

Hypertension and obstructive airways disease in the elderly

Achieving target blood pressure levels while maintaining good control of respiratory disease requires careful treatment choices but, given the range of agents available, can almost always be achieved.



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Systemic hypertension and obstructive airways disease – usually chronic obstructive pulmonary disease (COPD) or asthma – are very common in the elderly, and frequently coexist. Tobacco smoking is known to increase the impact of hypertension as a risk factor for cardiovascular disease, and airflow obstruction itself is an independent risk factor for future cardiovascular events.¹

Treating a patient with both hypertension and respiratory disease can be complex because a number of antihypertensive medications can affect the airways. Achieving target blood pressure levels while maintaining good control of respiratory disease requires careful choice of treatment. This article focuses on potential effects of treatments for

hypertension on airflow obstruction, and the possible effects of treatments for airflow obstruction on blood pressure. COPD is briefly described in the box on page 40.²⁻⁵

Lung changes with ageing

Even in the healthy elderly population, lung function declines with age. Airway size becomes smaller, mainly as a result of alterations in the supporting connective tissue. The diameter of the alveolar ducts increases and the alveolar surface declines, changes that are thought to be due to alterations in the relative proportions of elastin and collagen that affect lung compliance and airway support. Chest wall compliance may decrease, due

IN SUMMARY

- Think of obstructive airways disease in elderly patients when commencing treatment for hypertension.
- COPD should be sought in patients with other smoking related diseases.
- Smoking cessation and treatment of modifiable risk factors, including obstructive sleep apnoea, are vital for managing COPD and hypertension and for reducing cardiovascular risk.
- Thiazide diuretics, calcium channel blockers and angiotensin II receptor antagonists appear to be relatively safe in patients with airflow obstruction.
- ACE inhibitor side effects of cough and bronchospasm do not appear to be more frequent in patients with airflow obstruction, but may be more troublesome if they occur.
- Beta blockers are generally contraindicated in patients who have reversible airflow obstruction.
- Beta blockers are best avoided in patients with COPD, but cardioselective beta blockers may be considered for cautious use in mild or moderate COPD if there is a compelling indication.

to a combination of kyphosis and arthritis, and respiratory muscle strength declines. These changes result in a progressive decline in forced expiratory flow in one second (FEV₁) and vital capacity with age that is independent of tobacco smoke or environmental exposures. The effects mimic those observed in emphysema (Figure 2), and can put an elderly patient in a compromised respiratory position, even without the added burden of asthma or COPD.

Lifestyle modification

Many of the lifestyle changes that improve quality of life and breathlessness in patients with airways disease are also effective in lowering blood pressure and reducing cardiovascular risk. Smoking cessation is essential. Good nutrition and weight management should be strongly encouraged – overweight and obesity are associated with an increased risk of hypertension, and excess weight is also associated with increased breathlessness in patients with airflow obstruction. Exercise training, in the form of either a formal pulmonary rehabilitation program or a home or community based program, is a vital component of managing patients with COPD and can also improve blood pressure control.

Pharmacotherapy for hypertension

Initial therapy for systemic hypertension will depend on the individual patient's characteristics, including the presence of other cardiovascular risk factors (such as tobacco smoking) and associated medical conditions (such as diabetes mellitus). The aims of treatment are to restore blood pressure to a prespecified target blood pressure level and reduce overall cardiovascular risk; the target will depend on an individual's combination of cardiovascular risks. Thiazide diuretics, calcium channel blockers, angiotensin II receptor antagonists and possibly angiotensin converting enzyme (ACE) inhibitors may be suitable first line therapy (see Table).⁶

Thiazide diuretics

Thiazide diuretics remain first line therapy for the majority of patients with uncomplicated systemic hypertension;⁶ no direct studies of the use of these agents have been performed in hypertensive patients with COPD or asthma. There is a theoretical risk that thiazides – as potassium losing drugs



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– may indirectly worsen carbon dioxide retention in hypercapnic COPD.⁷ This is very rarely a clinical issue in patients with stable COPD, but it is sometimes observed in hospital patients with unstable COPD using high dose diuretics. Hence, caution is recommended when prescribing diuretics to treat patients with unstable, hypercapnic COPD.

Corticosteroids and beta agonists may also increase potassium loss, so regular monitoring of electrolyte levels or use of a potassium sparing diuretic should be considered in patients taking any of these treatments, and particularly if they are taking a combination of treatments. Results from one study have suggested that thiazides interfere with mucus production,⁸ but this does not seem to be a clinical problem. There are also potential benefits of diuretics in patients with lung disease, as peripheral oedema due to right heart failure, malnutrition or other causes is common in this group.

