The Effect of Rapid Respiratory Viral Diagnostic Testing on Antibiotic Use in a Children’s Hospital

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Background: Acute viral respiratory disease is the most common reason for pediatric hospitalization in the United States. Viral illnesses may be mistaken for bacterial infection, and antibiotic therapy may be prescribed. Over-prescribing of antimicrobials for viral illness is a factor contributing to increasing antimicrobial resistance among bacterial pathogens encountered in pediatrics.

Objective: To determine if the availability of a rapid diagnostic test for respiratory viruses would affect antibiotic use in a children’s hospital.

Design: Retrospective medical record review.

Setting: A 232-bed urban children’s hospital.

Participants: All hospitalized infants and children who underwent rapid testing (SimulFluor Respiratory Screen; Chemicon International Inc, Temecula, Calif) for respiratory viruses by direct fluorescent assay (DFA) during 2 successive winter seasons.

Main Outcome Measures: Rates of antibiotic prescribing in DFA-positive and DFA-negative patients during the 2 study periods.

Results: During the first winter season, DFA-positive patients had fewer days using intravenous antibiotics (2.4 vs 4, \( P = .04 \)), fewer days using oral antibiotics (0.25 vs 2.5, \( P = .04 \)), and fewer discharge prescriptions for oral antibiotics (37% vs 52%, \( P = .02 \)) when compared with DFA-negative patients. Intravenous antibiotics were initiated less often for DFA-positive patients during the second winter season than during the first (26% vs 44%, \( P = .008 \)).

Conclusions: Direct fluorescent assay testing was associated with a decrease in inappropriate antibiotic use. The availability of rapid viral diagnostics is an important tool for decreasing antibiotic prescribing in pediatric patients.

Arch Pediatr Adolesc Med. 2002;156:1230-1234

Acutely viral respiratory disease is the most common reason for pediatric hospitalization in the United States.1 Respiratory syncytial virus (RSV), influenza A and B, and parainfluenza are common causes of disease, and result in syndromes that may require hospitalization (bronchiolitis, pneumonia, and croup).2-5 In young children, viral illnesses often result in fever, leading to diagnostic evaluations for bacterial disease and to empiric antibiotic use. Pediatricians prescribe antibiotics in 20% of cases of upper respiratory infection, 40% of cases of bronchiolitis, and as many as 100% of cases of pneumonia, even though the majority of these illnesses are thought to be viral.6-9 Recent data indicate that patients with documented viral illnesses are less likely to have a bacterial infection than those without viral illness.10-13 Empiric antibiotic therapy is, therefore, usually unnecessary in patients with viral illness. This inappropriate use contributes to antimicrobial resistance among bacterial pathogens encountered in pediatrics.7-9,14

Accurate rapid detection methods for viruses have recently become available.15-17 The effect of viral diagnostics on hospital length of stay and treatment costs has been assessed in single studies of adult and pediatric populations.16,17 Likewise, data regarding the effects of viral diagnostics on antibiotic prescribing practices for hospitalized children are limited.17,18 We sought to investigate whether the results of rapid viral testing for multiple respiratory viruses would affect antibiotic use among hospitalized patients in an urban children’s hospital.

METHODS

SETTING

The study was conducted during 2 consecutive winter seasons at Primary Children’s Medical Center (PCMC), a 232-bed children’s hospital that serves as a community hospital for...
Salt Lake County, Utah, and as a tertiary referral center for the intermountain West. The emergency department evaluates 33 000 children per year, and there are approximately 10 000 admissions to the hospital each year.

All admitting physicians and house staff received a mailing in December 2000 notifying them of the availability of direct fluorescent assay (DFA) testing for respiratory viruses in the clinical microbiology laboratory. We hypothesized that clinicians would be less likely to prescribe antibiotics and more likely to discontinue antibiotics if rapid and reliable viral diagnostic tests were available.

We reviewed the effects of testing during 2 consecutive winter seasons. Study period 1 was the first winter season during which DFA testing was offered, encompassing December 20, 2000, through February 13, 2001; study period 2 was in the second winter season, after DFA testing had been available for 1 full year, and included 2 weeks between December 27, 2001, and January 9, 2002. Both study periods encompassed weeks of high viral activity in our community (positive DFA results for PCMC, by week, can be viewed online).

During study period 2, DFA testing was ordered more frequently, and the peak of the respiratory viral season was shorter; therefore, we were able to enroll the needed patients for comparison for a shorter period.

DFA TESTING

The clinical microbiology laboratory began testing nasal wash specimens for respiratory viruses on December 20, 2000, using the SimulFluor Respiratory Screen (Chemicon International Inc, Temecula, Calif). The assay tests for respiratory syncytial virus (RSV); influenza A and B; parainfluenza viruses 1, 2, and 3; and adenovirus were performed by DFA. The manufacturer reports an overall sensitivity of between 98% and 100%, and specificity between 84% and 100% when compared with viral culture.

