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Asthma in the older adult

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ABSTRACT

Objective: The older adult population is increasing worldwide, and a significant percentage has asthma. This review will discuss the challenges to diagnosis and management of asthma in older adults. **Data Sources:** PubMed was searched for multiple terms in various combinations, including asthma, older adult, elderly, comorbid conditions, asthma diagnosis, asthma treatment, biologics and medication side effects, and adverse events. From the search, the data sources that were utilized included peer reviewed scholarly review articles, peer reviewed scientific research articles, and peer reviewed book chapters. **Study Selections:** Study selections that were utilized included peer reviewed scholarly review articles, peer reviewed scientific research articles, and peer reviewed book chapters. **Results:** Asthma in older adults is frequently underdiagnosed and has higher morbidity and mortality rates compared to their younger counterparts. A detailed history and physical examination as well as judicious testing are essential to establish the asthma diagnosis and exclude alternative ones. Medical comorbidities, such as cardiovascular disease, cognitive impairment, depression, arthritis, gastroesophageal reflux disease (GERD), rhinitis, and sinusitis are common in this population and should also be assessed and treated. Non-pharmacologic management, including asthma education on inhaler technique and self-monitoring, is vital. Pharmacologic management includes standard asthma therapies such as inhaled corticosteroids (ICS), inhaled corticosteroid-long acting β -agonist combinations (ICS-LABA), leukotriene antagonists, long acting muscarinic antagonists (LAMA), and short acting bronchodilators (SABA). Newly approved biologic agents may also be utilized. Older adults are more vulnerable to polypharmacy and medication adverse events, and this should be taken into account when selecting the appropriate asthma treatment. **Conclusions:** The diagnosis and management of asthma in older adults has certain challenges, but if the clinician is aware of them, the morbidity and mortality of this condition can be improved in this growing population.

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Introduction

Asthma is commonly thought of as a disease of children and young adults, yet a significant percentage of the older adult (>65 years old) population in the United States is affected [1]. Data from the 2012 National Health Interview Survey (NHIS) reported a 7.8% prevalence of asthma among people 65 to 74 years old and 6% prevalence in those aged 75 years and older [2]. Over the next 40 years, the older adult population is predicted to double, and with this the prevalence of asthma in older adults will increase significantly. Asthma in older adults is becoming a serious health

issue, as they have the highest hospitalization and mortality rates for asthma, yet it is commonly underdiagnosed and undertreated [1,3]. In addition to an increase in morbidity and mortality, asthma in older adults can be challenging to diagnose due to multiple comorbid conditions and a broad differential diagnosis of other diseases that can produce symptoms similar to asthma. The management of asthma in older adults is often complicated by medication side effects, diminished cognition and co-morbid conditions limiting the use of appropriate treatment. Additional medications, including biologics, have been also been approved for

asthma therapy. This review includes a clinical vignette and up to date didactic review of the existing literature to discuss the importance of this problem and the approach to the diagnosis and treatment of asthma in the growing older adult population.

Methods

Clinical vignette: could this be asthma?

A 70 year-old man was referred to an allergist/immunologist for shortness of breath of 6 years duration and nasal allergy symptoms. He had recently been discharged from a hospital where he was admitted for bronchitis and atypical chest pain. His discharge diagnosis was end-stage COPD and he was prescribed an albuterol nebulizer. Since his discharge, he had been wheezing 3–5 days and nights per week and had difficulty walking half a block. Upon questioning, he admitted to having suffered from asthma when he was “young” and had seasonal nasal and ocular allergies since age 20 that turned perennial about 5 years ago. He lived in a house with 2 cats that were allowed in his bed and had a smoking history of 50 pack years but quit one year earlier. His past medical history was significant for coronary artery disease (history of an acute myocardial infarction and coronary artery bypass grafting in 1998), symptomatic gastroesophageal reflux disease, dyslipidemia, diabetes (type 2), hypertension, osteoarthritis, and benign prostatic hyperplasia. His current medications during the initial evaluation included albuterol by nebulizer and MDI, carvedilol 25 mg, olmesartan 20 mg, clopidogrel 75 mg, metformin 1000 mg, ezetimibe 10 mg, fenofibrate 145 mg, pravastatin 40 mg, and finasteride 5 mg.

