Concurrent Serious Bacterial Infections in 2396 Infants and Children Hospitalized With Respiratory Syncytial Virus Lower Respiratory Tract Infections

Kevin Purcell, MD, PharmD, RPh; Jaime Fergie, MD

**Background:** At Driscoll Children’s Hospital (Corpus Christi, Tex), we observed that most infants and children hospitalized for treatment of respiratory syncytial virus (RSV) bronchiolitis and/or pneumonia received broad-spectrum intravenous antibiotics despite having typical RSV signs and symptoms and positive RSV–rapid antigen tests on admission. Physicians were concerned about the possibility of concurrent serious bacterial infections, especially in infants younger than 3 months and in those with infiltrates present on the chest x-ray films.

**Objective:** To report the frequency of concurrent serious bacterial infections in infants and children hospitalized for treatment of RSV lower respiratory tract infections.

**Methods:** The medical records of 2396 infants and children admitted to Driscoll Children’s Hospital with RSV bronchiolitis and/or pneumonia during 7 RSV seasons from July 1, 1991, through June 30, 1998, were reviewed.

**Results:** There were positive cultures obtained from initial sepsis/meningitis workups on admission in 39 infants and children (1.6%). Of these, 12 (31%) were positive blood cultures and 27 (69%) were positive urine cultures. There were no positive cerebrospinal fluid cultures. All of the positive blood cultures contained either *Staphylococcus epidermidis*, *Staphylococcus warneri*, or *Bacillus* species, which are common contaminants. None of the patients received a standard 10-day course of intravenous antibiotic therapy. All of the positive urine cultures were typical urinary tract pathogens. All of the patients were treated.

**Conclusions:** Concurrent serious bacterial infections are rare in infants and children hospitalized with RSV lower respiratory tract infections and the empiric use of broad-spectrum intravenous antibiotics is unnecessary in children with typical signs and symptoms of RSV bronchiolitis.

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**AT DRISCOLL Children’s Hospital, a tertiary care pediatric teaching hospital in Corpus Christi, Tex, we observed that infants and children hospitalized for treatment of respiratory syncytial virus (RSV) bronchiolitis and/or pneumonia usually received broad-spectrum intravenous (IV) antibiotics despite having typical signs and symptoms of RSV and positive RSV rapid antigen tests on admission. Once started, antibiotics were almost always continued until discharge. Since many infants and children had fever at admission in addition to a several-day history of rhinorrhea, congestion, and wheezing, physicians were concerned about the possibility of concurrent bacterial infections, especially in infants younger than 3 months and in those with infiltrates present on chest x-ray films. Based on our experience and the literature,1-7 we believed that concurrent serious bacterial infections on admission were rare in infants and children hospitalized with RSV lower respiratory tract infections. We also thought that the empiric use of broad-spectrum IV antibiotics was unnecessary in infants and children with typical signs and symptoms of RSV bronchiolitis and possibly even detrimental. Hall et al8 showed in a large, prospective study that the treatment of RSV lower respiratory tract infections with broad-spectrum IV antibiotics actually increased the risk for bacterial superinfection. These investigators also found that 2.0% of infants and children hospitalized for treatment of RSV infections had concurrent serious bacterial infections on admission (types of infections not reported). Simultaneous infection with RSV and other respiratory pathogens has been documented by Tristan et al9 and 2 cases of bacterial pneumonia10,11 have been reported in infants with bronchiolitis based on posi-
SUBJECTS AND METHODS

As part of a study assessing the effectiveness of a multifaceted academic detailing program on physician-prescribing of ribavirin and antibiotics, the medical records of 2396 infants and children admitted to Driscoll Children’s Hospital with RSV lower respiratory tract infections during 7 RSV seasons from July 1, 1991, through June 30, 1998, were reviewed. Subjects were identified via a medical records search for International Classification of Diseases, Ninth Edition (ICD-9) discharge diagnoses of RSV bronchiolitis or RSV pneumonia. Only medical records of infants and children with positive RSV rapid antigen tests or nasopharyngeal viral cultures positive for RSV as recorded in the microbiology section of the laboratory results were reviewed. Data were collected on age, sex, dates of admission, lengths of stay, pediatric intensive care unit admissions, ribavirin use, antibiotic use, initial sepsis/meningitis workup culture results, and presence of risk factors associated with increased morbidity and mortality as defined in the 1993 American Academy of Pediatrics guidelines for ribavirin use.

Antibiotic use was defined as the prescribing of a broad-spectrum IV antibiotic (second- or third-generation cephalosporin) in the admission orders. Oral antibiotics were not considered. Subsequent physician orders were reviewed to determine if the IV antibiotic was continued. A sepsis work-up included blood and urine cultures while a meningitis work-up included blood, urine, and spinal fluid cultures. Only sepsis/meningitis workups done on admission (the first day of hospitalization) were included. Bacterial infections were considered to be concurrent if they were present along with RSV infections at the time of admission and identified through the initial sepsis/meningitis work-up. This is in distinction to secondary (subsequent) bacterial infections as identified by Hall et al10 that arose during hospitalization in association with the treatment of RSV infections with broad-spectrum IV antibiotics.

Descriptive statistics were performed with SPSS (SPSS Inc, Chicago, Ill). The institutional review board at Driscoll Children’s Hospital approved this research project.

