension, osteoporosis and vertebral fractures. Systemic maintenance corticosteroids are however indicated for severe, uncontrolled asthma indicated at the higher steps of the GINA treatment recommendations [31].

A qualitative survey of elderly Australian asthmatics observed that 37% of respondents were concerned about medication side-effects. Further, 41% reported side-effects from their preventer medication most commonly including voice changes and a sore dry throat. Fifty-one prevent reported adverse outcomes from their reliever medication, particularly tremor. Such concerns constitute a significant barrier to regular asthma medication use [13, 30].

Beta-2 agonists are recommended as first line reliever therapy in asthma guidelines [31, 32]. Across the entire population  $\beta$ -agonists are superior bronchodilators and have a more rapid onset action than anti-cholinergic medication. However, there is a reduced expression/function of beta receptors in the lung related to ageing. Cholinergic receptors appear to function independently of ageing. As a consequence, there is a reduction in response to  $\beta$ -agonist bronchodilator therapy associated with ageing which has not been seen with anti-cholinergics. Indeed, some elderly patients respond better to anti-cholinergics than to beta agonists [33]. These findings have not translated into specific treatment guidelines.

Elderly patients with severe allergic asthma should also be considered for omalizumab therapy. The GINA guidelines [31] recommend this medication as "Step 4" add-on treatment. A subgroup analysis demonstrated that elderly patients also gain benefit from this medication [34].

Elderly patients are often prescribed a number of medical treatments for medical comorbidities. There is a list of medication that can trigger or exacerbate asthma. For example,  $\beta$ -blockers are prevalent and used for hypertension and ischemic heart disease. There are case reports of timolol, a non-selective beta blocker, used for glaucoma triggering severe and fatal bronchospasm [35]. Non-steroidal anti-inflammatory medications used for osteoarthritic pain, highly prevalent in the elderly population, can also exacerbate asthma.

Lack of access to medical care is a problem in the elderly population. Medical visits may represent a significant financial hardship in the elderly population where in retirement income

is often fixed. Further, physical frailty is also likely to exacerbate the difficulties of visiting medical doctors [13, 36]. Finally, there has been qualitative research reporting that elderly patients are reluctant to seek emergency care because they believe they are not deserving [37]. These factors are likely to contribute to reduced utilisation of medical care.

Elderly patients have a reduced perception of airflow obstruction [11, 12]. There is also a reduced cough reflex [38]. These factors are also likely to contribute to delayed presentation of asthma exacerbations. In order for asthma action plans to be effective in older age-groups they should observe the differences in the elderly population and be tailored to individuals [39].

Population-based studies have consistently demonstrated under-treatment of asthma in the elderly. In a community sample [14], of those with definite asthma, thirty nine percent were on no asthma treatment which included 6/20 patients with severe asthma. Further, only forty percent were using reliever medications and thirty percent inhaled corticosteroids.

### Self management of asthma

Asthma action plans are an important strategy in asthma management. They are important in that they are effective in improving asthma outcomes in the paediatric and adult population when provided in written form [40]. Evidence from a case-control study of people who had died from asthma showed that the presence of an action plan was a major protective factor against death from asthma [40]. Of concern, there is evidence that action plans are less likely to be provided to elderly asthmatics [39]. In a survey of elderly asthmatics 66% participants wanted more information about their asthma. The preferred method was a conversation with a doctor or receipt of written information sheets [30]. A qualitative study of primary care physicians surprisingly revealed that action plans were not a priority in patient asthma management. These observations were partly explained by the perceived barriers in primary care such as the short consultation duration [41]. Asthma education strategies have largely been developed in paediatric and mixed age-groups [42] so that evidence of effectiveness of asthma self-management education in older age-groups is sparse [4, 30]. Whilst some studies of educational strategies for asthma specifically targeted to older people provide evidence of efficacy [43] the evidence is not uniform [44], suggesting that further study in the area of what constitutes an effective educational strategy in older people with asthma is indicated.

