Improving Patients with Advanced Chronic Airflow Obstruction

Kasik and Alexander (Chest 1982;82:571) urge caution in the long-term use of bronchodilators in patients with advanced chronic airflow obstruction (CAO). Further, they advise a critical assessment of therapeutic response and urge that only patients with either symptomatic improvement or statistically significant objective functional improvement be continued on long-term bronchodilator therapy. On first reading, one would have difficulty quarreling with this advice, but perhaps there is more to the story than meets the eye.

It is true that we do not have as many well-designed controlled clinical trials in therapy of CAO as we do in asthma, but the studies we do have frequently show definite benefit to many patients. For example, the study, purported to show benefit in only six of 40 patients,¹ can be interpreted differently. In this study, the authors required significant objective response to bronchodilator therapy in three criteria, ie, FVC increase of greater than 15 percent, FEV₁ increase of greater than 15 percent, and FEF₂₅₋₇₅ increase of 25 percent or more. The FEF₂₅₋₇₅ was not done by the isovolume method for calculating postbronchodilator response, and thus, improvement was underestimated. If one accepts improvement in either FEV₁ or FVC, then the number of responders was 25 out of 40 or more than 50 percent. Often, the only response seen to either oral or inhaled bronchodilators is a FVC response, and this may be correlated with symptomatic improvement.

In a second report by the same authors, isoproterenol responsiveness was found in patients with advanced CAO when they were receiving placebo, but not when they were receiving oral theophylline.² The authors explain this difference on the basis of bronchodilator effectiveness of oral theophylline therapy. A direct quote is, "We believe the response to isoproterenol challenge during oral theophylline was blunted because the airways were already maximally bronchodilated." Thus, here too is the conclusion that theophylline was an effective bronchodilator in these patients.

Another study reported statistically significant improvement in peak expiratory flow rate, FEV₁, and FVC in patients receiving therapeutic levels of theophylline as assessed by blood levels, but three had undesirable side effects from theophylline.³ Although the conclusion that symptom scores were not significantly improved was reported, no data were offered for careful scrutiny. Further, the authors wondered whether the design of the diary card was not well suited to detect subjective changes.³

Chronic airflow obstruction in older patients with a chronic stable FEV₁ of 1 L or less carries a very bad prognosis, and the disabling symptoms are well known by all experts in the field. These patients need all the help they can get, and even if one achieves an apparently trivial improvement in vital capacity, airflow and/or symptomatic benefit, the therapy is likely worthwhile. In addition, there is also the possibility of slowing the progress of disease in the long run which is something that has never been studied.

Our therapeutic armamentarium today includes, not only theophylline, but inhaled and orally administered beta agonists, corticosteroids, and anticholinergics. It is likely that all of these drugs should be tried in systematic fashion guided by the patients' symptoms and simple objective measurements of improvement available via office spirometry. Sometimes surprising benefit is found, such as statistical improvement in response to corticosteroids.⁴ In fact, corticosteroids may enhance the bronchodilator effects of beta agonists and possibly even theophylline.

From a pragmatic standpoint, the therapeutic approach should proceed along the following lines, in my opinion. Start somewhere, ie, begin with some drug of potential benefit such as an inhaled or oral bronchodilator followed by a trial of corticosteroids with continued use of bronchodilators if no response or an inadequate response is the immediate result. It may be wise to begin with an inhaled beta agonist and determine its response. The availability of more specific, longer-acting agents makes this even more attractive than in years past. The second step might well be a theophylline with a decision whether or not to continue guided by symptoms and simple spirometric tests. Oral beta agonist therapy would be an alternative at this point. A therapeutic trial of corticosteroids should be strongly considered, again guided by symptomatic response and objective functional measurements. After maximum benefit has been achieved by
step therapy, consolidation of the program is the next strategy arriving at a therapeutic regimen which will maintain maximum benefit with minimal or no side effects. This approach will likely benefit many patients with CAO.

All of this of course is conducted on an "open" basis without the objectivity of double-blind randomized crossover trial of each therapeutic agent. This is how we treat patients in the real world today. Almost always, a critical assessment of benefit can be achieved by consensus between patient and physician for the purpose of planning long-term care. This step approach has the potential for improvement of large numbers of patients with chronic airflow obstruction.

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**REFERENCES**


**The Optimal Approach to Identifying the Cause of Lower Respiratory Tract Infection**

*Although an extensive literature exists on the various methods of sampling lower respiratory tract secretions (LRTS) in lower respiratory tract infections (LRTI),¹ the clinical importance and role for each method in identifying the cause of LRTI remains an area characterized by confusion and controversy. By answering a series of questions, we believe that the reasons for this confusion can be elucidated and a way of resolving the controversy achieved.*

*Why Is an Accurate and Reliable Lower Respiratory Tract Secretion Sampling Method Theoretically Needed?*

Ideally, the treatment of LRTI includes the selection of the most effective, safest, and cheapest antibiotic. Theoretically, selecting the most appropriate antibiotic can be done only after accurately identifying the cause of the LRTI. We believe that attaining this ideal in treatment is more difficult today than ever and increases the need for accurate sampling methods of LRTS. We believe this is true for the following reasons: (1) There is an ever-increasing spectrum of potential pathogens that includes new organisms, such as _Legionella pneumophila_, as well as those that have only recently been documented to be pathogens, such as _Streptococcus viridans_ species.² (2) There is an ever-increasing number of available antibiotics that makes the choice of the most suitable antibiotic increasingly difficult. (3) There is an ever-increasing diversity of patients at risk for unusual infections that presents the clinician with an even more complex situation in trying to determine the specific cause and optimal therapy. (4) The unknown impact of widespread use of the pneumococcal vaccine on the spectrum of LRTI adds to the uncertainty of predicting the cause of the infection. (5) Short of analyzing LRTS, there is frequently no other way of identifying the cause of LRTI.

*What Is the Most Accurate Method of Obtaining Lower Respiratory Tract Secretions in Patients With Lower Respiratory Tract Infections?*

The techniques that can be used to obtain or evaluate LRTS range from the totally noninvasive (expectorated sputum analysis) to the moderately invasive (nasotracheal suctioning, flexible fiberoptic bronchoscopy using a protected wire brush in telescoping cannulas with distal occlusion) to the invasive (transtracheal aspiration and percutaneous lung aspiration). The available data would suggest that the accuracy of techniques used to obtain and analyze LRTS varies inversely with the invasiveness of the procedure;² that is, expectorated sputum analysis is the least accurate method, while percutaneous lung aspiration and transtracheal aspiration are the most accurate. Flexible fiberoptic bronchoscopy using telescoping cannulas would appear, at this time, to be in an intermediate position, or, at best, equal to transtracheal aspiration.⁴⁵

*Why Are the Most Accurate Methods of Obtaining Lower Respiratory Tract Secretions Not Routinely Used?*

We believe that the main reasons for the limited use of transtracheal aspiration and percutaneous lung aspiration are as follows: (1) a fear of potential complications; (2) the lack of widespread experience and training among physicians in performing these procedures; (3) the increased time and effort involved in carrying out these procedures; and (4) the lack of studies that have clearly defined the roles of each of the methods.¹

*Why, Despite the Large Number of Studies Done on Methods to Obtain Lower Respiratory Tract Secretions, Does so Much Controversy and Confusion Exist?*

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