On physical exam, the patient was an ill-appearing elderly male, with conjunctival chemosis, swollen nasal mucosa, enlarged turbinates, reduced breath sounds bilaterally, prolonged exhalation and wheeze (inspiratory and expiratory). Office spirometry pre- and post- bronchodilation (nebulized albuterol 2.5 mg and ipratropium bromide 0.5 mg) was performed and his pre-bronchodilator FEV₁% predicted was 39% and FVC% predicted was 52%. Post-bronchodilator spirometry revealed an 11% improvement in FEV₁% predicted and a 21% improvement in FVC % predicted. An allergy evaluation revealed a total IgE of 402 IU/mL and positive specific IgE to dust mites, cat dander, grass pollen, European olive and ragweed. The patient was started on fluticasone/salmeterol 500/50 bid and albuterol MDI 180 mcg with spacer q6 h for 5 days, nasal saline and nasal mometasone 200 mcg daily, ocular ketotifen fumarate 0.025% prn, rabeprazole

20 mg daily and GERD precautions. After 5 days, the patient felt significantly better and FEV₁% predicted increased to 53% predicted. His fluticasone/salmeterol dose was tapered to 250/50 mcg 1 inhalation twice a day and albuterol by MDI with spacer prn. His cardiologist was contacted to discuss changing carvedilol to a beta-selective blocker but the cardiologist deferred the recommendation.

Results

One month later, the patient returned and had no shortness of breath but his FEV₁% predicted was 46%. On examination he had reduced breath sounds but no wheezes or rhonchi. The patient was given ipratropium bromide (42 mcg) by MDI with spacer and his FEV₁% predicted increased to 54% after 30 min. His medication regimen was changed to budesonide/formoterol 320/9 mcg BID through spacer + tiotropium bromide 18 mcg daily. Two months later, the patient indicated he was doing well and had rarely needed to use his rescue medication. Office spirometry showed an improvement in the FEV₁% predicted to 67%. Allergy avoidance measures were reviewed with the patient, but the patient refused to remove the cats from his home or bedroom. Four months later, the patient left the practice as felt that he was stable enough on his medical regimen.

Discussion

Diagnosis of asthma in older adults: clinical history and objective measures

History

To establish a diagnosis of asthma in older adults, it is important to first understand that the general characteristics of asthma still apply and need to be considered. The NAEPP Expert Panel 3 Guidelines (2007) and Global Initiative for Asthma®, outlines three main components for the diagnosis of asthma: (1) patient has episodic symptoms of airflow obstruction or airway hyperresponsiveness is present, (2) airflow obstruction must be at least partially reversible, and (3) alternative diagnoses are excluded [3,4]. Excluding alternative diagnoses is a significant challenge in older adults, as multiple common diseases such as heart disease (including coronary heart disease, heart failure, hypertension), diabetes, Alzheimer’s dementia, COPD, osteoarthritis, amongst others may cause symptoms or impede the process of obtaining information needed to establish an accurate asthma diagnosis [5]. Hence, the guideline recommended method for establishment of diagnosis of a detailed medical history is

considerably more significant in older adults [3,4]. Additional recommended methods for diagnosis of asthma include a physical exam focusing on the upper respiratory tract, chest, skin and spirometry to demonstrate obstruction and assess reversibility and additional studies to exclude alternate diagnoses [3,4]. Reversibility is thought to be demonstrated by an increase in FEV₁% predicted of $\geq 12\%$ and ≥ 200 ml from the baseline value or by an increase of $\geq 10\%$ of predicted FEV₁ after inhalation of a short-acting bronchodilator such as albuterol [3,4]. Compared to children, older adults tend to have diminished response to bronchodilators as a result of airway remodeling and loss of elastic recoil that comes with age [6].

