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Asthma and COPD: differences and similarities

With special reference to the usefulness of budesonide/formoterol in a single inhaler (Symbicort®) in both diseases

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SUMMARY

Asthma and chronic obstructive pulmonary disease (COPD) both have a high prevalence worldwide and yet each condition remains underdiagnosed. Despite a number of common features, these inflammatory respiratory syndromes have distinct clinical outcomes. COPD represents a greater economic burden than asthma because it has a less favourable prognosis and is associated with greater morbidity and mortality. Therefore, it is important to distinguish between these two diseases at an early stage, so that appropriate therapy can be prescribed to prevent deterioration. However, effective treatments that may be used in both conditions can minimise the effects of misdiagnosis and maximise the impact of treatment without the associated complexity when both conditions occur together. The current review summarises the differences and similarities of asthma and COPD, in terms of risk factors, pathophysiology, symptoms and diagnosis, to provide greater understanding of the role of budesonide/formoterol in a single inhaler in both diseases.

Keywords: Asthma; COPD; budesonide; formoterol; comparison

PREVALENCE AND ECONOMIC BURDEN OF ASTHMA COMPARED WITH COPD

Despite clear guidelines for asthma (1–3) and chronic obstructive pulmonary disease (COPD) (4,5), both conditions remain underdiagnosed (6–10). With a high global prevalence (11), asthma and COPD place a considerable burden on patients, society and healthcare systems alike.

Prevalence and Mortality Rates

Recent surveys suggest that 5.1 million people in the UK (approximately 9% of the UK population) are currently being treated for asthma (12,13) and that in the USA 10.5 million people (approximately 4% of the US population) experienced an asthma attack during 1999 (14,15). COPD has a similar prevalence to asthma in the USA, with around 10 million Americans (approximately 4%) reporting physician-diagnosed COPD in 2000 (15,16), although this figure may be underestimated (16). UK figures for 1997 reveal that COPD affected 1.36% of the female population and 1.65% of the male population, thus showing an increasing trend (from 0.80 and 1.36%, respectively, in 1990) (17). On the basis of the current trends, it is estimated that COPD will rank fifth in the world in order of disease burden by 2020 (18).

According to a report commissioned jointly by the World Health Organization and the World Bank, COPD is one of the few major public health problems where the mortality rate continues to escalate (Figure 1) (19). An increase in some of the major risk factors for COPD has led to the prediction that it will become the third major cause of death by the end of the next decade, falling only behind ischaemic heart disease and cardiovascular disease (CVD) (19). Surprisingly, respiratory disease (including respiratory cancer) accounts for greater mortality in the UK (24% of total deaths) than either coronary heart disease (21%) or non-respiratory cancer (19%) (20). Asthma is responsible for just 1% of these respiratory disease deaths, whereas as many as 20% are due to COPD (20). It is striking that in the USA, more than half of all deaths from respiratory disease are caused by COPD (21).

Economic Impact

The widespread morbidity caused by respiratory disease translates into substantial treatment costs. Medication accounts for the largest expenditure in the treatment of asthma (22), but in COPD, which is more of an economic burden than asthma, the major cost factor is hospitalisation as a result of exacerbations (23). The relative costs of asthma and COPD in both the UK and USA (Figure 2) demonstrate that COPD is associated with a greater economic burden than asthma, even though asthma is more widespread.

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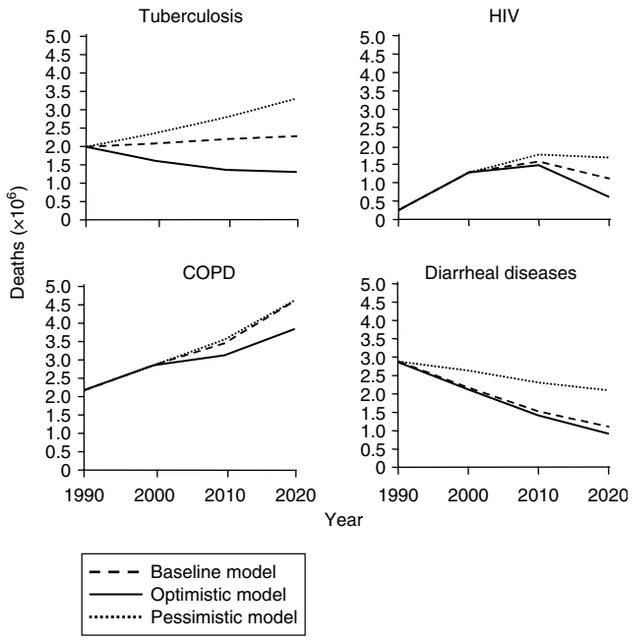