ACE inhibitors

Many ACE inhibitors are available, and these are particularly useful for treating patients with systolic, and probably diastolic, cardiac dysfunction and heart failure.⁶ ACE inhibitors have been shown to reduce cardiovascular risk in patients with multiple risk factors, especially hypertension

continued

and diabetes. The benefits and side effects of treatment are likely to be class effects, and it is advisable to monitor electrolytes.

Cough is the most common side effect, being reported by 10 to 20% of patients.⁹ Bronchoconstriction has been reported

but appears to be much less frequent. Cough and bronchoconstriction are both probably due to suppression of kininase II: angiotensin converting enzyme catalyses the conversion of angiotensin I to angiotensin II but also inhibits kininase II, which may lead to an increase in bradykinin

and substance P in the lung. Bradykinin induces cough and bronchoconstriction in susceptible patients by stimulating sensory C-fibres and phospholipase A2. Substance P is a neurotransmitter for C-fibres and can induce bronchoconstriction.¹⁰

ACE inhibitors are safe in the large

COPD: an underdiagnosed disease of the elderly

COPD is mainly a disease of the elderly, with a prevalence that increases steeply with age. It is the third leading cause of the total burden of disease and injury in the Australian population, outranked only by ischaemic heart disease and stroke.²

Tobacco smoking remains the most important cause of COPD: about half of all smokers develop some airflow obstruction, and between 15 and 20% have clinically significant disease (Figure 1).³ Other causes include:

- exposure to occupational dust and fumes, including organic dust
- outdoor and indoor air pollution (including environmental tobacco smoke)
- bronchial hyperresponsiveness
- α_1 -antitrypsin deficiency
- recurrent respiratory infections in childhood.

Even in patients with severe disease, COPD is significantly underdiagnosed. Symptoms often develop gradually, and shortness of breath may be attributed to normal ageing or deconditioning or erroneously attributed to coexisting heart failure. COPD should be suspected in all smokers, particularly those with other smoking related diseases.

Clinical examination has poor sensitivity for detecting mild to moderate COPD and for assessing its severity; spirometry remains the most useful method of diagnosing, assessing and monitoring

patients with the disease. Severity can be rated according to the COPDX plan as mild, moderate or severe.³ Patients who are most likely to run into trouble with drugs that worsen airways disease are those with moderate or severe disease.

There is overlap between COPD and asthma. Many patients with COPD have some reversibility of airflow obstruction with bronchodilators; conversely, some nonsmokers with chronic asthma develop irreversible airflow obstruction. Both new-onset asthma and persistent asthma are more common in the elderly than is often appreciated, and rates of hospitalisation for asthma are highest in people who are 65 years of age and older.⁴

Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is common, conservatively estimated to affect 4% of middle aged men. OSA may coexist with COPD, and may complicate management of COPD.⁵ Recognition and treatment are important for reducing overall cardiovascular risk, improving overnight oxygen levels (which may be already compromised by airways disease) and potentially improving blood pressure control. Risk factors for obstructive sleep apnoea overlap those for hypertension (e.g. increasing age, tobacco smoking and obesity); obstructive sleep apnoea is also an independent risk factor for hypertension.

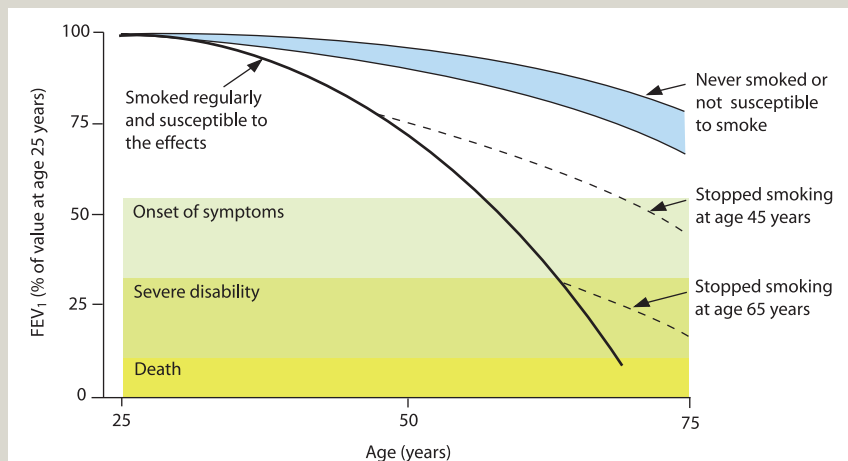


Figure 1. Time course of COPD. The decline in FEV₁ for a hypothetical susceptible smoker and the effect of stopping smoking early or late in the course of COPD is shown, along with the decline for a hypothetical nonsmoker and nonsusceptible smoker.

FROM REFERENCE 3 (AND ADAPTED FROM FLETCHER C, PETO R. THE NATURAL HISTORY OF CHRONIC AIRFLOW OBSTRUCTION. *BMJ* 1977; 1: 1645-1648).