Taking a detailed medical history, including description of symptoms, time of onset, duration, triggers, and ameliorating factors, is essential. History of wheezing, particularly during expiration, is commonly found, but not necessary for diagnosis and is not a reliable indicator of airflow limitation [7]. In addition to recurrent wheeze, history of cough, especially a nighttime cough, recurrent difficulty breathing or dyspnea, and recurrent chest tightness are symptoms often seen in asthma [7]. History of these symptoms must be placed in context with knowledge of the status of the older adult's co-morbid conditions, including past history of childhood or young adult asthma and allergic rhinitis [7]. Older adults are likely to have multiple medical conditions such as coronary artery disease, hypertension, Alzheimer's dementia, COPD, chronic sinusitis, gastroesophageal reflux disease and osteoarthritis [5]. Some of these co-morbid conditions can also cause wheezing. For example, a patient with acute left ventricular heart failure and associated pulmonary edema, may present with cough and wheezing. Understanding the patient's cardiac history, as well as a full examination, evaluating for other signs of heart failure such as lower extremity edema, weight gain and elevated jugular venous pulse would help distinguish the two potential diagnoses. To further complicate the diagnosis, older adults have a decreased perception of bronchoconstriction. Two studies found that older adults had poorer recognition of airway resistance compared to younger adults [8,9]. This reduced perception of dyspnea may be due to a decline in cognition as seen in Alzheimer's dementia, or deconditioning from reduced mobility [7]. Some patients with "known" COPD are misdiagnosed. In a patient with a known diagnosis of COPD, obtaining history of symptoms that are worsened by exercise, pollen, changes in weather, strong emotional expression, mold, house-dust mites, viral infection (all

known triggers of asthma) can portend a potential diagnosis of asthma-COPD overlap (ACO) [10]. When taking a patient's history, an emphasis on the onset of asthma symptoms can be helpful as those with earlier onset are more likely to have an allergic component [7].

Additionally, occupational or home exposures are important to assess for alternative pulmonary conditions or identify triggers of asthma [10]. A detailed physical examination, including the upper airway for evidence of chronic sinusitis and nasal polyps, a common chronic disease in older adults, is essential for ruling out alternative additional diagnoses [7].

In this particular case, the history included many characteristics suggestive of asthma including nocturnal predominant wheezing, childhood history of asthma, clinical history of environmental allergies, and recent history of severe episodes of respiratory decompensation requiring steroid injection. Confounding the diagnosis, includes his significant past medical history of coronary artery disease, type 2 diabetes, as well as his social history of extensive smoking/tobacco exposure. Physical examination findings of allergic rhinoconjunctivitis such as conjunctival chemosis, swollen nasal mucosa, and enlarged turbinates suggest asthma as these two conditions are often co-existing. Prolonged exhalation and expiratory wheezes may also be seen in asthma but are nonspecific [7]. Additional objective measures are needed for further evaluation of this older gentleman.

Objective measures: unique challenges with objective measures of asthma in the older adult

Diagnosis of asthma in older adults follows a comparable algorithm for objective testing as for general population [1,7]. Thus, presence of clinical suspicion of asthma (history suggestive of episodic dyspnea, wheezing, cough or chest tightness) with objective testing either measuring reversibility to airway obstruction or hyper-responsiveness to bronchial provocation is vital to establish asthma [1]. Demonstration of reversibility on spirometry with $\geq 12\%$ or more improvement (and minimum 200 ml) after intervention with a short acting β -agonist or ICS-SABA in older adults or a 20% improvement in PEF from baseline after medication is considered significant reversibility [7]. There are some special considerations however, as they pertain to older adults with asthma. Physiologic changes with age can affect effort and terminal 'scooping' (i.e. end expiratory curvilinearity), which may be a normal finding in older adults [11]. The terminal scooping may incorrectly be