Figure 1 Projected increase in mortality from 1990 to 2020 for tuberculosis, human immunodeficiency virus (HIV), chronic obstructive pulmonary disease (COPD) and diarrheal diseases in baseline, optimistic and pessimistic scenarios (reprinted with kind permission from Elsevier) (19)

With better methods for diagnosing COPD – in particular to distinguish it from asthma – and identifying and reducing risk factors, appropriate management at an early stage may help to lower the healthcare burden. The advantage of treatments such as budesonide/formoterol in a single inhaler is their capacity for use in both conditions. This minimises the effect of misdiagnosis and maximises the impact of treatment without the associated complexity when both conditions occur together. This review summarises the differences and similarities of asthma and COPD, in terms of risk factors, pathophysiology, symptoms and diagnosis, to provide a greater understanding of the role of budesonide/formoterol in a single inhaler in both diseases.

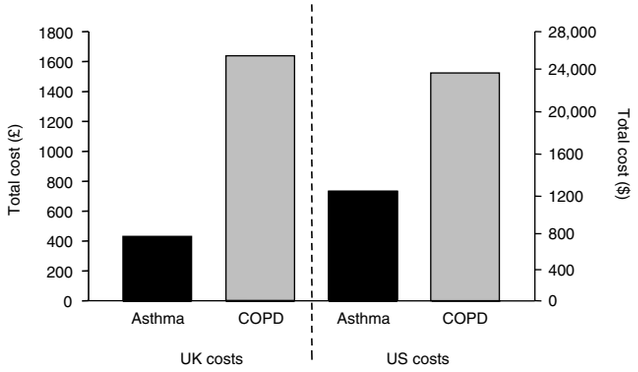

Figure 2 Total costs per patient of asthma and chronic obstructive pulmonary disease in the UK and USA (12,22,24,25)

RISK FACTORS

Asthma and COPD can be distinguished in terms of the major risk factors associated with each condition, although some putative risk factors are common to both diseases (Table 1).

In atopic individuals, the primary risk factor for asthma is exposure to allergens; consequently, many patients with asthma display high serum levels of immunoglobulin E (26,27). In addition to cigarette smoking, risk factors for non-atopic asthma include increasing age, lower social class and urban dwelling (28).

Cigarette Smoking

Cigarette smoking is the major aetiological cause of COPD, but while cessation of smoking is the only intervention known to slow the progression of this disease, there are no reports that this can reverse pulmonary damage. One report showed that cigarette smoking results in an 80–90% risk of developing COPD (29); 50% of elderly smokers are currently suffering from COPD according to the GOLD (5) and British Thoracic Society/Scottish Intercollegiate Guidelines Network (4,30). The traditionally low incidence of smoking in the female population could explain the bias against diagnosing COPD in this group (31). However, the rate of smoking in women has risen over the last 10 years (32) and correlates with the increase in age-adjusted death related to COPD in this group. In contrast, age-adjusted death due to COPD remains higher, yet constant, in the male population (21).

Genetic Factors

Epidemiological evidence indicates a strong association between α_1-antitrypsin deficiency and the development of emphysema and COPD (33–35). Although α_1-antitrypsin deficiency accounts for only 1–2% of emphysema cases, individuals with this deficiency have a high risk of developing emphysema, particularly if they are smokers (36). Other genetic influences on COPD include genetic polymorphisms in the promoter region of the proinflammatory mediator, tumour necrosis factor alpha (37) and a polymorphic variant of the gene encoding epoxide hydrolase (38).

As in COPD, allergic asthma may also be inherited, although the lack of a precise phenotypic profile for this disease presents a significant obstacle to genetic analysis studies. Nonetheless, several candidate genes for asthma have been identified and a detailed overview can be found in the report by Heinzmann and Deichmann (39).

A factor that is likely to become more important in the treatment of asthma and COPD is the influence of glucocorticoid receptor genotypes on sensitivity to corticosteroids. One of the four main receptor haplotypes, a variation without intron B, was recently shown to be associated with enhanced sensitivity to glucocorticoid therapy (40), whereas other variations have been associated with resistance to corticosteroid therapy (41).

