Pharmacoeconomics in Pediatric Asthma

In Canada throughout the 1990s, inhaled corticosteroids (ICS) have been the treatment of choice, and we continue to view ICS as the mainstay of treatment for persistent asthma in children, except for those whose disease is so mild that they only require infrequent, as-needed β₂-agonist treatment. Corticosteroid dosage should continue to be individualized, and the minimum effective dose should be used.

In this issue of CHEST (see page 1835), Bisgaard et al present a retrospective pharmacoeconomic analysis based on their recent randomized controlled trial of asthma therapy in infants and toddlers with an average age of 28 months. This study reports that the percentage of patients with one or more exacerbations was significantly lower in those treated with fluticasone, 200 μg/d (20%) or 100 μg/d (26%), than in those treated with placebo (37%), and was accompanied by significant improvements in overall asthma control in both active treatment groups. The dose-response curve for fluticasone administered through a spacer (Babyhaler; Glaxo Wellcome; Middlesex, UK) was, however, relatively flat. Not so long ago, this dramatic reduction in exacerbations would have been enough to ensure not only approval of the product but formulary coverage. Now we have to go one step further and formally assess the study outcomes from a pharmacoeconomic standpoint.

When formally assessed in pharmacoeconomic studies, the cost of asthma care is quite staggering. In the United States, the costs of asthma have been estimated to be just over $6 billion per annum, which accounts for 1% of the total US expenditure on health, and asthma costs are approximately 1% of the health budgets of most countries.

What costs do we need to consider when assessing the cost of asthma care in such a pharmacoeconomic study? When formally assessed, the cost of asthma care includes the components of both direct and indirect costs. Direct costs include inpatient care, emergency visits, physician visits, nursing services, ambulance use, drugs and devices, blood and diagnostic tests, research, and education. Indirect costs or morbidity costs include school days lost, traveling, waiting time, and lost productivity for the caretaker of asthmatic children.

Direct costs of asthma have been shown to exceed indirect costs (accounting for 61% of total adult and pediatric costs in Canada and 53% in the United States). The major cost of direct care are medications and exacerbations requiring hospital treatment. Pharmacoeconomic assessments must therefore focus on more than just drug acquisition costs. Such assessments are sometimes foreign to those of us performing efficacy clinical trials, as such costs may not seem immediately obvious.

Total asthma management must be considered as in the article by Bisgaard et al, as one study has shown that asthma education has also decreased asthma morbidity, hospital admissions, and costs in the pediatric population. Education is, however, most effective when accompanied by effective medical therapy. Clearly, interventions that produce or prevent hospitalization in patients with asthma will have comparatively significant potential impact on cost and treatment of disease. To improve asthma management, international guidelines have been introduced that recommend appropriate diagnosis, patient education, and increased use of prophylactic therapy. Underuse of prescribed therapy, which includes inhaled corticosteroids, or noncompliance contributes to the poor control of asthma and increased costs.

When we assess the cost of care, we also need to know who will be paying for the medication. The new drug may have an increased acquisition cost, which may have to be paid for by the patient.

Unfortunately, many families in North America may not have a drug plan to cover their children’s medications, or a co-payment may be required. Many drug plans developed are specifically aimed at seniors and not at the pediatric population; therefore, the cost of medication can fall on young parents, some of whom may not be covered by employer insurance or social assistance. Other family members may also suffer from asthma, adding the burden of the direct drug costs on the individual family.

Pharmacoeconomic studies are crucial, as now many third-party payers, such as government and private health-care plans, are requiring these studies to be performed in order to decide if they will reimburse the claim. Therefore, the cost of asthma must not focus on “drug acquisition” cost, ie, the cost of an individual medication; it should be described, as in this article, as part of the continuum of asthma care in keeping with national guidelines and quality management. We are all too frequently faced with a family without the independent means or third-party coverage for individual pharmaceutical items. This may have profound implications on whether the individual prescription item is filled at the pharmacy and on adherence to the regimen. Physicians need to recognize the importance of providing effective therapy to minimize total costs. In essence, by achieving asthma control, direct and indirect medical costs can be substantially reduced. Thus, in this age group of asthmatic children, the use of inhaled corticosteroid
fluticasone, 200 mg/d, as in this study, can more than repay any acquisition cost by reducing hospital admissions and emergency department visits. Adherence to guidelines on appropriate diagnosis, education, and therapy should reduce the overall cost and is a solid case on which a physician can help an individual to obtain coverage. Studies of pharmacoeconomics are critically important in order to help facilitate equal access to individual medications across all levels of society. Prospective assessment is required not only during phase-III clinical trials but also when care is delivered in accordance with national guidelines.

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REFERENCES
6 Joyce DP, McIvor RA. Use of inhaled medications and urgent care services: study of Canadian asthma patients. Can Fam Physician 1999; 45:1707–1713

Streamlining Methacholine Challenge Testing

The diagnosis of asthma is usually made after careful consideration of a patient’s individual history and the demonstration of reversible airway obstruction. Those are the easy ones. For many patients with some combination of cough, wheezing, dyspnea, and chest tightness, the diagnosis may remain unclear after initial history, physical examination, and spirometry. In such cases, the methacholine challenge test (MCT) has become the most widely used method of evaluating the likelihood that a given patient’s respiratory symptoms represent asthma. Making a diagnosis of asthma with confidence should lead to appropriate therapy. Refuting the diagnosis can lead to a broadened differential diagnosis that includes less common disorders with similar nonspecific symptoms whose diagnosis is often greatly delayed, such as endobronchial lesions, interstitial lung disease, or pulmonary vascular disease.

Increasing quantities of inhaled methacholine, a synthetic derivative of acetylcholine, induce increasing degrees of bronchospasm in susceptible individuals. Normal subjects may also experience some degree of short-lived airways narrowing if administered large amounts of methacholine, but their degree of bronchospasm typically plateaus after a modest decrease in FEV1. The clinical utility and techniques for the MCT have been recently authoritatively reviewed.1 Individuals experiencing a significant amount of airflow limitation (defined as a ≥ 20% fall in FEV1, compared to baseline) in response to a threshold concentration of methacholine (typically < 16 mg/mL of inhaled methacholine) are considered to have airways hyperresponsiveness (AHR), ie, a positive MCT result. The MCT has excellent sensitivity in identifying patients with asthma, but AHR can occur in other conditions, including viral tracheobronchitis, COPD, and congestive heart failure. Even patients with allergic rhinitis who are without chest symptoms may have a positive MCT result. Absence of AHR to methacholine challenge provides strong evidence against the diagnosis of current asthma.

The increasing significance of the MCT as a clinical and research tool is evidenced by Figure 1, which shows the number of MCT publications listed for each year from 1970 to 2000 in the National Library of Medicine PubMed directory. The search was performed using the phrase, “methacholine challenge” OR “methacholine inhalation” AND asthma. Nine citations were recovered for the entire 1970s, 165 citations for the 1980s, and 471 citations for the 1990s.

The MCT is not the only form of bronchial challenge that is clinically useful for diagnosing asthma. While inhalation of allergens and other specific inflammation-inducing agents remains the province of a few highly specialized centers, histamine inhalation has been popular in Europe. Airway challenges to respiratory heat and/or water loss reliably produce bronchospasm in asthmatics but not in normal subjects.9 Exercise testing is an unreliable method of respiratory heat and water challenge because of the difficulty in standardizing the challenge variables of minute ventilation, challenge pe-