interpreted as evidence of obstruction. Additionally, baseline cardio-respiratory capacity, general debilitation and co-morbidities affecting performance by affecting respiratory mechanics that could lead to poor effort and non-acceptability of that assessment [12]. Technical difficulties in performing a complex task such as spirometry successfully may be affected by cognitive capacity or dexterity [13,14]. A study examining quality of spirometric performance in older adults reported that 18.2% (approximately 1 in 5) patients were unable to perform according to specified criteria [15]. The study concluded that age by itself was not a risk factor for poor performance but both cognitive and functional impairment can play a significant role [15]. Home monitoring or in-office PEF which is more dependent on patient effort may amplify the issues of incorrect assessment of older adults with asthma [16,17]. Thus conventional assessments of obstruction and reversibility may be confounded by variables unique to older adults. In the case of normal spirometry or sub-threshold reversibility, measuring airway hyper-responsiveness is recommended either by direct provocation with methacholine or exercise challenge testing, even in the older adult [7]. Additional considerations arise however with regards to bronchial provocation procedures in older adults especially with respect to contraindications which may preclude its use [18]. Presence of concurrent cardiovascular comorbidity (in particular a recent heart attack or stroke) and inability to perform a satisfactory spirometry (as noted above) may limit the applicability of this clinically useful test in older adults [19]. Furthermore, differences in metabolic rates in the older age group due to altered pharmacokinetics of medications could potentially influence the spirometric observations [12]. Similar issues can be potentially expected with testing such as cardio-respiratory exercise testing as physical conditioning, body habitus, and poor cardiopulmonary reserve may affect the results. At present, measurement of exhaled nitric oxide or sputum analysis are not included in the assessments for definition of asthma, but even if they were included challenges would exist. For example, exhaled nitric oxide levels are positively associated with age even after adjusting for multiple variables potentially confounding the assessment in older adults with asthma [20,21]. Thus, older adults pose unique challenges to assigning a correct diagnosis of asthma. Awareness of these challenges is crucial for proper management as well as monitoring asthma in older adults.

Monitoring asthma in older adults

A key concept in the management of asthma is accurate self-monitoring, thereby identifying inadequate control and facilitating necessary medication adjustments. Options for self-monitoring include the use of a written asthma action plan (AAP), with or without the use of a peak flow meter (PFM). In fact, the current NIH guidelines specifically recommend that all patients with asthma are provided an AAP which includes two aspects: (1) daily management and (2) recognizing and handling worsening asthma [3].

The use of asthma action plans has been evaluated in multiple studies. While the majority of studies (both pediatric and adult) have had positive results [22–25], this is not universally true [26,27]. Among older adults, one observational study found no difference in asthma outcomes for those who had been given an AAP or PFM compared to those who had been given neither (though baseline asthma severity was not controlled in that study) [28]. However another prospective study by Buist et al. found that, when compared to baseline, an AAP (with or without PFM) significantly improved outcomes including asthma quality of life and FEV1 [29]. It therefore appears reasonable to provide older adults with asthma an AAP to assist with self-monitoring. In addition, the AAP should be as simple as possible and printed with large fonts.

The question of whether to use a PFM in addition to the AAP is more controversial. PFMs are recommended for those who have difficulty perceiving symptoms [2], and this is more common among older adults [30,31]. Although a study of older adults with asthma found improvement with an AAP, there was no difference between those who did and did not use a PFM [29]. Importantly, all participants in that study were provided four 90-min educational sessions, which may have influenced the results. This appears to be the only prospective study of PFM use among older adults. Among children and general adult populations, there are multiple studies that show benefit of a PFM [32–34], along with many that show lack of benefit [35,36]. A confounding factor may be that many patients do not use peak flow meters correctly [37]. Older adults may have difficulties with manual dexterity and vision, which could cause additional difficulties when using a PFM. Therefore, the use of a PFM in older adults is best utilized for those who have difficulty perceiving symptoms. If incorporated into self-management, it is extremely important that older adults are taught to use the PFM correctly. Furthermore, there is no significant relationship

between PEFR and FEV1, and thus, PEFR monitoring without FEV1 can lead to delayed recognition of worsening asthma.

