

ASSESSMENT AND MANAGEMENT OF ASTHMA AND CHRONIC OBSTRUCTIVE PULMONORY DISEASE (COPD) – CONVERGING APPROACHES

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ABSTRACT

This review compares the methods of assessment and treatment objectives used for asthma and COPD. There is now a significant amount of convergence between the two diseases in these areas. It is now well recognised that both are inflammatory diseases. Anti-inflammatory therapy with inhaled corticosteroids (ICS) forms the basis of asthma therapy (and are underused in many countries, including Pakistan), but there also is now very good evidence that ICS reduce bronchial inflammation in COPD, especially when used in combination with long-acting beta₂-agonists.

Guidelines recommend that asthma assessment in routine practice, is based upon an evaluation of the level of asthma control; COPD assessment is moving towards something very similar, but it is termed health status measurement. Simple standardised methods designed for use in routine practice are now available for both purposes.

Treatment in both conditions also now has two objectives:

- 1. To reduce symptoms to achieve control (in asthma) and improved health status (in COPD);*
- 2. Preventative therapy to reduce the risk of exacerbations.*

In asthma, exacerbations are associated with a risk of hospital admissions and death and in COPD the same risks apply, but now with good evidence that exacerbations also speed disease progression.

The treatments that are available for asthma can, if used properly, achieve high levels of control. Whilst new drugs are welcome, good application of existing drugs would very greatly reduce the burden of this disease on patients and healthcare systems. New treatments are steadily becoming available for COPD and there is now much that can be done to reduce the burden of this disease. Both diseases are eminently treatable.

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IMPACT OF ASTHMA

The impact of asthma remains great. Data from the Asthma Insights and Reality in Pakistan (AIRIP) study conducted in 2005 show that the level of asthma control is very poor. Over 20

percent of adults and over 30 percent of children reported 2 or more severe episodes per year and over 50% reported sleep disturbance more than twice a week. Data from elsewhere in Asia, but not including Pakistan showed that nearly 70% of asthmatics utilized urgent health care and 30% were hospitalized once in a year. In that survey, only 25% of patients were using inhaled corticosteroids (ICS). Data from AIRIP suggest that only 5% of asthmatics in Pakistan use ICS. This is a remarkable observation, since ICS are an extremely effective treatment for asthma. This observation should be compared with data from Finland. That country had a national plan to manage asthma, based upon the use of ICS. Over a twenty-year period there was a striking drop in asthma admissions and asthma deaths that was largely attributable to effective and consistent use of ICS.

ASTHMA TREATMENT ASSESSMENT

International guidelines for asthma, such as those from GINA (<http://www.ginasthma.org/>),

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emphasise the importance of achieving control of the disease. Various criteria have been set for the level of control, but these are essentially clinical. As the GINA guidelines point out, when patients are controlled they can:

- Avoid troublesome symptoms night and day
- Use little or no reliever medication
- Have productive, physically active lives
- Have (near) normal lung function
- Avoid serious attacks

This is a very important list of objectives since it emphasizes the fact that asthma management should be directed towards almost complete suppression of the disease and normalization of a patient's life. It is noteworthy that whilst lung function is included in the list, it is only one of five objectives, the rest of which are purely clinical and assessed through the patient's report of their symptoms and the effect that asthma has on their lives, not by physiological measurement.

The concept of control has importance in the everyday life of asthmatic patients, but recent studies have shown that is of greater significance than that. Current asthma control is a predictor of the level of future control, but perhaps more importantly, the level of current control was a predictor of the frequency of severe exacerbations weeks and months later.

Whilst the guidelines emphasize control, the definitions are not very user-friendly, but GINA recommends a number of very simple measures of asthma control that can be used in the clinic routinely. There is a very good correlation between two of them - the Asthma Control Questionnaire (ACQ) which, in its original version included peak flow (PF) measurement, and the Asthma Control test (ACT) which does not require PF measurement. The ACT requires just two minutes to complete and can be done by the patient in the waiting room. [Note: a recent study compared four shortened versions of the ACQ that don't require PF measurements and found them all to be reliable].

The ACT has now been subjected to a number of validation studies, a cutoff score of 20 (the ACT goes from 5 (worst) – 25 (best)) corresponds well with the cutoff between GINA defined control and partly controlled. However, even more importantly, it has been shown that for each 1-point fall in ACT score below 20, the risk of a severe exacerbation within a year increases by approximately 10%, so that an ACT score of 15 is associated with a 60% increase in risk of exacerbation compared to a score of 20. Other studies have shown that activity limitation, work

impairment and absenteeism is much higher in patients with an ACT score <20 compared with those with scores ≥ 20. So – a simple 2-minute questionnaire provides a reliable assessment of the current impact of asthma on the patient's daily life, a predictor of their level of control in the future and an indicator of the risk of them having an exacerbation over the next year. A great deal of clinically useful information for such a short investment of (the patient's) time.