Table 1 Risk factors for asthma and chronic obstructive pulmonary disease (11)

	Asthma		*COPD*	
Degree of certainty	*Environmental factors*	*Host factors*	*Environmental factors*	*Host factors*
Established	Allergen exposure Occupational sensitisers	Atopy Gender	Cigarette smoking Some occupational exposures	α_1-antitrypsin deficiency
Good	Respiratory infections Drugs and food additives	Low birth weight	Air pollution (SO_2 and particles) Poverty, low socioeconomic status Alcohol Environmental tobacco smoke in childhood	Low birth weight Bronchial hyperresponsiveness Family history
Putative	Smoking		Other occupational exposures	Genetic predisposition
	Air pollution Diet		Adenovirus infection Dietary deficiency of vitamin C	Blood group A IgA nonsecretor

COPD, chronic obstructive pulmonary disease; SO_2, sulphur dioxide; IgA, immunoglobulin A.

Gender

The influence of gender on asthma changes with age; childhood asthma is more common in boys, while females are diagnosed with asthma more frequently in the adult population (42,43). COPD is more common in males than females (21,44), which may be related to differences in smoking intensity, however, after adjusting for this variable, women appear to develop more severe airflow obstruction than men (45,46). Several environmental factors also contribute to the onset of both asthma and COPD.

Allergens and Other Factors

Asthma can be induced by animal proteins, plant proteins and both organic and inorganic chemicals; a detailed list of asthma sensitisers is updated regularly on the French website Association Asthme & Allergies (http://asmanet.com) (47). Asthma may also be related to the westernised lifestyle where the high hygiene standards have reduced exposure to allergens, such that natural desensitisation is impeded (48).

Exposure to occupational hazards, such as dust (e.g. in gold and coal mining) (49), gas (e.g. in cadmium mining) (50) and wood smoke (51) may precipitate symptoms of COPD and aggravate respiratory problems in patients with asthma.

Low birth weight, which may itself be the result of environmental factors, can predispose an individual to asthma (52) or COPD (53), because the normal decline in lung function that occurs with increasing age starts from a lower peak value. Childhood experiences, including recurrent viral or bacterial respiratory infection (54–56), exposure to cigarette smoke and a lack of certain dietary elements, e.g. n-3 polyunsaturated fatty acids (57), also appear to increase the chances of developing chronic airway inflammation later in life. This interaction of both host and environmental factors can lead to either reversible or long-term changes in airway pathology.

UNDERLYING PATHOPHYSIOLOGY OF ASTHMA AND COPD

Pathophysiological changes – either anatomical (airway remodelling) or cellular (inflammation) – are associated with respiratory disease in asthma and COPD. Improved understanding of these changes (Table 2) has increased our knowledge of the effects of various treatments at the pathophysiological level. For a more detailed overview of the pathology of these diseases see Jeffery (58–59) and Saetta and Turato (60).

In brief, asthma entails airflow obstruction predominantly caused by bronchoconstriction and reticular basement membrane enlargement, which correlate well with both the frequency of asthma attacks (61) and airway hyperresponsiveness (62). Inflammation is also important and associated with high numbers of eosinophils and $CD4^+$ lymphocytes (63).

COPD also exhibits airway narrowing with reactive oxygen species-induced cellular damage (64,65). The presence of goblet cells (mucous metaplasia) in the peripheral airways (66) and mucus hypersecretion (67) have also been documented. Although it has been found that neutrophils and macrophages are predominant in COPD inflammation (59,68,69), there have been several reports of eosinophilia in both stable COPD (69,70) and during acute exacerbations (71), which suggests a potential role for inhaled corticosteroid treatment in COPD. Recent pathology work shows that increasing inflammation exists with increasing COPD severity (72). In the end stages of the disease, very active inflammation is present, which could suggest that COPD remains amenable to treatment even in these stages.

Although asthma and COPD exhibit many differences, they share several common features, and therapies targeting such aspects can be of benefit in both conditions. Such treatment at the pathophysiological level will lead to amelioration of the various symptoms of asthma and COPD.

Table 2 Airway remodelling and inflammatory cell changes in asthma and chronic obstructive pulmonary disease (58,59)

Feature	*Asthma*	*Chronic obstructive pulmonary disease*
Airway remodelling		
Epithelium	Fragile	Metaplastic
Reticular basement membrane	Thickened	Not thickened
Fibrosis	Unlikely	Present
Vessels	Angiogenesis	Likely angiogenesis
Bronchial smooth muscle	Increased in large airway	Increased in small airway
Glands	Hypertrophy	Hypertrophy
Emphysema	No	Yes
Inflammatory cells		
$CD4/CD8^+$ ratio	3 : 1	1 : 2
Neutrophils*	-1.5	2.2
Eosinophils*	93	3.5
Macrophages*	0	8.6

*Values given as fold change in the number of cells vs. healthy control subjects.