Management of asthma in older adults

Pharmacologic treatment

According to the NAEPP Expert Panel 3 Guidelines (2007) and the Global Initiative for Asthma®, our patient with a history of dyspnea, inspiratory/expiratory wheezing and significant reversibility following bronchodilator categorizes him as having a diagnoses of severe persistent asthma and places him under step 5 therapy: initiation of high dose inhaled corticosteroids, long acting beta agonist or leukotriene antagonist and if needed oral corticosteroids and/or the initiation of omalizumab [3,4]. There had been a black box warning for combination inhaled corticosteroid and long acting beta agonist products in asthma for 14 years, however, in December 2017, this was removed by the FDA due to multiple safety trials [38].

This stepwise guideline approach for asthma care should be used as a guide with focus on the specific asthma phenotype when determining the most effective asthma medications for the particular patient. Our patient's phenotype involves underlying Asthma with COPD overlap or ACO in a patient over 70 years of age. Although initiation of inhaled corticosteroids in patients over 50 diagnosed with asthma leads to diminished emergency room visits [39] and appears to be superior to leukotriene antagonists based on a retrospective review of prospective studies comparing the 2 agents [40], further investigations pertaining to the use of inhaled corticosteroids in patients diagnosed with ACO over the age of 70 are needed.

Prospective and retrospective studies support the addition of long acting beta agonists to inhaled corticosteroids in patients over 65, which showed increase in time to first exacerbation, diminish in rescue SABA, nighttime awakenings [41] and less hospitalizations and death [42]. In patients over 70 diagnosed with ACO a small study revealed the initiation of inhaled corticosteroid/LABA combination led to an improvement in FEV1 [43]. Since our patient has COPD features he may respond to long acting muscarinic antagonist (LAMA) [44]. LAMA offers additional benefit by diminishing bronchoconstriction seen in patient's taking beta blockers from unopposed increase in cholinergic transmission [45] and acting as an anti-inflammatory agent by reductions in IL-6, IL-8, LTB4 levels [46]. In September of 2015, the FDA approved use of tiotropium as add on therapy for

asthma. The addition of LAMA to inhaled steroids is superior to doubling of inhaled corticosteroids and non-inferior to the use of a LABA and inhaled steroids in both objective and subjective measures [47–49]. One could assume that this medication would be ideal for older patients with a diagnosis of ACO though current studies are mixed on whether older or younger patients diagnosed with asthma receive the most benefit. Although younger patients with better bronchodilator response from SABA respond best to LAMA addition, other factors indicating benefit include having a higher cholinergic tone as indicated by slower heart rates and a lower FEV1/FVC ratio as seen in our patient [50]. Studies investigating the addition of LAMA to ICS/LABA combination show the most significant improvement in FEV1 and peak flows occurred in subjects with lower FEV1 and history of tobacco use [51,52], possibly resulting from an anti-inflammatory effect since use of LAMA has been associated with diminished FeNO levels [53]. Although there was a reduction in severe exacerbations requiring systemic steroid use with the addition of LAMA to ICS/LABA, these studies failed to show significant benefit in subjective measures including AQLQ scores and electronic asthma diary. Future randomized prospective studies focusing on patients over 70 with ACOS are needed to accurately assess the benefit of LAMA to ICS/LABA in our patient. Review of inhaler technique should also be added as part of the monitoring.

The newest agents for asthma are biologic therapies. In many trials, patients over 65 are often excluded, however, some studies have looked at the efficacy of omalizumab, a recombinant humanized monoclonal anti-IgE antibody, in older adults [54,55]. One study evaluated omalizumab over a four month period in 174 asthma patients 50 years or older, and compared them with 297 patients younger than 50 years [54]. FEV1 improved in 60% of patients 50 years and older and improved in 69% of the younger age group [54]. There was a reduction in asthma symptoms in both groups [54]. Adverse event rate was similar in both groups [54]. Another study evaluated omalizumab in 19 patients who were over 65 years old [55]. This study also demonstrated lower rates of exacerbations and hospitalizations and no significant adverse events [55]. More recent biologic therapies approved for asthma include mepolizumab, reslizumab, benralizumab, and dupilumab. Additional studies are needed to evaluate their efficacy specifically in older populations.