MANAGEMENT OF ASTHMA

All guidelines emphasize regular assessment and stepping up ICS dose to achieve control. That approach was tested in the GOAL study, which compared ICS alone with ICS+LABA. The study confirmed what the guidelines recommend - that patients with regular symptoms but not receiving ICS responded very well to ICS alone (using a step-up approach), so that at the end of the year, over 60% were well controlled. There was a slightly better level of control in those using ICS+LABA, but this difference was small (about 5% more patients controlled). By way of contrast, in patients who were symptomatic despite receiving ICS before entering the study, the additional benefit of ICS+LABA over ICS alone was clearly larger (15 % more patients controlled). At the end of one year nearly 80% of patients were at least well-controlled. This contrasts starkly with the 5% of controlled patients in AIRIP.

One of the criticisms of GOAL was that it was all one way – up-titrating the ICS dose. Recently there have been a number of studies that suggest that once controlled (for at least 3-6 months), it is more effective to halve the dose of ICS than to stop the LABA. One point to emphasize here is that maintenance treatment means just that, at least for adults. One very important property of ICS is broncho-protection against the various triggers that can cause exacerbations. There is no good clinical marker for this, it is best assessed using bronchial-provocation tests such as methacholine challenge. Studies have shown that bronchial hyper-responsiveness takes a long time (in excess of one year to develop fully). It is much slower than the lung function or symptomatic response, however it is lost quickly, even if the patients have been on ICS for 2 years. The patients may not be aware of the loss of protection until they have their next viral upper respiratory tract infection that “goes to their chest” and causes an exacerbation. The point is that preventative therapy for asthma is based on probabilities – like treating hypertension to prevent stroke or myocardial infarction. The clinician doesn't know when or in whom the protection is needed, they just know that the average patient is at risk and requires treatment to minimize that

risk.

More recently an approach to using low dose ICS+LABA as both preventer and reliever has been advocated. Numerous studies have shown that the time to first exacerbation is prolonged, but a recent meta-analysis has shown that the level of control using this approach is less good than that obtained with a guideline directed step up approach. This treatment regime has also been shown to be inferior to medium high dose ICS alone in reducing airway inflammation.

ASTHMA TREATMENT SUMMARY

- Targets inflammation (usually with ICS ± LABA)
- Primary treatment objective is good symptom control
- Good control is associated with fewer severe exacerbations.
- Guidelines recommend stepping up ICS dose until controlled and then stepping down
- Good control requires prolonged maintenance therapy

COPD PATHOPHYSIOLOGY

The underlying inflammatory nature of asthma has been understood for a long time and is even taught to patients, however the importance of inflammation in COPD has been recognized for little more than a decade. Yet the degree of inflammation differs from that in asthma only in kind, not degree (although there is a correlation between the severity of airflow limitation and the level of inflammation). In COPD, neutrophils, macrophages, CD4+ and CD8+ cells are among a number of inflammatory cells that have an increased presence, even in patients with mild airflow limitation. In the airways, inflammation leads to airway wall thickening, remodeling and broncho-constriction. In the alveoli there is destruction of alveoli (emphysema) with loss of elastic recoil. This results in early airway collapse at the onset of expiration. Airway and lung parenchymal damage both lead to expiratory airflow limitation – the characteristic feature of COPD. Most patients have elements of both diseases, but it is not known why an individual patient may have more of one component than another. As an aside, there is an impression that biomass-fuel induced COPD, more a disease of women than men, may produce more of an airway disease picture than one of emphysema. This, together with the patient's gender may lead to a mis-diagnosis of asthma.

COPD PREVALENCE AND BURDEN

COPD has a high level of prevalence worldwide. Unfortunately data for Pakistan are not

yet available (but a study is in progress) but the BOLD study showed that across a number of sites in different countries it was 12% for men, and 9% for women. In Turkey, for example it was 6% in women and 15% in men. The impact of COPD on the patient is very high. In a North American and European study, 60% of COPD patients had restriction of normal physical activity and nearly 50% had disturbance in the performance of household chores. Patients with COPD underestimate the impact of the disease on themselves, 75% of patients who had to stop when walking at their own pace judged that they had only mild or moderate disease and more remarkably, 35% of those who were too breathless to leave the house thought their disease was only mild-moderate.

Health status measurements provide a more reliable measure of the effect of the disease on the patient, a study performed with the St George's Respiratory Questionnaire (SGRQ) show that people diagnosed with COPD after having been picked up in a screening programme had SGRQ scores that were clearly above the normal range. For reasons that are not understood, COPD patients ignore or underestimate the effects of their disease unless specifically assessed.

COPD ASSESSMENT

Traditionally, COPD assessment has been based upon FEV₁ measurement, but this just measure airflow limitation and cannot distinguish between two entirely different pathophysiological processes – airways disease and emphysema. It is now well established that the FEV₁ correlates very poorly with breathlessness, impaired health status and poor exercise intolerance. Until recently, however, assessment of health status has not been possible in routine practice, but the development of the COPD Assessment Test (CAT) has enabled reliable health status measurements to be made in a routine clinical setting. It only takes the patient 2 minutes to complete the questionnaire and 30 seconds to score. The CAT seems to behave very much like the much more complex SGRQ and holds great promise as a means of assessing symptom severity and impact and as a simple method of monitoring the patient.