SYMPTOMS, OVERLAP, DIAGNOSIS AND DISEASE OUTCOMES OF ASTHMA AND COPD

Despite differences in the underlying pathophysiologies of COPD and asthma, several distinctive symptoms are shared between the two diseases, which means that differential diagnosis is more difficult. Furthermore, in special patient populations such as the elderly, diagnosis can be especially problematic, and there are incidences where asthma and COPD may exist together. Therefore, treatments that can minimise the effects of misdiagnosis and maximise treatment benefits when the two conditions occur together are particularly important, as the disease outcomes of asthma and COPD are very different.

Symptoms

Asthma patients present with bronchoconstriction, which causes wheeze, shortness of breath, chest tightness and cough. The essentially reversible, underlying pulmonary inflammation in this disease is associated with recurrent, but intermittent, exacerbations (11) that can be controlled with appropriate medication (2). Exacerbations in asthma can, however, be difficult to pinpoint and patients need to treat worsening symptoms to avoid them.

COPD patients also experience severe cough, often with sputum production, associated with excess mucus (67) and airway inflammation (73), both attributed to chronic bronchitis. Along with fixed airway obstruction and emphysema, these factors have all been shown to contribute to airway limitation, exhibited as shortness of breath (74,75). Repeated and increasingly frequent exacerbations in COPD are associated with increased inflammation (76) and may require the use of antibiotics (77) or steroids (5). These exacerbations can lead to acute respiratory failure (5) and are associated with long recovery times (6 days to 5 weeks) (78). As exacerbations have such a huge impact on patients' lives, treatments that prevent or reduce the frequency of exacerbations are increasingly important. Pulmonary damage in COPD is progressive and essentially non-reversible, although smoking cessation generally leads to improvements in airflow, specifically forced expiratory volume in 1 s (FEV_1) (79). However, patients' lung function may deteriorate several years after they have stopped smoking.

Despite these distinctive symptoms, asthma and COPD remain underdiagnosed (6,8–10,30,80). As both conditions have several major symptoms in common, these alone are not sufficient to make a differential diagnosis. Although variability in symptoms or a history of wheezing is more indicative of asthma, and chronic sputum production is more suggestive of COPD, coexistent conditions such as respiratory infection can further complicate diagnosis (81,82).

Diagnosis

Patient history is frequently used for the differential diagnosis of asthma and COPD in primary care. Family history or a seasonal variability of symptoms are good indicators of asthma (2), while COPD is the more likely diagnosis if, in addition to these symptoms, the patient is aged at least 45 years (30) and has a history of smoking. Ideally, the diagnosis based on patient history will be confirmed by spirometry and whether lung-function abnormalities are reversible in response to bronchodilator and inhaled corticosteroid therapy, as recommended by international guidelines (2,5). The introduction of community-based spirometric screening – either of smokers or of the whole population – has been proposed to identify individuals at risk of developing COPD (83), although the benefits and cost-effectiveness of this approach have yet to be determined.

In primary care, several problems may be encountered when attempting to distinguish between asthma and COPD. Although asthma may be confused with viral respiratory tract infections in infancy, the presence of symptoms in the elderly is more likely to be interpreted as COPD (84), fibrosing lung disease or cardiac left ventricular failure. Further confusion is seen between COPD and occupational asthma, with a misdiagnosis leading to inappropriate therapy and the

persistence of symptoms. Miravitlles and colleagues (85) concluded that, although primary care screening is possible, fewer cases of COPD were diagnosed correctly in this setting than in cases where patients were referred to a specialist.

In COPD, a postbronchodilator $FEV_1 < 80\%$ predicted, coupled with an FEV_1/forced vital capacity ratio $< 70\%$, confirms the presence of airflow limitation that is not fully reversible, which is a hallmark of this disease (5). In contrast, good bronchodilator reversibility leads to a more likely diagnosis of asthma (5). However, even a significant reversibility does not exclude COPD (5). Further tests that allow an accurate distinction to be made between the two conditions include an assessment of hyperinflation (via either intrathoracic gas volume measured by plethysmography or functional residual capacity determination) and lung diffusion capacity (DL_{CO} single-breath technique). Hyperinflation is a more consistent phenomenon in COPD than in asthma; while a reduction in DL_{CO} is found more frequently in COPD patients than in the healthy population (11). However, a more practical approach to distinguishing between asthma and COPD is to use spirometry, because compared with the specialised equipment required to measure the above parameters, spirometers are smaller, less expensive and more appropriate for the assessment of disease severity in a primary care setting.

