Tips from Other Journals

Tips from Other Journals are written by the medical editors of *American Family Physician.*

The trade names of drugs listed in Tips from Other Journals are based on what is currently available and not necessarily the brand of drug that was used in the study being discussed.

Clinical Rule Predicts Risk of Respiratory Syncytial Virus Infection

Background: Respiratory syncytial virus (RSV) is a common cause of lower respiratory tract infection in children younger than one year. It is estimated that 44 percent of children in the United States receive medical attention for RSV infection in the first year of life, and 95 percent of those are treated by their primary care physician or in an emergency department. About 40 percent of children who are infected develop recurrent wheeze; therefore, RSV results in significant medical costs and reduces health-related quality of life.

Known risk factors for RSV include prematurity, young age, male sex, heart and lung disease, Down syndrome, no or limited breastfeeding, presence of siblings, day care attendance, and exposure to tobacco smoke. Clinical prediction rules have been developed to predict the need for hospitalization of preterm infants, but not for healthy term infants likely to be treated as outpatients. Because RSV can be prevented with risk-factor modification, Houben and colleagues developed a clinical prediction rule to identify healthy term infants at high risk of RSV lower respiratory tract infection in the first year of life.

The Study: Two large urban hospitals in the Netherlands invited all term newborns (at least 38 weeks' gestation) without major congenital anomalies to participate in a prospective birth cohort study. Of 1,080 eligible newborns, 341 (32 percent) participated in the study. Parents who declined to participate commonly cited the protocol that required daily measurement collection. Baseline characteristics were similar in participants and nonparticipants. At the onset of any respiratory episode, parents recorded their child's daily respiratory symptoms, including cough and wheeze, and obtained nasal/throat swabs. Lower respiratory tract infection was strictly defined as moderate or severe cough or any wheeze for two or more days. The presence of risk factors was ascertained from hospital birth records (sex, gestational age, birth weight, and birth month), and from parental questionnaires completed when the children were one month and one year of age.

The primary outcome was the diagnosis of RSV lower respiratory tract infection, determined by clinical symptoms and the presence of RSV RNA detected from polymerase chain reaction of the swabs sent in by parents. Secondary outcomes included RSV lower respiratory tract infections requiring primary care attention, the prevalence of wheeze in the first year, and the impact of wheeze on the child's health-related quality of life as determined by responses to a preschool quality-of-life questionnaire. The association between each risk factor and the presence or absence of RSV lower respiratory tract infections was analyzed through univariate regression; risk factors predictive of RSV were included in multivariate regression analysis. Factors most related to developing RSV were included in the prediction rule. Individual scores were determined by assigning points for each variable and adding the results.

Results: Of the 298 newborns with complete data, 42 (14 percent) developed RSV lower respiratory tract infections. Of these 42 newborns, 27 (64 percent) visited a primary care physician and three were hospitalized. The final reduced regression model included four independent predictive variables: day care attendance and/or the presence of older siblings (two points); high parental education levels (one point); birth weight greater than 8 lb, 13 oz (4 kg; one point); and birth date between April and September (one point). Children at lowest risk (score of 0 to 2) had an absolute risk of developing RSV of 3 percent, whereas children at ▶

highest risk (score of 5) had an absolute risk of 32 percent. The authors theorized that parents with a higher education level may seek medical care earlier to obtain a formal diagnosis. The authors also suggested that a larger birth weight may be associated with a longer labor and altered immunity. Children diagnosed with RSV were twice as likely to wheeze during the first year of life as children who were not infected (62 versus 36 percent; $P = .003$), and they visited a physician more often for respiratory problems (48 versus 30 percent; $P = .03$).

Conclusion: This clinical prediction rule identifies children at the highest and lowest risks of RSV lower respiratory tract infections, which can help target preventive and monitoring strategies.

AMY CRAWFORD-FAUCHER, MD

Source: Houben ML, et al. Clinical prediction rule for RSV bronchiolitis in healthy newborns: prognostic birth cohort study. *Pediatrics.* January 2011;127(1):35-41.

