

Barriers to measuring and achieving optimal outcomes in pediatric asthma

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To measure the effectiveness of any therapeutic endeavor, a set of defined outcome measurements must be performed, or the task of determining the effectiveness of any therapeutic step becomes difficult. With asthma, however, in which case it is difficult to establish the initial diagnosis, beginning a program of outcome measurements regarding any therapeutic interaction is nearly impossible. Conventional means are thwarted at the outset. One way of approaching the problem of obtaining reproducible outcomes data is to examine those areas in which measurements can be made and determine the barriers to obtaining the data. Establishing a good medical history is a critical step that, in general, is especially difficult with very young children, and tools that provide objective measurements that are used in the normal evaluation of older children are of little use in the very young child with asthma. Parts of the physical examination are difficult to perform in very young children, and findings associated with asthma can be found in other clinical states. In this age group, diary keeping suffers from the same problems and issues that are related to obtaining an accurate medical history. Barriers also exist to obtaining the best outcomes. The choice of medications for the very young child is limited; there are several typical adherence problems, and information about adverse effects is limited. (*J Allergy Clin Immunol* 2001;107:S482-4.)

Key words: Wheezing episode, reproducible outcome data, medication delivery issue, psychosocial issue, adherence, medication phobia

To measure the effectiveness of any therapeutic endeavor, a set of defined outcome measurements must be performed. These vary significantly, depending on disease state, a disease state's level of severity, setting of service, and the patient's age. Disease-specific measurement tools have been created and validated in appropriate populations for most chronic disease states. Without such measurement tools, the task of determining the effectiveness of any therapeutic step becomes extremely difficult, if not impossible.

In performing any longitudinal study of children with

asthma, it is essential to establish the baseline period; for asthma, this is not clear. Although there may be predisposing genetic factors, the diagnosis is rarely made with the first wheezing episode. It is common to call the first episode bronchiolitis, particularly when associated with signs of a viral infection. Within the patient's first year of life, a reluctance to diagnose a chronic illness may even cause this diagnosis to be repeated on the second episode of wheezing. In older children and adults, however, a wheezing episode is presumptive evidence for a diagnosis of asthma. When it is difficult to establish the initial diagnosis, it becomes difficult to begin a program of outcomes measurements regarding any therapeutic interactions.

A review of the literature and any personal experience in dealing with young children lead one to appreciate the complexity of trying to establish objective, or even subjective, consistent measurement tools for this age group.¹ The barriers to establishing these measurements are multifactorial and include such issues as communication difficulties, lack of objective measurements, lack of existing standardized data, and use of nonobjective third parties to obtain data.

One way of approaching the problem of obtaining reproducible outcome data is to look at those areas in which measurements can be made and determine the barriers to obtaining the data. In this fashion, other ways of obtaining data may be found.

HISTORY

The establishment of a complete medical history and analysis of key information in the medical history are critical steps in building a diagnosis and assessing the clinical state of the patient. This essential aspect of care is significantly altered when the patient is younger than 5 years of age, however.

To begin with, young children do not have the language development or skills to verbalize their problems, nor do they have an understanding of their body that can help the history-taking process. Children cannot describe their headaches, nausea, or degree of dyspnea. They cannot provide helpful information about time and spatial relationships. Clinicians would love to know when the symptoms first began and what the exacerbating factors are, but these are usually observational facts rather than actual ones.

We are thus dependent on second-hand information about the child and the symptoms. Simple questions (such as: How often does the child wake during the night with symptoms? How much difficulty is there with activity? What are the precipitating factors?) may not have easy answers. The questions must be restated, such as "When

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did you first notice...?" Answers to these questions depend on the observer's acuity level and bias (how often does a guardian who smokes say that smoke causes his or her child to cough?) and the observer's own understanding of the question and how it translates into observable symptoms. For example, a child may often awaken during the night with some symptoms, but only when it is associated with the parents' awakening will it be reported.

To overcome this particularly difficult barrier, certain key questions must be formulated to try to gather the critical information. These may include questions relating to trouble with feedings, trouble with any active behavior, or observation of the child coughing when laughing.

MEASUREMENT TOOLS

In the normal evaluation of older children and adults with asthma, several tools can be used to obtain objective measurements. These tools include home measurements with peak flow meters, office measurements with spirometry, and hospital measurements with plethysmography.² Because these measurements entail some cooperation and consistent effort by the patient, they are of little use in the routine care of the very young child. Although hospital-based physicians and investigators can perform some measurements, these are not practical in most children with asthma. The inability to have objective measures to follow leaves the clinician with a more difficult task of estimating changes in small, or even large, airway function. Sometimes a complete medical history can give an overall idea as to the functionality of the lungs, but this is not an accurate tool and depends on too many variables, such as an objective and accurate medical history, an observer who is really attuned to small changes in the activity level of the child, and airway dysfunction.