Asthma and COPD are both divided into four categories of severity, according to symptoms and lung-function tests (2,5); treatment strategy is selected on the basis of this classification. Despite the recommendations of published guidelines (2,5), spirometry seems to be underused by primary healthcare practitioners for the diagnosis of airway disease (6), mainly because of budget constraints. Spirometric assessment should, however, be encouraged and if used more, it is thought that many more cases of asthma and COPD would be diagnosed correctly, leading to appropriate medication being prescribed earlier with more satisfactory outcomes for both conditions.

Disease Overlap

The significant overlap in symptoms and some risk factors between asthma and COPD increases the likelihood of misdiagnosis. Indeed, among patients previously diagnosed with asthma by their general practitioner, re-evaluation by an allergy specialist showed that 59% had asthma, 7% had both asthma and COPD and 34% had no asthmatic disease (8). Misdiagnosis and underrecognition of respiratory disease is particularly common in elderly individuals. A study of patients aged 65 years or older and meeting strict criteria for asthma revealed that one in five asthmatic patients had received an improper diagnosis of COPD and a quarter of asthmatic patients did not receive any diagnosis of respiratory disease (82). Potential barriers to proper diagnosis in this elderly population included respiratory symptoms being considered a normal part of ageing, disability, a lack of functional assessment being performed, and atypical clinical features (82). Asthma is often considered to be a disease of childhood or young adulthood, despite the fact that disease progression and/or relapse in patients who had experienced remission can occur later in life and that first onset of asthma may occur in late adulthood (1).

While there is clearly some overlap between asthma and COPD, there are also circumstances when the two conditions can occur together (11). For example, individuals with asthma who smoke or are exposed to other noxious agents that cause COPD may develop COPD-type pathology in addition to preexisting asthma-related inflammation (5). Therefore, among asthma patients in whom response to usual treatment has deteriorated, the development of COPD should be considered. The high incidence of concurrent respiratory disease was highlighted in a recent survey of over 2900 individuals in the USA, where 7% were diagnosed with asthma, 11% had COPD and a further 4% met criteria for both conditions (86). Table 3 provides an overview of clinical clues to aid the differential diagnosis of asthma and COPD.

Table 3 Clinical clues for a differential diagnosis of asthma and chronic obstructive pulmonary disease

Clinical consideration	*Asthma*	*COPD*	*Potential overlap*
Risk factors	Family history of asthma	Current or past smoking	Asthmatics who smoke run risk of developing coexistent COPD
	Allergy		
Patient age	Younger age	Older age	Asthma is underrecognised in the elderly and often misdiagnosed as COPD in these patients
Symptoms	Wheeze	Cough with sputum production	Comorbid conditions such as respiratory infections can cause atypical symptom presentation
	Variability of symptoms		
Spirometry	Reversible	Non-reversible	Some loss of reversibility may be seen over time in asthma

COPD, chronic obstructive pulmonary disease.

Disease Outcomes and Patient Treatment Challenges

Pulmonary damage caused by asthma is essentially reversible, either spontaneously or in response to clinical intervention (11,74), though lung function continues to decline more rapidly in patients with asthma than in those without (87). Indeed, lung function tests for peak expiratory flow and FEV_1 can be used to assess the risk of mortality (88). Since the risk of COPD increases with age and since there is no documented evidence that current treatments can reverse the decline in lung function associated with this disease, it is associated with a higher mortality rate than asthma (89). In addition to higher mortality rates, comorbidity is also more significant in patients with COPD than in those with asthma.

Allergic rhinitis and other respiratory conditions prevail in asthma patients (90), but COPD patients are susceptible to more debilitating complications. One study involving 591 subjects found that locomotive diseases, insomnia, sinusitis and migraine were common in patients with COPD compared with matched controls (91). Other studies have observed that extrapulmonary effects, such as hormonal abnormalities (92), and skeletal and muscle dysfunction are prevalent in COPD, particularly during the latter stages of the disease (93,94). It is therefore essential that treatments used in COPD have a favourable safety profile, given that most patients are older and more vulnerable to the effects of taking multiple medications.

One important consideration is the effect of corticosteroids, which are frequently used in the treatment of both conditions, on both muscle strength and bone mass. Osteoporosis is a common complication in COPD, particularly in female patients and smokers, and may be aggravated by the use of corticosteroids in the treatment of airway inflammation (95). Although oral corticosteroids can be associated with an increased fracture risk (96) and myopathy (97,98), they are usually restricted to short-term use in favour of inhaled corticosteroids, such as budesonide, which localise the drug directly to the lung. Several studies have indicated that inhaled corticosteroids do not affect inspiratory muscle function (99), or increase either the risk of osteoporosis (100) or the number of bone fractures (ISOLDE study) (101,102), and do not have a clinically significant effect on bone mineral density (103).