### Medication adherence

Medication non-adherence is a problem when managing any medical patient and asthma is no exception. Patients with severe asthma who are non-adherent have poor symptom control, increased reliever medication, and increased emergency department presentations and hospital admissions [45]. Krishnan and colleagues [46] used electronic medication monitoring in asthmatics following discharge from hospital with an asthma exacerbation. Within seven days of discharge there was fifty percent non-adherence to both inhaled and oral corticosteroids [46]. In an important study, Sin et al. [47] identified 6,254 consecutive admissions to hospital with asthma in Ontario Canada in patients aged over 65 years. Those patients identified as users of inhaled steroids post discharge by collecting an additional inhaled corticosteroid medication within 90 days of discharge were 29% less likely to be readmitted to hospital with asthma and 39% less likely to experience 'all cause mortality' over a 1-year follow-up period [47]. This study supports the efficacy of inhaled corticosteroids in older people.

Non-adherence can be unintentional. Community based studies describe suboptimal drug delivery with both metered dose inhalers (MDI) and dry-powder devices in an elderly population [48, 49]. These observations highlight the need to consider the capacity of the elderly population when prescribing asthma medication. Firstly, elderly patients require sufficient cognitive capacity to learn, plan and sequence the correct inhaler technique. Allen et al. [49] observed that the uptake of successful inhaler technique (both MDI and turbohaler) is unlikely to be successful in an elderly population with a reduced Mini-Mental State Examination (MMSE). In those with a MMSE >23 18/19 subjects correctly used an MDI.

Physical capacity also needs to be considered when prescribing asthmatic medications. Dry powder inhalers require sufficient inspiratory flow generated by the patient in order to generate adequate drug delivery. Severe arthritis and dyspraxia affecting the hands can also adversely affect the ability to achieve the coordination required to ensure adequate drug delivery. The addition of spacer devices can improve the performance of MDIs and are routinely recommended. MDI and MDI and spacer technique was taught to 40 naïve elderly (mean age 78) patients with obstructive airways disease. Following the education session 30% of MDI patients had inadequate technique compared to only 8% of the MDI and spacer patients. Further, MDI and spacer was the preferred delivery device of the patients [50]. Importantly, effective device education can improve technique and can be utilised in

the pharmacy [51]. For those symptomatic asthmatic patients with significant cognitive or physical disability nebulised preventer medication is an alternative.

Non-adherence to asthma treatment can also be intentional. The physician must consider the possible risk factors for intentional non adherence so they can be addressed proactively. These factors can broadly be considered as physical, financial, treatment related and psychosocial [52]. Physical and financial barriers to treatment adherence are due to difficulties of access to medication which can indicate the physical incapacity of older age and the restrictions of retirement-incomes in older people. Treatment-related side effects are a major concern to older people with a survey of over-55 year old Australian patients indicating that 37% were worried about treatment side effects while 41% reported experiencing side effects from asthma medication [30].

Bozek et al. [53] identified poor cognition and depression as major risk factors for poor adherence in an elderly asthmatic population. Poor compliance was associated poor asthma control as measured by the Asthma Control Test. Further, one year of close monitoring (electronic diary and drug packages) of these patients had a positive impact on adherence. Moreover in those effectively treated, asthma and cognition were seen to improve [54].

## CONCLUSION

Asthma in the elderly is associated with significant morbidity and mortality and requires careful monitoring. People over age 65 with asthma have fewer symptoms of asthma and are less likely to report and present to medical care. The inhaled therapies required to control asthma are often not taken adequately because of physical or cognitive disability more evident in the elderly population. Elderly patients also intentionally do not take their asthma medications for a broad range of reasons and the physician needs to carefully identify these factors in considering a symptomatic patient. Current controversies in the management of older people relate to the utility of asthma management education in this group, the effectiveness of current treatment algorithms which are dominantly derived from younger age-groups and the cellular phenotype of asthma in the older person. To answer these questions, further specific work in basic disease mechanisms are required as well as work studying the application of current treatment regimens for asthma to the older population, including education to ensure that improved asthma outcomes are achieved.

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