Specimens were prepared by cytospin and tested using the SimulFluor Respiratory Screen, followed by SimulFluor influenza A/influenza B; and SimulFluor parainfluenza 1, 2, and 3; or adenovirus stains if the screen was positive. During study period 1, viral respiratory culture testing was performed on all specimens using 4 shell vials, with 72-hour and 10-day exit stains. Sensitivity and specificity of the DFA was based on comparison with viral cultures. Because of the excellent sensitivity and specificity of the assay observed during the first year of use, during study period 2, viral respiratory culture testing was performed only for parainfluenza DFA-positive specimens and for DFA-negative specimens. Testing with DFA was performed 3 times daily during study period 1, and 5 times daily during study period 2. The laboratory charge was US $32 for DFA testing during study periods 1 and 2. There were no institutional protocols in place regarding DFA testing during either of the study periods.

PATIENT ASCERTAINMENT AND DATA COLLECTION

The microbiology records were queried for all patients who had respiratory viral DFA testing performed during the 2 study periods. Patients who had DFA testing were eligible for inclusion in the study if they were admitted to the hospital. During study period 1, review of paper medical records for enrolled patients was performed. Data were abstracted from the discharge summary, medication administration record, and microbiology records. Data included demographics, admitting and discharge diagnosis, results of DFA and bacterial cultures, inpatient antibiotic therapy, and discharge prescriptions for antibiotics. Patients with positive and negative DFA results were compared. During study period 2, the medical records at PCMC were computerized. The computerized discharge summaries, medication administration records, and microbiology records were reviewed, and data collected included admitting diagnosis, DFA and bacterial culture results, whether intravenous antibiotics were administered during the hospital stay, and discharge prescriptions for antibiotics. Patients admitted during study period 2 were compared with those in study period 1.

STATISTICAL ANALYSIS

All data were entered into a computerized database (Access 97; Microsoft Inc, Seattle, Wash). Comparisons between DFA-positive and DFA-negative patients were made using either a 2-sample inference for proportions (Statit Custom QC; Statware Inc, Corvalis, Ore), the t test, Fisher exact test, or χ² analysis (SPSS Inc, Chicago, Ill). Multiple logistic regression was performed to analyze variables related to intravenous antibiotic use. In the model, intravenous antibiotic use was the dependent variable, and DFA result, time to DFA result, and patient age were the independent variables. The effect of specific viral diagnoses on antibiotic prescribing was analyzed using χ² analysis.

RESULTS

PATIENTS

During study period 1 (8 weeks), 229 admitted patients had DFA testing performed. During study period 2 (2 weeks), 109 admitted patients had DFA testing performed. The most common admitting diagnoses for patients in both study periods were bronchiolitis, pneumonia, and fever, representing 61% in study period 1 and 71% in study period 2. The ages of patients in study period 1 ranged from 4 days to 19 years (mean age, 29 months), and in study period 2, age ranged from 11 days to 18 years (mean age, 17.3 months, P = .02). Additional patient information is given in the Table.

DFA TESTING

During study period 1, 104 (45%) of 229 patients had positive DFA results. The viruses identified included RSV (66%); influenza B (16%); parainfluenza 1, 2, and 3 (10%); and influenza A (7%). During study period 2, 57 (52%) of 109 had positive DFA results, and the viruses identified included RSV (74%); influenza A (16%); parainfluenza 1, 2, and 3 (7%); and adenovirus (3%). Patients who...
were 3 years old or younger were more than twice as likely to have a positive DFA result when compared with those who were older than 3 years (odds ratio [OR], 2.4; 95% confidence interval [CI], 1.2-4.8; \( P = .005 \)).

The turnaround time for DFA results for patients during study period 1 was 8.6 hours, and during study period 2, it was 4.5 hours. The sensitivity of DFA testing for 1112 specimens processed at PCMC during the first 9 months of testing was 87%, and the specificity was 94%.\(^{21}\) Information regarding the sensitivity and specificity of the DFA testing for individual viruses can be found online.\(^{22}\)

### BACTERIAL INFECTION

During study period 1, 1 (<1%) of 104 DFA-positive patients had a culture-confirmed bacterial infection, compared with 16 (12.8%) of 125 in the DFA-negative group (\( P < .001 \)). During study period 2, 1 (1.8%) of 57 DFA-positive patients had confirmed bacterial infection, compared with 7 (13.5%) of 52 DFA-negative patients (\( P = .02 \)). When both study periods are combined, 2 (1.2%) of 161 DFA-positive patients had culture-proven bacterial infection, compared with 23 (13%) of 177 DFA-negative patients (\( P < .001 \)). Patients who tested negative for viral infection by DFA were 11.9 times more likely to have culture-confirmed bacterial infection than those who tested positive (95% CI, 2.65-38.6).