Along with osteoporosis, CVD is highly prevalent (19) and is one of the three major causes of death in COPD patients (104). One of the possible risk factors for developing CVD is the use of β_2-agonists (105), which are now indicated in the current treatment guidelines for both COPD (5) and asthma (2). However, β-blockers are one of the principal medications used in CVD and when used in conjunction with β_2-agonists, this can result in partial adverse interactions (105). Indeed, β-blockers are contraindicated in asthma patients as they can induce fatal or life-threatening asthma (106).

A further complication that is commonly associated with chronic illness, such as COPD, is depression, particularly if patients are receiving long-term oxygen therapy (107). This comorbid condition can have a detrimental effect on health-related quality of life (HRQL). One study involving 109 patients (mean age 71 years) with severe COPD found that 57% demonstrated significant depressive symptoms (107). Depression and anxiety may also be linked to exacerbations, with recurrent exacerbations being more likely to occur in COPD patients who report signs of anxiety and/or depression ($p < 0.05$ vs. normal patients) (108). Many patients experience extensive respiratory symptoms and comorbid conditions, resulting in substantial polypharmacy, which may have a major impact on the everyday lives of patients and their families. Given these factors, and the inevitably poor prognosis of COPD, it is not surprising that this condition causes significant depression in many patients. Therefore, clinically meaningful reductions in symptoms and comorbid syndromes are of high priority in such chronic diseases. As such, treatments that can minimise the effects of misdiagnosis and maximise treatment benefits without the associated complexity when the two conditions occur together are important tools in the management of asthma and COPD.

MANAGEMENT OF ASTHMA AND COPD

Asthma treatment guidelines (1–3) aim to ensure that control is gained and maintained using a stepwise approach, tailoring treatment both to the severity of the asthma and to the individual day-to-day needs of the patient, employing the lowest effective medication dose. Current COPD guidelines (5) also advocate a stepwise approach to treatment based on disease severity, with more focus towards preventing disease progression. Effective management strategies in both diseases should therefore reduce symptoms and exacerbations and improve patient HRQL.

In moderate-to-severe COPD, the preferred treatment is a bronchodilator, with the introduction of inhaled corticosteroids in the event of exacerbations or worsening disease in steroid-responsive patients (5). Several controlled clinical studies have demonstrated the efficacy of short-acting β_2-agonists, anticholinergics and long-acting β_2-agonists for bronchodilation in COPD patients (109–114). Although the prescription of bronchodilators for COPD is accepted, the role of inhaled corticosteroids is less well established despite increasing evidence of their efficacy and their recommendation in current treatment guidelines (5). Results from numerous clinical studies have demonstrated clinical benefits for using inhaled corticosteroids in COPD, including symptom relief (115–118), improved lung function (101,115,117,119,120), a reduction in the frequency and severity of exacerbations in severe disease (101,117,118,121) and improved health status (101). Furthermore, it has been shown that inhaled corticosteroids reduce the number of COPD-related mortalities (122). Current guidelines state

that inhaled corticosteroids are only suitable for use in patients with documented spirometric steroid responsiveness or those with $FEV_1 < 50\%$ predicted (5). However, as discussed earlier, the emerging evidence of eosinophilia in COPD and the clinical benefits of inhaled corticosteroids, in some COPD patients, suggest that these agents may warrant further investigation.

There has been some debate regarding whether inhaled corticosteroids can slow the disease progression in patients with COPD (123). Although several large studies have failed to show a significant difference in the rate of FEV_1 decline between treatment with inhaled corticosteroids and placebo (101,102,116,124), a meta-analysis of these studies showed that inhaled corticosteroids do slow the FEV_1 decline significantly (125). Commenting on these contradictory outcomes, Burge and Lewis (123) suggested that while FEV_1 decline is a valid endpoint, it can also be difficult to analyse. The marked reduction in morbidity and mortality seen among patients with COPD receiving inhaled corticosteroids (122,126,127) lends further support to a role for these drugs in altering disease progression, as does the significant reduction in exacerbation rate highlighted by another systematic review of studies (128).