Non-pharmacologic treatments

Education

Asthma education is a critical element of successful asthma management – so much so that the NIH asthma guidelines lists ‘Education for a partnership in asthma care’ as one of the four essential components in asthma management [3]. These guidelines note that strong evidence supports self-management education in the clinic as well as home setting, and should address items such as recognition of asthma symptoms, trigger identification, steps to take during an attack, and use of an asthma management plan. Unfortunately for older adults, those with late onset asthma are far less likely to receive education compared to younger populations or even to older adults with early onset asthma [56,57].

There have been a number of trials that demonstrate asthma education programs specifically tailored to older adults can improve outcomes. Baptist et al. performed a randomized controlled trial of a 6-session group and telephone self-management educational program, and found significant improvement in asthma control and quality of life compared to the control group [58]. Other authors have similarly found tailored education for older adults can improve adherence to asthma controller medications, exacerbation rates, inhaler device technique, self-care behaviors, and asthma action plan use [59–61]. Overall, the evidence suggests that educational programs for older adults with asthma are an effective therapeutic modality. Education may also involve family members as well as colleagues and friends of the patient.

Breathing exercises/pulmonary rehab

Older adults with asthma frequently use complementary and alternative techniques to manage their asthma, though they rarely discuss these with their physician [62]. Among the most commonly used techniques are breathing exercises. While a formal pulmonary rehabilitation program is frequently recommended in COPD, there have been a few small trials evaluating pulmonary rehabilitation among older adults with asthma [63–65]. Overall, these trials have been positive for outcomes such as quality of life and occasionally respiratory function parameters, though effects on endpoints such as hospitalizations and ED visits have not been adequately investigated. Other trials investigating breathing exercise techniques (i.e. yoga breathing, breathing retraining, etc.) have also shown improvements in multiple outcomes and may be considered as an ancillary therapy, though these

studies were not conducted in an exclusive geriatric population [66,67].

Special treatment considerations.. According to the World Health Organization, the major chronic conditions affecting people aged 65 years and older include cardiovascular diseases, hypertension, stroke, diabetes, cancer, chronic obstructive pulmonary disease, and musculoskeletal conditions [68].

Gastroesophageal reflux disease (GERD) is also a common associated condition. The prevalence of GERD in asthma patients is approximately between 42 and 69% [69]. Older adults may not experience typical reflux symptoms of heartburn and may present with anorexia, weight loss, anemia, or dysphagia [70]. Thus, older adults with GERD may benefit from a more comprehensive gastroesophageal evaluation [70]. Once the diagnosis is made, behavioral and lifestyle changes can be initiated [71]. Patients on medical therapies, including antacids, Histamine 2 receptor (H-2) antagonists, and proton pump inhibitors, should be monitored closely due to potential side effects [70].

As reported by the National Institute on Aging, arthritis affects 45% of men and 56% of women over the age of 65 years in the USA [72]. Arthritis and the medications for its treatment can interfere with the management of asthma [5,73–76]. Furthermore, researchers in Taiwan recently suggested that rheumatoid arthritis and ankylosing spondylitis may increase the prevalence of asthma [77,78]. Arthritis affects manual dexterity, leading to difficulty in the handling of inhalers, particularly metered dose inhalers (MDI) [5,79]. Arthritis can also affect the performance of activities of daily living [5,72,73]. Various gadgets have been developed to ease the use of MDI [5,79]. Dry inhalers are recommended, although these require higher inspiratory flow rates which may be difficult for older adults to generate [5]. Inhaler technique acquisition and retention also require proper cognitive function [80]. The high prevalence of poor eye sight, hearing difficulties, depression and cognition may compound the difficulty not only with inhalers but with the overall management of asthma and its comorbidities [5,72,74]. Older adults with asthma may require hospitalization for their asthma more often than their younger counterparts. Hospitalizations can cause a lingering cognitive decline. Hand-held and conventional nebulizers should be considered if a patient cannot handle any inhaler after repeated instruction and training. Arthritis medications may also affect the management of asthma [74,75].