RESULTS

The mean±SD age of our patients was 237±251 days. Almost all of the patients (95.3%) were younger than 2 years, with 79.0% younger than 1 year, 33.6% younger than 90 days, 11.9% younger than 6 weeks, and 6.1% younger than 30 days. Most of the patients were boys (59%). The mean±SD length of stay was 5.2±5.6 days and 8.3% of the patients were admitted to the pediatric intensive care unit, with 7.3% requiring mechanical ventilation. Although most of the patients were otherwise normal and healthy, 10.3% were premature and 17.0% had an underlying disease. The most common underlying diseases were congenital heart disease (6.3%), bronchopulmonary dysplasia (4.9%), neurological problems (3.2%), multiple congenital anomalies (1.4%), and metabolic disorders (0.9%). Broad-spectrum IV antibiotics (second- or third-generation cephalosporin) were prescribed on admission in 70.5% of all patients. Once started, antibiotics were continued until discharge 97.0% of the time. The overall RSV mortality rate was 0.25%.

Positive cultures from the initial sepsis/meningitis work-ups were obtained on admission in 39 patients (1.6%). Of these, 12 (31%) were positive blood cultures and 27 (69%) were positive urine cultures. There were no positive cerebrospinal fluid cultures. All of the positive blood cultures were either Staphylococcus epidermidis, Staphylococcus warneri, or Bacillus species, which are common contaminants. Data were not collected on whether these patients had clinical evidence of sepsis syndrome. However, none of the patients received a standard 10-day course of IV antibiotic therapy for sepsis. All of the positive urine cultures grew only one organism and 74% (20) occurred in boys. The bacteria isolated were typical urinary tract pathogens. All of the patients in this study were treated for urinary tract infections.

COMMENT

In our study, very few infants and children hospitalized with RSV bronchiolitis and/or pneumonia had concurrent serious bacterial infections. Our results are consistent with the findings of one large prospective study and several other smaller retrospective studies. Hall et al10 found that 13 (2%) of 635 infants and children hospitalized for treatment of RSV lower respiratory tract infections had concurrent bacterial infections on admission. The types of bacterial infections identified were not reported for these patients. Liebelt et al11 found no cases of concurrent serious bacterial infections in 211 infants younger than 90 days with bronchiolitis. Kuppermann et al12 also found no cases of bacteremia in 156 children younger than 2 years with bronchiolitis. However, 1.9% of these patients had urinary tract infections. Greenes and Harper13 found a 0.2% rate of bacteremia in 411 children aged 3 to 36 months with bronchiolitis. One child had a positive blood culture for S pneumoniae. Antonow et al14 found that 4 (1.5%) of 262 infants younger than 60 days with signs and symptoms typical of bronchiolitis had concurrent serious bacterial infections. Three infants had urinary tract infections and 1 had a blood culture positive for S pneumoniae.

The positive blood cultures obtained from the patients in this study were due to contaminants. This underscores the principle that in a population with a low incidence of disease, a positive result has an extremely low positive predictive value. Thus, only 1.1% of the patients in our study may have had actual concurrent serious bacterial infections on admission. All of the pa-
patients had urine cultures positive for organisms. However, a 1.1% frequency of positive urine cultures may be explained by asymptomatic bacteriuria and does not necessarily represent cases of true concomitant urinary tract infections. Wettergren et al. found a 0.9% frequency in girls and a 2.5% frequency in boys of bacteriuria during the first year of life. The 1.1% frequency of bacteriuria in our study patients is consistent with these data. Hoberman et al. reported a 3.5% prevalence of urinary tract infections in febrile infants among those with a possible source of fever (eg, bronchiolitis, otitis media, etc). The authors concluded that asymptomatic bacteriuria was an unlikely explanation for all of the positive urine cultures since the frequency of 3.5% observed was substantially greater than the mean value reported in symptom-free infants by Wettergren et al.

Although there is a practice guideline for the treatment of infants and children aged 0 to 36 months with fever without a source, there is no guideline that specifically addresses the treatment of febrile infants and young children with clinical evidence of viral infections. Fever occurs in 45% to 65% of infants and children hospitalized with RSV lower respiratory tract infections. The cost of performing sepsis/meningitis workups in all of these infants and children, as well as the discomfort to the child (and stress to the family), is significant. Antonom et al. found that 49.6% of infants younger than 60 days admitted with bronchiolitis underwent sepsis workups. The infants who underwent sepsis workups had an average total charge of $4507 and a length of stay of 3.4 days compared with $2998 and 2.8 days for those not undergoing workups. Additionally, the cost of continuing broad-spectrum IV antibiotics until discharge 97.0% of the time in infants and children with RSV lower respiratory tract infections, as observed in our study, can be significant in terms of dollars spent and the potential development of antibiotic resistance.

This retrospective study has several limitations. The database was assembled as part of an academic detailing study. Only general patient demographics and specific data that were needed to assess the outcomes of a multifaceted academic detailing program were collected. No data were obtained on temperature, white blood cell count with differential cell count, or chest x-ray film. Also, data were not collected on the number of infants and children who underwent sepsis/meningitis workups, only on the number of patients with positive cultures. However, even though not all of the patients had cultures obtained, it is unlikely that any other patients had serious bacterial infections, although some cases of asymptomatic bacteriuria may have been missed. All patients were observed in the hospital for an average of 5.2 days and review of their medical records did not reveal any subsequent readmissions for missed bacterial infections.

Concurrent serious bacterial infections are rare in infants and children hospitalized with RSV lower respiratory tract infections. Performing all of these cultures (full sepsis/meningitis workups) on admission in infants and children with typical signs and symptoms of RSV bronchiolitis and a positive RSV rapid antigen test, even in the presence of fever, is unnecessary and adds to the cost, discomfort, and stress of the hospitalization. However, laboratory testing for bacterial infections should be considered in severely ill-appearing infants and children with atypical signs and symptoms or clinical courses due to the small but real possibility of concurrent serious bacterial infections.

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Corresponding author and reprints: Jaime Fergie, MD, Driscoll Children’s Hospital, Corpus Christi, TX 78411 (e-mail: fergie@driscollchildrens.org).

REFERENCES