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Figure 2. High resolution chest CT scan of a 70-year-old woman with emphysema. Extensive emphysematous changes with bullae are visible in both lungs.

majority of patients with obstructive airways disease. Only a limited number of studies of cough and bronchial reactivity in patients with COPD or asthma have been performed, and most have not shown an increase in cough or bronchospasm induced by ACE inhibitors in patients with underlying airways disease, compared with those without underlying airways disease.¹⁰ However, patients have usually been continued on their maintenance bronchodilator treatment in these studies.

Table. Antihypertensives for patients with obstructive airways disease⁷

Optimal

None established

Possible

- Thiazide diuretics
- Calcium channel blockers
- Angiotensin II receptor antagonists

Contraindicated or to be used with caution

- Beta blockers
- Beta blockers with alpha blocking activity
- ACE inhibitors (monitor for side effects of cough or bronchoconstriction)

Asthma and bronchospasm are rare as side effects of treatment with ACE inhibitors, but need to be recognised if they occur because the effects are likely to be more disabling in patients with underlying airways disease. Replacing the ACE inhibitor with another should not be tried because patients who experience cough or bronchospasm when using one agent in this class generally have the same problem with others. The cough will usually settle within a month after drug withdrawal.¹⁰

Angiotensin II receptor antagonists

Angiotensin II receptor antagonists probably have similar effects to ACE inhibitors in heart failure or renal disease, or after myocardial infarction. However, angiotensin II receptor antagonists do not inhibit kininase II and thus do not lead to accumulation of bradykinin and substance P. Cough is an uncommon side effect, and most studies suggest that its incidence is similar in patients receiving treatment or a placebo. There are, however, case reports of bronchoconstriction with angiotensin II receptor antagonists,¹¹ which is possibly related to inhibition of endogenous nitric oxide release in the airways. Clinical experience with use of these drugs in patients with use of airways disease is limited, and they may not be entirely free of the side effects of ACE inhibitors.⁷ Overall, angiotensin II receptor antagonists are a reasonable choice in patients with airways disease who, because of cough or bronchospasm, are intolerant of ACE inhibitors.

Calcium channel blockers

Long acting calcium channel blockers are useful for treating hypertension, particularly in elderly patients with angina or isolated systolic hypertension.⁶ There have been no studies on their use in hypertensive patients with airways disease. Calcium channel blockers may modestly decrease bronchial reactivity,¹⁰ and thus may have beneficial but probably neutral airway effects in patients with airways disease.

Beta blockers

Beta blockers are very useful in patients with both hypertension and coronary heart disease and are increasingly used in treating heart failure. In patients with airways disease, however, this is the class of antihypertensive agents most likely to cause side effects. Beta blockers increase airway resistance and generally should not be used in patients with asthma or other reversible airways disease – the severity of the bronchoconstrictor response is unpredictable, and occurs mainly in this group.⁷ There is usually little to no effect in healthy people, but severe bronchoconstriction can be seen even in those with mild asthma with beta blocker use.

Most of the airway side effects that are caused by beta blockers are related to interference with beta-2 mediated bronchodilatation. Beta-2 receptors are the main adrenoreceptors on airway smooth muscle; beta-1 receptors account for 10 to 30% of receptors on submucosal glands and alveolar walls. The cardioselective beta-1 blockers (atenolol, metoprolol, bisoprolol [Bicor]) have less effect than nonselective drugs (e.g. propranolol) on lung function, although their cardioselectivity may be lost at higher doses. The cardioselectivity is also relative, and airflow obstruction can certainly worsen at therapeutic doses of a cardioselective drug. Decline in lung function with non-cardioselective drugs can be seen in mild and moderate COPD, as well as in severe COPD.¹²

Nonselective beta blockers with intrinsic sympathomimetic activity (pindolol, oxprenolol) may cause less bronchoconstriction than beta blockers without this activity. However, they remain contraindicated in asthmatic patients, and in those with airflow obstruction.⁷

If a patient with severe hypertension and COPD is unable to tolerate other classes of antihypertensive medications, a cardioselective beta blocker could be trialled while maintaining optimal bronchodilator treatment.¹⁰ However, the

potential benefits must be weighed against the potential risks. For treatment of hypertension alone, in general it is likely that other suitable agents can be found. The benefit–risk ratio will also need to be considered in a patient with additional indications for beta blockade, such as heart failure or angina, and mild underlying airways disease. Spirometry is recommended at baseline for assessing the severity of the airways disease and degree of reversibility, and over time to monitor for any decline. Referral to a respiratory physician for review of airways disease should be considered if significant airways disease is present and/or to a cardiologist for review of treatment if a beta blocker is needed.