Inhaled corticosteroids form the basis for regular maintenance treatment in asthma (2) and have been shown to reduce symptom severity and exacerbation risk (129,130). As disease severity intensifies, the dose of inhaled corticosteroid may be increased. However, results from several long-term, controlled studies have shown that a more clinically beneficial option is to add a long-acting inhaled β_2-agonist (130–137). A particular advantage of the long-acting β_2-agonist formoterol is that it has an onset of bronchodilator effect as rapid as that with salbutamol, coupled with a duration of action as long as that with salmeterol (138). Therefore, the pharmacological properties of formoterol provide a unique combination of the early onset of a reliever medication and the convenience of a long-lasting medication. Current guidelines for asthma management recommend that once symptom control has been achieved, asthma maintenance therapy should be reduced gradually to the lowest effective dose required to maintain control (2), thus minimising side effects and costs. Patients who could manage their own disease by increasing or decreasing medication in response to worsening or improving symptoms would need fewer visits to the physician. An analysis of studies demonstrating the success of a self-guided management approach highlights the benefits of including a written plan, as well as the regular supervision and revision of medication regimens (2,139,140). A recent Swedish study investigated asthma treatment through patient-controlled adjustable maintenance dosing with budesonide and formoterol in a single inhaler (141). This, and a similar study in Canada, demonstrated that patients were able to use the plan to control their asthma effectively at a lower overall drug load (141,142). In another study in asthma, adjustable maintenance dosing with budesonide and formoterol in a single inhaler reduced exacerbations and use of reliever medication compared with fixed dosing with salmeterol and fluticasone in a single inhaler (143).

In contrast to the adjustable-dosing approach for treating asthma, medication is not usually reduced once COPD symptoms are controlled, since lung function decline is irreversible with current therapeutic options, and it is important to maintain HRQL. Withdrawal of maintenance treatments, such as inhaled corticosteroids, has been shown to increase the risk of exacerbations and is associated with significant deterioration in HRQL (118,144).

The regular use of controller medication is often neglected by both COPD and asthma patients (145,146). Several reasons for non-adherence to medication schedules have been proposed, including increasing complexity of the treatment regimen (147,148), lack of immediate relief from symptoms with inhaled corticosteroids compared with bronchodilator therapy (9,149) and apparent improvement of symptoms (150). Adherence to therapy is important in the management of any disease, particularly in asthma, to gain maximum treatment efficacy (151). Therefore, it is important to design a simple, but effective, treatment programme to maximise adherence in patients with asthma and COPD.

A positive solution to the problem of poor adherence in asthma and COPD is by using therapies containing both an inhaled corticosteroid and a long-acting β_2-agonist in a single inhaler (117,120,152–154). The bronchodilator and anti-inflammatory agents have different mechanisms of action, which may give greater relief from airway obstruction with no more side effects than would be expected for the classes of monocomponents. Indeed, inhaled corticosteroids and long-acting β_2-agonists are well tolerated and highly efficacious when used together for the treatment of asthma or COPD, improving lung function, reducing symptoms and preventing exacerbations (120,155–157).

In asthma, the use of budesonide/formoterol in a single inhaler may be particularly beneficial as the dose–response curves of these two drugs (133,158) may allow patients to control their disease simply by increasing or decreasing the number of inhalations. Moreover, the safety of treatments that contain both an inhaled corticosteroid and a long-acting β_2-agonist has been demonstrated in several long-term studies (117,118,120,152). Improved efficacy of combination therapies over individual delivery of the monocomponents has also been shown (159), and a sustained synergistic effect between these two classes of drug has recently been reported (160). The benefits of more effective treatment include reduced dose and drug load and better disease control. Furthermore, combining these agents in a single inhaler is also cost-effective (161,162). A treatment regimen that addresses all of these concerns will therefore facilitate the successful management of both respiratory diseases.

Other pharmacological agents used in both asthma and COPD include anticholinergics, theophylline and oral

corticosteroids. Although the addition of leukotriene inhibitors to inhaled corticosteroids may improve asthma control (163), current guidelines state that further studies and clinical experience are needed with these agents (2). Oxygen therapy is the first-line treatment for patients hospitalised with severe, acute exacerbations of asthma or COPD (2,5). All COPD patients with $FEV_1 < 40\%$ predicted, or clinical signs suggestive of right ventricular failure or respiratory failure, should be considered for measurement of arterial blood-gas tensions followed by oxygen therapy, where appropriate (5). The administration of oxygen for more than 15 h per day has been shown to increase the survival of patients suffering from severe COPD and to improve HRQL (164). In this way, appropriate management strategies with effective treatments have been shown to reduce the exacerbations and symptoms associated with both asthma and COPD, thereby improving patients' HRQL.