The importance of exacerbations of COPD has been recognized increasingly. They are quite unlike asthma exacerbations, from which the patients recover quickly if treated correctly, a single well-treated COPD exacerbation has a large and long-lasting (weeks and months) effect on patients' health. Repeated exacerbations lead to faster loss of FEV₁ and greater deterioration in health over time. In many respects COPD exacerbations are one of the most important features of COPD. There is a correlation between FEV₁ assessed using GOLD grading, with

increasing risk of exacerbations being associated with more severe airflow limitation', but it should be recognized that this a population-based risk estimate. Recently it has been shown that a patient's history of exacerbations is a reliable predictor of future exacerbations, which is much more appropriate to clinical practice since it is an individual-patient based risk estimate.

It is clear that future COPD assessment systems will move away from Spirometric measurements towards clinical approaches based upon symptomatic impact and risk of exacerbations and death. This is becoming analogous to asthma in which assessment focuses on the level of control of the disease and identifying patients at risk of an exacerbation.

COPD treatment

As with assessment, treatment of COPD is differentiating into two components:

Symptomatic

- o Reduce symptoms
- o Improve exercise capacity
- o Improve health status

Risk Reduction

- o Reduce the risk of exacerbations
- o Slow the rate of disease progression
- o Reduce mortality.

Again the analogy with treatment of asthma becomes clear: treatment is both symptomatic and preventative.

The other development that is influencing COPD treatment is the evidence that anti-inflammatory therapy based on ICS significantly reduces a number of airway markers of inflammation, this effect being greatest when ICS and LABA are combined'. Importantly, if the ICS are discontinued the anti-inflammatory effect is lost. COPD has not yet advanced down the road travelled in asthma 20-30 years in which the emphasis has been on anti-inflammatory therapy being the first treatment, with long-acting bronchodilators being added secondarily, however that journey has begun.

Compared with a decade ago, treatments for COPD are much more effective. There are several choices of drugs that reduce the risk of exacerbations. Once daily tiotropium – a long-acting antimuscarinic (LAMA) appears more effective than twice daily salmeterol, but the margin of advantage is small (10% reduction). This should be compared with the 30% reduction in exacerbation rate reported when ICS+LABA (fluticasone+salmeterol) was compared to

salmeterol alone in patients with severe or very severe obstruction. At the other end of the severity spectrum, there is clear evidence that ICS+LABA reduces exacerbations in patients with moderate airflow limitation.

There is an increasing wide range of symptomatic treatments, with good evidence for worthwhile efficacy with tiotropium and a new 24 hour acting long-acting beta₂-agonist (indacaterol). One drug may not produce enough symptomatic benefit so ICS may be added to LABA and LAMA may be added to LABA. Long-term studies have shown that the health status benefits of ICS+LABA (fluticasone+salmeterol) and LAMA may be sustained for at least 3-4 years'. Key to the use of symptomatic treatment is the obligation on the prescribing physician to review the patient and evaluate symptomatic treatment – there is no point in prescribing a drug for symptoms that confers no perceivable benefit to the patient. There are now numerous choices and combinations, so it is possible to ring the changes to the patient's benefit.

Before leaving this discussion of treatment it is important to remember that the most effective treatments are also the cheapest. Smoking cessation is a key factor to slow disease progression and pulmonary rehabilitation produces benefits greater than anything that comes from an inhaler.

CONVERGENT MANAGEMENT APPROACHES FOR ASTHMA AND COPD

From the foregoing it is clear that there are increasingly similarities of approach to the management of asthma and COPD. The assessment methods are now very similar - both require an estimate of the risk of exacerbations and a routine measurement of the symptomatic impact of the disease. That symptomatic impact is called 'lack of control' in asthma and 'impaired health status' in COPD. Simple routine questionnaires are now available for both disease and are taking over from lung function measurements in guiding treatment decisions and for routine monitoring.

The focus of treatment in asthma is on anti-inflammatory therapy as first-line and whilst that point has not yet been reached in COPD, it is likely to come within a decade. The treatment objectives in the two diseases are different; those in asthma are directed towards complete suppression of symptoms, since this is achievable, whereas in COPD abolition of symptoms is not yet possible. However, COPD guidelines emphasize the importance of achieving maximum symptomatic improvement. The broad approaches to treatment are becoming similar – emphasizing preventative therapy as being different from

symptomatic and rescue treatment. Asthmatic patients may require addition of long-acting bronchodilator if the preventative treatment does not suppress symptoms. They may also benefit from 'rescue' inhaler use, but such short-acting treatment is rarely of much value to COPD patients - since their symptoms are far more persistent; in them long acting symptomatic therapy is required, however the principles are similar between the two diseases.

KEY MESSAGES

- Asthma and COPD are both inflammatory conditions.
- It is easy to make simple and reliable assessments of the key clinical features of both diseases – exacerbations and symptoms
- Both diseases require maintenance preventative treatment
- Both may require symptomatic treatment with long-acting bronchodilators
- Both require regular review to step up and down in asthma and ad or replace in COPD

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**GRANT SUPPORT, FINANCIAL
DISCLOSURE AND CONFLICT
OF INTEREST**

None Declared