Carvedilol (Dilatrend, Kredex), a non-selective beta blocker that has alpha blocking activity, is generally used in the treatment of heart failure, not of hypertension alone. It appears to be well tolerated in patients with COPD, but asthma is a contraindication. Combined alpha and beta blockers should be used with great caution in patients with any airways disease because the alpha blockade may fail to prevent bronchoconstriction caused by the beta blockade.⁷

Combination and alternative therapies

Patients who have severe hypertension or hypertension that is not controlled by a single agent may require combination therapy.⁶ The recommendations for use of single medications in patients with coexisting airways disease also apply to their use in combinations.

Some patients are either resistant to or intolerant of the usual initial therapies. In such individuals, alternatives include prazosin, which is an alpha blocker, and also methyl dopa (Aldomet, Hydopa) or clonidine (Catapres), which are centrally acting antiadrenergic agents. There is little information on their effects in airways disease, but clonidine may variably increase airway responsiveness in patients with

asthma.⁷ Given the lack of guidelines for using these drugs in this situation, use in patients with airways disease should be cautious.

The direct acting vasodilator hydralazine (Alphapress) is not reported to cause airway side effects, but studies are lacking. It is often used in combination with a beta blocker, and its use in patients with airways disease is likely to be limited for that reason.

Pharmacotherapy for asthma or COPD

Inhaled treatments

Bronchodilator treatments do not usually worsen hypertension, but cardiovascular side effects can occur with some medications. The inhaled short acting beta-2 agonists salbutamol (Airomir, Asmol, Epaq, Ventolin) and terbutaline (Bricanyl) remain recommended for relief of intermittent wheeze and dyspnoea in asthma and COPD. Palpitations and, less commonly, tachycardia are known side effects, particularly in the elderly. Short acting anticholinergics (ipratropium bromide) are also useful in COPD.³ There is no evidence of worsening of hypertension with either of these medication groups.

The inhaled long acting beta-2 agonists, salmeterol (Serevent) and eformoterol (Foradile, Oxis Turbuhaler), are useful in asthma control in combination with an inhaled corticosteroid. Combined preparations are commercially available of salmeterol and fluticasone (Seretide) and of eformoterol and budesonide (Symbicort Turbuhaler). Long acting beta-2 agonists are not listed on the PBS for treating COPD, although they have been shown to have benefits.³ Palpitations and tachycardia are seen, particularly in the elderly, and can be troublesome. Aggravation of hypertension, however, does not appear to be a problem.

Tiotropium bromide (Spiriva), a long acting anticholinergic, is a useful maintenance treatment for patients with COPD. Cardiovascular side effects, including

hypertension, do not appear to be a clinical problem.

Theophylline (Nuelin) is rarely used these days for COPD or asthma because of its narrow therapeutic index and significant side effects.³ Some COPD patients with disabling breathlessness may find it helpful, but it is not advised in patients with severe hypertension. Cardiac arrhythmias are a known side effect – this is of particular concern in patients with COPD, who often have other risk factors for coronary artery disease.

In patients with COPD who have a documented response or severe COPD with frequent exacerbations, it is possible to use an inhaled corticosteroid, beclomethasone (Qvar), budesonide (Pulmicort) or fluticasone (Flixotide).³ The role of these agents in managing patients with persistent asthma is well established. Inhaled corticosteroids are not currently listed on the PBS for use in COPD, but may have benefits in these situations. Some systemic absorption occurs, with potential for easy bruising, cataract formation and osteoporosis, but worsening of hypertension is not seen to be a clinical problem. Results from a recent study suggest that a very low dosage of inhaled corticosteroid (50 to 200 µg/day) may reduce the risk of myocardial infarction.¹³

Systemic treatments

Use of short term high dose oral corticosteroids for exacerbations of asthma or COPD is often associated with retention of fluid and development or worsening of pre-existing hypertension. Blood pressure should be monitored in patients on this treatment. The effect is dose related, improves as the dose is reduced and is not associated with long term blood pressure change. Some patients may require adjustment of antihypertensive medication, but generally observation is all that is needed. Long term oral corticosteroids are rarely required in asthma or COPD; if used, the dose should be reduced to the minimum possible.

continued

Conclusion

Obstructive airways disease should always be considered in an elderly patient before antihypertensive treatment is commenced, especially if there is a history of smoking or suggestive clinical features. Spirometry is a valuable tool for diagnosing and monitoring airflow obstruction. Aggressive control of risk factors is important for cardiovascular risk reduction, as well as improving disease control and symptoms in both hypertension and COPD. The presence of airflow obstruction may modify pharmacotherapy for hypertension but, given the range of drugs available, good control of blood pressure without worsening of airways disease can almost always be achieved. **MT**

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