HEALTH-RELATED QUALITY OF LIFE

Improving HRQL is an important objective in the management of any disease and is usually achieved by effective suppression of debilitating symptoms. Achieving this is dependent upon the ability to identify disease severity accurately (165), so that treatment can be tailored closely to each patient's requirements.

Symptomatic COPD and asthma can impact considerably on patients' everyday lives. In COPD, the ability to perform even basic activities, such as walking up stairs, taking a bath or getting dressed, can be affected (166). The control of exercise-induced asthma in children is particularly important, as the inability to take part in sporting activities has a large impact on both their physical fitness and HRQL (167). It should, however, be noted that patients with COPD have constant symptoms that can vary in severity, whereas patients with asthma experience periods of worsening, but are often symptom free with appropriate medication. In both diseases, symptom worsening not only leads to reduced HRQL but also accounts for many days away from places of employment or school.

Along with symptom deterioration (168,169), exacerbations are another major factor in reducing HRQL in both COPD and asthma (146,170,171). Emotional stability can be affected by acute exacerbations and, as discussed earlier, patients suffering from chronic lung diseases commonly experience feelings of depression or anxiety, even if pulmonary-function parameters appear to be stable. Ferrer and colleagues (172) reported that even patients with mild COPD reported dramatically impaired HRQL compared with the general population. This demonstrates the importance of monitoring HRQL to provide patients with the best possible care.

Monitoring HRQL in response to treatment provides useful information for directing management strategies (173). In a recent study, patients were provided with HRQL questionnaires immediately before consultation with a physician. On the basis of their responses, practitioners were able to incorporate appropriate counselling or patient education into the consultation that may not otherwise have been deemed necessary based purely on the outcomes of pulmonary-function tests (174). Several HRQL questionnaires have highlighted the detrimental effects of acute exacerbations of asthma or COPD on patients' HRQL. Quality of life scores from recent, long-term controlled clinical studies, using the Asthma Quality of Life Questionnaire (AQLQ) (175), the self-administered Short-form 36 survey (176) or the St George's Respiratory Questionnaire (SGRQ) (177), correlated strongly with scores for symptoms (including shortness of breath and wheeze), but not lung function (168,171). Direct measurement of HRQL, rather than inference from the results of lung-function tests, is therefore more likely to facilitate the detection of morbidity (178,179).

Disease-specific instruments, such as the SGRQ (177), the AQLQ (175) and the Chronic Respiratory Disease Questionnaire (180), have been used successfully to monitor improvements in clinical parameters that correlate well with improvements in HRQL following therapeutic intervention (181–183). Several studies have used these questionnaires to elucidate the effects of both inhaled corticosteroids (184) and single-inhaler therapies (budesonide and formoterol in a single inhaler) (120,153) on the HRQL of patients with either asthma or COPD. These studies demonstrated that inhaled corticosteroids, used either alone or in conjunction with a long-acting β_2-agonist, can significantly improve the HRQL of patients with asthma and COPD.

By using measurements of HRQL alongside lung function testing and symptom detection, a comprehensive picture of the effects of inhaled corticosteroids and long-acting β_2-agonists in asthma and COPD can be obtained. The positive outcomes with such treatments serve to emphasise the importance of their role in the management of both conditions.

CONCLUSIONS

COPD and asthma have an increasing global prevalence and place a significant burden on patients, carers and healthcare systems. The aims of COPD and asthma management are therefore to ease this burden and improve patient HRQL through the reduction of symptoms and exacerbations. Differential diagnosis is particularly important in the management of these diseases, because even though they share many symptoms they have very different clinical outcomes. There are also numerous risk factors associated with each disease, such as smoking or exposure to allergens, which should be reduced to minimise their effects on disease progression. Furthermore, the possibility that both conditions may exist together should not be overlooked, especially given the high

prevalence of each disease and the association of both diseases with smoking.

Our increased understanding of the underlying pathophysiologies of asthma and COPD has facilitated the development of several effective controller medications. Therapies such as budesonide/formoterol in a single inhaler and combined fluticasone/salmeterol have been shown to be particularly effective at improving patients' lung function and reducing symptoms and exacerbations in both asthma and COPD. This results in clinically relevant improvements in HRQL that are clearly detectable by the patient. In addition, budesonide/formoterol is the only single-inhaler therapy suitable for patient-controlled adjustable-dosing regimens in asthma.

In conclusion, COPD and asthma are distinct diseases with particular pathologies, risk factors and outcomes, both of which, depending on the choice of drug, could be effectively treated with the same medications.

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