Monotherapy vs. Combination Therapy for the Management of Mild Asthma

Background: Asthma treatment aims to reduce symptoms, exacerbations, and long-term complications by using the lowest dose possible to minimize adverse effects. Patients with mild persistent asthma (who comprise up to 70 percent of all persons with asthma) can be treated with low-dose inhaled corticosteroids, whereas those with moderate asthma often require an inhaled corticosteroid and a long-acting beta agonist. In patients with moderate to severe asthma, studies have shown more benefit with a low-dose inhaled corticosteroid combined with a long-acting beta agonist than with inhaled corticosteroids alone. In the few studies of patients with mild asthma, the results indicate that these treatment options have similar effectiveness. Postma and colleagues conducted a randomized controlled trial to evaluate the effectiveness of monotherapy with the inhaled corticosteroid ciclesonide (Omnaris) versus the combination inhaled corticosteroid and long-acting beta agonist fluticasone/salmeterol (Advair) in patients with mild asthma.

The Study: The authors randomized 657 patients with a clinical diagnosis of mild persistent asthma to three groups: placebo, ciclesonide in a dosage of 160 mcg daily, or fluticasone/salmeterol in a dosage of 100/50 mcg twice daily. Patients participated in a two-week run-in period and were allowed to use salmeterol (Serevent) as a rescue medication. Criteria for randomization to treatment after the run-in period included a predicted forced expiratory volume in one second of 80 percent or more, reversible airway obstruction, limited use of rescue salmeterol, no nighttime asthma symptoms, and a daytime symptom score of 3 through 9. Patients were excluded if they had ever smoked, had an asthma exacerbation within two months of the run-in period, were hypersensitive to inhaled corticosteroids, had chronic obstructive pulmonary disease, were thought to be noncompliant, were intolerant of short-acting beta agonists, or had started immunotherapy. The primary outcome was time to the first severe asthma exacerbation (defined as a more than 30 percent decrease in peak expiratory flow from baseline on two consecutive days, or the need for oral corticosteroids, hospitalization, or other emergency treatment). Patients also recorded daytime and nighttime asthma symptoms (scale 0 to 4: 0 = no symptoms; 4 = unable to carry out daily activities, or awake most of the night because of asthma symptoms).

Results: Only the fluticasone/salmeterol treatment increased the time to first exacerbation ($P = .0002$) and decreased the risk of having a first severe asthma exacerbation during the 12-month study ($P = .0002$). In addition, pulmonary function improvements were noted only in the fluticasone/salmeterol group ($P < .0001$). However, when compared with placebo, ciclesonide achieved levels of daily asthma control similar to those of fluticasone/salmeterol. This was measured by the median number of poorly controlled asthma days (1.5, 1.8, and 6.2 days per 12 months for ciclesonide, fluticasone/salmeterol, and placebo, respectively); the median number of asthma symptom–free days (31, 23, and 17.5 days per 12 months for ciclesonide, fluticasone/salmeterol, and placebo, respectively); asthma symptom scores (ciclesonide, $P = .0015$; fluticasone/salmeterol, $P = .0007$); and reduced rescue medication use (ciclesonide, $P = .0001$; fluticasone/salmeterol, $P = .0005$).

Conclusion: Although the combination treatment of fluticasone/salmeterol increased pulmonary function and time to first exacerbation, ciclesonide monotherapy was able to control symptoms of daily asthma in persons with mild persistent asthma. These results demonstrate that monotherapy with an inhaled corticosteroid may be considered as a first-line approach in patients who have mild persistent asthma and normal pulmonary function.

SAWALI SUDARSHAN, MS III

Source: Postma DS, et al. Comparison of the effect of low-dose ciclesonide and fixed-dose fluticasone propionate and salmeterol combination on long-term asthma control. *Chest.* February 2011;139(2):311-318. ■