Prednisone may worsen depression and cognitive defects [74]. NSAIDs including aspirin can lead to worsening asthma, although the prevalence asthma-exacerbated respiratory disease in older adults is not well established.

Minimizing treatment risks and side effects in older adults

Medications play a crucial role in the treatment of adults with asthma [81]. While the medications used to treat asthma have side effects, these adverse effects may be augmented in older adults due in part to age-related changes in pharmacodynamics and pharmacokinetics and the concurrent use of multiple medications known as polypharmacy [82]. A review of several studies found that polypharmacy is considered to be the most important factor associated with adverse drug reactions [82]. Over a third of men and women between 75 and 85 years of age take at least five prescription medications and nearly 50% of older adults take one or more medications that are not medically necessary [83,84]. In order to minimize treatment risks and the side effects of asthma medications in older adults it is important to reconcile patient medications (prescribed and over the counter) at each visit. Further, patients should be strongly encouraged to notify all their health care providers when starting a new medication (prescription or over the counter) so the side effects and treatment risk can be assessed. Special considerations of the adverse effects of commonly used asthma medications in older adults are discussed below.

Bronchodilators are first line treatment for acute symptomatic control of asthma. Stimulation of β -2 adrenergic receptors leads to an increase in sympathetic system activity, reduction in adenyl cyclase responses and increased inhibitory G protein expression. This cascade of events leads to smooth muscle relaxation and bronchial dilatation. Side effects of short-acting β -agonists (SABAs) include tachycardia, tremor, a dose dependent decrease in serum potassium levels and dose dependent prolongation of the QT interval on EKG [85]. Due to different age related physiologic response to β -adrenergic receptor stimulation, these side effects may be more pronounced in older adults [5,85,86].

Anticholinergics may be an effective alternative to long-acting β -agonists (LABAs) in the older adult population. The adverse effects of anticholinergic medications, include dry mouth, urinary hesitancy, constipation, and increased ocular pressure. These effects may be more pronounced in older adults as

they may have underlying co-morbid conditions (glaucoma, benign prostatic hypertrophy) or take medications (ferrous sulfate, anti-hypertensives) that have similar side effects, such as constipation and dry mouth. Caution should be used in patients with glaucoma and to limit deposition in the eye, a spacer should be used with the MDI and a mouthpiece, not a facemask, should be used when administering the nebulized form [87,88].

Theophylline should be used cautiously, or even avoided, in older adults due to its narrow therapeutic range and toxic events. Older adults have several risk factors that may increase the plasma theophylline level, such as reduced clearance, various underlying diseases and multiple co-administered drugs [89]. After theophylline treatment has been initiated, therapeutic drug monitoring is required so theophylline toxicity does not occur. Theophylline toxicity can cause seizures, atrial fibrillation, supraventricular tachycardia, ventricular ectopy, and ventricular tachycardia [89].

The use of systemic corticosteroids can have deleterious effects in the older adult population with an increased risk of bone fractures, cataracts, muscle weakness, back pain, bruising, and oral candidiasis [90]. Additionally, they can provoke confusion, agitation, and changes in glucose metabolism [90]. Inhaled corticosteroids may be a better alternative for use in older adults but it may cause local adverse effects such as hoarseness, dysphonia, cough, and oral candidiasis, which can be reduced with the use of a spacer [90].

As asthma and allergies often co-exist even in older adults, caution to the side effects of common allergy medications should also be discussed with patients with both conditions. First generation antihistamines such as chlorpheniramine, diphenhydramine and hydroxyzine can cause confusion, blurred vision, constipation, urinary retention and dry mouth. These adverse effects may affect older adults greater due to their underlying medical conditions. As many of these antihistamines are available over the counter, it is essential to obtain an accurate list of all medications a patient is taking (Table 1).