The DFA-positive patients with dual viral and bacterial infections both, were diagnosed with pneumonia. The pathogens identified were RSV and *Staphylococcus aureus* bacteremia and influenza A and *Haemophilus influenzae* bacteremia.

### ANTIBIOTIC USE

During study period 1, 44% of DFA-positive patients received intravenous antibiotics during their hospital stay, compared with 45% of DFA-negative patients. However, the duration of intravenous antibiotic therapy was significantly shorter for DFA-positive patients compared with DFA-negative patients (2.5 days vs 4.0 days; \( P = .04 \)). At the time of hospital discharge, DFA-positive patients were less likely to receive a discharge prescription for oral antibiotics (37% vs 52%; \( P = .02 \)).

During study period 2, DFA-positive patients were significantly less likely to have intravenous antibiotic administration initiated when compared with DFA-positive patients from study period 1 (26% vs 44%; \( P = .008 \)). At the time of hospital discharge, 37% of DFA-positive patients received prescriptions for oral antibiotics, which was the same percentage as during study period 1. Approximately 50% of the discharge prescriptions for oral antibiotics for DFA-positive patients during both winter seasons were written for otitis media, and approximately 50% were written for pneumonia.

In the multiple logistic regression model using data from both study periods, a negative DFA result was significantly associated with an increase in intravenous antibiotic administration. Patients who were DFA-negative were 2.3 times as likely to receive intravenous antibiotics than patients who were the same age and DFA-positive (95% CI, 1.5-3.6; \( P < .001 \)). The turnaround time for the test was not a significant variable in the model. Children with RSV infection were 3.2 times less likely to receive intravenous antibiotics than patients with other viruses or no viruses identified (95% CI, 1.8-5.4; \( P < .001 \)).

### COMMENT

Overprescribing of antibiotics for viral respiratory infections is a significant problem in pediatrics and is believed to play a major role in increasing antibiotic resistance among common bacterial pathogens in the United States. Professional organizations, including the American Academy of Pediatrics (Elk Grove Village, Ill), the American Academy of Family Physicians (Leawood, Kan), and the Centers for Disease Control and Prevention (Atlanta, Ga) have published guidelines on the judicious use of antimicrobials in pediatric upper respiratory infections.\(^{23}\) The Infectious Disease Society of America (Alexandria, Va) and the World Health Organization (Geneva, Switzerland) have both issued policy statements regarding the containment of antimicrobial resistance, and both emphasize the importance of the clinical microbiological laboratory.\(^{24,25}\)

The availability of rapid, accurate diagnostic testing that can identify viral infections has tremendous potential to limit the inappropriate use of antimicrobials. Relatively few studies, however, have demonstrated this. A study among adults compared patients with viral infections detected by conventional culture-based methods, with those that had infection detected by rapid methods.\(^{26}\) During the rapid testing period, detection of viruses was associated with shorter hospital stays and improved antibiotic stewardship.\(^{16}\) In the United States, 2 studies have shown that the rapid detection of influenza A is associated with decreased antibiotic use in children.\(^{18,26}\) A study from Hong Kong also showed a decrease in antibiotic use for children with influenza A or B, parainfluenza, or adenovirus infection following the initiation of rapid viral diagnostic testing.\(^{17}\)

Our study sought to evaluate the effect of the availability of a single reliable diagnostic test for several common respiratory viruses on antimicrobial use. The DFA used in this study had excellent sensitivity and specificity, similar to what has been reported by others.\(^{15}\)

Our study demonstrates that positive DFA results for respiratory viruses are common among patients tested, especially in younger children. The DFA results during both study periods indicated that approximately 50% of pediatric patients tested were positive for 1 of the 7 viruses identified by the DFA assay. Children younger than 3 years were 2.4 times more likely to have positive DFA results than older children, as is consistent with other studies documenting the importance of recognizing respiratory viruses in this age group.\(^{3,5,13,27}\)

Among children tested with the viral DFA panel, DFA-positive patients had a lower risk of bacterial infection that could be detected by culture than did DFA-negative patients. Only 1.2% of DFA-positive patients had culture-confirmed concomitant bacterial infection. Other studies have found similar low occurrences of bacterial infection in pediatric patients with viral illness.\(^{10,11,13,28}\)
Overprescribing of antimicrobials for viral illness is a factor contributing to increasing antimicrobial resistance among bacterial pathogens encountered in pediatrics. This study demonstrates that the availability of an accurate and rapid diagnostic method for common respiratory viruses was associated with decreased use of antimicrobials in infants and children hospitalized for viral respiratory illnesses. Rapid and accurate viral diagnostic testing should be an important component of any plan for the containment of antimicrobial resistance.

Accepted for publication August 1, 2002.

Dr Byington is supported by the Robert Wood Johnson Generalist Physician Faculty Scholar Program.


We thank Charles Hoff, PhD, for his assistance with statistical analysis.

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