Markers of inflammation that are obtained after bronchoscopy could be another objective measurement of the diagnosis and response to treatment. Cells and enzymes are commonly evaluated in bronchoalveolar lavage fluid that is obtained in adult asthmatic patients. Few studies exist of bronchoalveolar lavage fluids in asthmatic children.³ Significant basal membrane thickening and high eosinophil levels in the airway mucosa have been found in bronchial biopsies of wheezing infants in whom asthma developed subsequently,⁴ but these findings suggest that the asthma's pathophysiologic state may develop significantly before any clinical signs or symptoms present themselves. If these observations were better understood and monitored, an earlier intervention with a better outcome might result. At present, reproducible, valid inflammatory markers with predictive value and clinical credibility are not yet available for asthmatic children under 5 years of age.⁵

Physical examination

The physical examination is another gross tool to give some assessment of the asthmatic child. Associated findings, such as atopic dermatitis, allergic shiners of the eyes, and rhinitis may be highly suggestive of asthma in a child with a history or physical findings com-

patible with asthma. Assessment of the lungs by observation, palpation, and auscultation can give some gross indication of lung function. Cyanosis, retractions, and hyperventilation are all signs of respiratory distress. Bilateral wheezing is the hallmark of asthma. All of these findings can be seen in other clinical states, however. It is almost impossible to judge small airway function during the physical examination of very young children. The child will not take a deep breath and perform a forced expiratory maneuver, which helps in small airway assessment. An increase in the thoracic cage diameter might signal that the process has been present for a longer period of time, but the finding provides no exact information.

Diaries

For a physician to base treatment plans on the basis of a recorded diary is often a dangerous step to take with very young children. In this age group, diaries suffer from the same problems related to obtaining an accurate medical history. Persons responsible for filling out these forms are often not accurate historians and do not have the child's perspective, but rather an observer's. Even measurements of medication used are often inaccurate with respect to numbers and timing of usage.

BARRIERS TO OBTAINING THE BEST OUTCOMES

One might think that with good measurement tools, the task of obtaining good outcomes becomes easier, but this is not the case with the treatment of disorders in the very young child.⁶ There are many other barriers that make the goal of optimizing outcomes difficult. These include medication issues, medication delivery issues, and psychosocial issues.

Medication choices

Unfortunately, the choice of medications for the very young child is limited by the formulations available, the limited testing of various dosing schemes, and the unknown dose-adverse effect relationships that may exist. The metabolism of the very young child is different from older children and adults. This undoubtedly affects the pharmacokinetics of medications that are administered in any form and the duration of action, peak effect, and even the general effectiveness of the medications used. These issues influence our understanding of the effect of medications on these children and the development of the optimal way of using them.

Although it is accepted that the inhaled delivery route is an excellent one for most asthmatic patients, this route is fraught with problems for the young child. We have no reliable method of measuring the inhaled amount that reaches the lungs and stomach. This is probably not a constant from dose to dose. There is scanty information regarding the relationship of inhaled medication on a per-kilo basis and its effectiveness and adverse effect ratios. Even with a spacer, inhaler use is probably not a very good choice for con-

sistent medication delivery. It may, however, be the best available mode of medication delivery for many children.

Adherence problems

Several adherence problems are associated with medication delivery. Dosing depends on many people, formulation, and taste problems. Mothers, and mainly grandmothers, tend to underestimate the importance of regular and continuous medication and various equipment inconsistencies. Where the medication is administered (home vs daycare), when it is delivered (work day and weekend schedules), and who is delivering the medication (parent, grandparent, caretaker, or teacher) are all factors that must be taken into consideration in planning a treatment schedule for the young child.

The major determinants of pediatric compliance include the patient's or parent's perception of the severity of the illness; a warm, understanding physician who allows enough time for meeting patient or parent needs and educating them adequately; and a simplified regimen coupled with explicit directions and follow-up care.⁷

Medication phobias

One of the most common physician-related problems that may affect obtaining optimal outcomes in children is steroid phobia, a widespread situation that is based on information regarding problems in the use of oral corticosteroids 20 years ago and now accompanying any type of steroid use. Unfortunately, the lack of consistent data regarding inhaled corticosteroids in the very young child has perpetuated this problem. When to use inhaled corticosteroids, the correct dosage, the safe duration of therapy, and the potential need for tapering therapy are all important issues that must be resolved to gain the confidence of physicians who use these medications in the very young child for prolonged periods of time.

Steroid phobia is not limited to providers. Most parents and grandparents have heard some negative stories related to steroids. With their lack of knowledge about this class of medication, their fears carry over to any steroid, preventing many from actually delivering the medication to the child in the fashion prescribed or recommended.

Adverse effects

Adverse-effects information is limited in this age group. Most adverse effects that have been described are based on observable signs and measurable symptoms in older children. Long-term effects on the central nervous system are generally not monitored. Often, subtle adverse effects (such as irritability and changes in feeding habits) are not captured. It is also known that dietary effects related to medications are not adequately studied in children younger than 5 years. There is limited knowledge on the effect of various illnesses and their medications on asthma medications.

With our incomplete understanding of asthma in the very young child and the treatments available, much information is still needed with respect to measuring appropriate outcomes and attempting to achieve them. With asthma being such a major problem in this age group, such issues should be a major focus of research for the immediate future.

Future research should be directed to identifying risk factors for asthma and defining the population; the complexity of measuring outcomes in wheezing infants (including asthma); evaluating adverse effects in the treatment of wheezing infants (including asthma); medication and behavior in the treatment of wheezing infants (including asthma); and compliance and behavior in the treatment of wheezing infants (including asthma).

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