Effects of medications used for other chronic diseases on asthma

As the mortality rates in older adults have declined and the population is living longer, older adults are more likely to have at least 2 co-morbid conditions (multimorbidity). Studies using administrative claims data and prevalence studies in community samples

Table 1. Medication considerations in older adults.

Pharmacotherapy	Side effect in older adults	Alternative therapy
Non-cardioselective β -blocker Topical β -blocker (ophthalmic solution) Bronchodilator: short-acting β -agonists	• Bronchospasm • Fatal asthma attack • Tachycardia, tremor, a dose dependent decrease in serum potassium levels • Dose dependent prolongation of the QT interval on EKG	Selective β blocker
Aspirin and NSAIDs Angiotensin Converting Enzyme inhibitor Anticholinergics	• Avoid use in patients with Aspirin sensitivity • Increased dry cough • Increased dry mouth, urinary hesitancy, constipation, and increased ocular pressure. • Avoid use in patients with Glaucoma	Acetaminophen Angiotensin Receptor Blocker Use a spacer with MDI and a mouthpiece (when used with nebulized form)
Theophylline	• Increased toxicity: seizures, atrial fibrillation, supraventricular tachycardia, ventricular ectopy, and ventricular tachycardia	
Systemic corticosteroids	• Increased risk of bone fractures, cataracts, muscle weakness, back pain, bruising, and oral candidiasis. • Provokes confusion, agitation and glucose metabolism changes	Inhaled corticosteroid
Inhaled corticosteroids	• Local adverse effects: hoarseness, dysphonia, cough, oral candidiasis	Use a spacer

have shown rates of multimorbidity to be greater than 60% in those aged 65–74 and over 80% in those aged ≥ 85 years [71]. With these high rates of multimorbidity in older adults, one must consider the effect medications used to treat co-morbid conditions have on asthma.

β -blockers are commonly used in the treatment of hypertension and congestive heart failure. The nonselective β -blockers (i.e. propranolol, nadolol and esmolol) may provoke bronchospasm, though the use of cardioselective β -blockers has a much lower incidence of bronchospasm [87]. Ophthalmologic solutions containing nonselective β -blockers (i.e. timolol) used to treat glaucoma should be avoided as their use have caused asthma exacerbations [87]. Aspirin and NSAIDs are often used by older adults for their cardioprotective and anti-inflammatory effects in the treatment of arthritis and degenerative joint disease. In patients with aspirin exacerbated respiratory disease (AERD), this can cause acute bronchospasm, nasal congestion, rhinorrhea and a rash. While AERD typically develops between ages of 20–50, patients with asthma that have never used aspirin or NSAIDs may not realize they have this type of asthma (AERD). Angiotensin converting enzyme (ACE) inhibitors used to treat hypertension and congestive heart failure may lead to dry cough further worsening symptoms of asthma.

Conclusion

This clinical vignette of a 70-year-old patient with ACO and significant comorbidities is all too commonly seen in practice. Clinicians caring for these patients need to remember to obtain a detailed clinical

history and physical examination, pulmonary function testing as they are paramount in establishing the diagnosis, especially in older adults. Unique challenges regarding the diagnosis of asthma in older adults include a poorer perception of dyspnea and technical issues in performing complex objective testing. The expanding pharmacologic treatment options for asthma are similar to younger adults. However, older patients are often at more risk for adverse effects and pharmacologic interactions. Difficulty with inhalers and cognitive impairment may interfere with management. Additional individual patient education may be necessary. Systematic assessment and thorough management of medical comorbidities are crucial. In summary, diagnosis and management of asthma in older adults has certain challenges, but if the clinician is aware of them, the morbidity and mortality of this condition can be improved in this aging population.

Disclosure statement

This manuscript was unfunded. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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