SHORT REPORT

Pulmonary and systemic bacterial co-infections in severe RSV bronchiolitis

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In 127 infants admitted to intensive care for RSV bronchiolitis, concomitant bacterial sepsis was a rare event. However, in the subgroup of intubated patients the incidence of bacterial pneumonia was 43.9% (95% CI 31.0–56.8%), half community acquired and half nosocomial. As clinical signs are not helpful in identifying these patients, tracheal aspirates have to be investigated microbiologically on a routine basis in order to start antibiotics in time.

About 10% of hospital admissions for respiratory syncytial virus (RSV) infection need intensive care unit (ICU) treatment.[1] Bacterial invasion may aggravate the clinical course. Neither percentage nor impact of bacterial co-infections on outcome in infants with severe RSV disease have been very well studied. Furthermore, it is not clear whether the described bacterial co-infections were community acquired or nosocomial.

The present study aimed at determining the proportion and aetiology of bacterial respiratory co-infections and sepsis in patients with RSV infection admitted to the ICU. To establish the diagnosis of bacterial pneumonia we took advantage of tracheal aspirate analysis which is possible in intubated patients. We further analysed whether bacterial co-infections influenced the clinical course. Our data are important in order to decide whether initial antibiotics are justified in infants severely affected by RSV.

METHODS

We included infants admitted with RSV bronchiolitis to the ICU of the University Children's Hospital of Zurich during 1997–2001. In patients with multiple admissions, only the first RSV episode was taken for analysis. Length of hospital and ICU stay, occurrence of bacterial pneumonia and sepsis, systemic inflammatory response syndrome (SIRS) on the day of ICU admission, use of antibiotics, artificial ventilation parameters, and mortality data were gathered from the records.

Respiratory compromise was quantified using: (1) highest oxygenation index (mean airway pressure × FiO_2/paO_2) in the first 24 hours of artificial ventilation; and (2) the respiratory severity score[2] on admission and before intubation in spontaneously breathing patients. According to their infectious state, the RSV patients were assigned to five groups (table 1).

RSV was identified in nasopharyngeal or tracheal aspirates by means of an antigen test (Test Pack Abbott). Sepsis was diagnosed when both a positive blood culture (pathogenic bacteria) and an SIRS were present. Bacterial pneumonia was diagnosed only in tracheally intubated patients and if their tracheal aspirate showed significant growth of relevant bacteria (table 2) and presence of a significant number of leucocytes (both ⩾2+ on a scale from no leucocytes/bacteria to 3+). Tracheal specimens were routinely taken in all intubated patients, either at ICU admission when already intubated or directly after intubation plus on clinical grounds thereafter. Pathogenic agents detected in samples from the first 48 hours after hospital admission were regarded as community acquired and thereafter as nosocomially acquired.

RESULTS

The inclusion criteria were met by 127 patients (median age 1.7 months, range newborn to 5.8 years). Fifty seven patients (45% of the whole sample) were mechanically ventilated (conventional ventilation 46; high frequency oscillation 11). The remaining infants were managed by non-invasive CPAP alone (n = 8), nasal prong oxygen alone (n = 53), and no supplemental oxygen at all (n = 9). There was one death (no SIRS, no bacterial co-infection).

Tracheal cultures were taken in all but one mechanically ventilated patients (in the first hour after intubation or at ICU admission if already intubated). There were 25 infants with concomitant bacterial pneumonia, resulting in a risk of bacterial pneumonia in intubated infants of 25/57 (43.9%, 95% CI 31–57%). About half of these infections were community acquired and half were nosocomial (table 1).

Overall, the incidence of sepsis was 3/127 patients (2.4%, 95% CI 0–5%); related to the number of blood cultures, this ratio was 3/75 = 4%. Two episodes were community acquired (table 1).

The five groups did not differ significantly in length of stay and respiratory parameters (table 1). Table 2 shows the bacteria isolated from tracheal aspirates and blood specimens.

During the first two hospital days, 73 patients were given antibiotics. Since only 14 patients had severe bacterial infections on admission (community acquired bacterial pneumonia/sepsis; table 1), 59 patients (46.5% of the whole patient sample) were initially unnecessarily treated with antibiotics. There was a high proportion of patients receiving antibiotics in the groups without bacterial pneumonia and/or sepsis (table 1: groups 1 and 2). In the SIRS positive, sicker looking infants, antibiotic use was higher (67%) than in the SIRS negative infants (53%) (p = 0.11, Fisher's exact test).

DISCUSSION

In infants hospitalised in the ICU for RSV bronchiolitis, sepsis was rare, as confirmed by others.[1] The risk of bacterial pneumonia in intubated infants was 43.9% and corresponded roughly with numbers found in non-ICU RSV patients (32% and 59%).[3 4] However, pneumonia in the latter patients was diagnosed on clinical signs and radiological findings only. In

Abbreviations: ICU, intensive care unit; RSV, respiratory syncytial virus; SIRS, systemic inflammatory response syndrome

Table 1 Length of stay, respiratory parameters, and antibiotic use in RSV patients with and without SIRS or bacterial co-infections

	Group 1 SIRS negative (no sepsis, no pneumonia) (n = 54)	Group 2 SIRS positive (no sepsis, no pneumonia) (n = 46)	Group 3 Bacterial pneumonia (no sepsis) (n = 24)	Group 4 Bacterial sepsis (no bacterial pneumonia) (n = 2)	Group 5 Bacterial sepsis and pneumonia (n = 1)	All patients (n = 127)
Community acquired bacterial pneumonia/sepsis	NA	NA	12 (50%)	1 (50%)	1 (100%)	14 (11%)
Length of hospital stay, days	11 (1–158)	9 (1–298)	10 (1–168)	12, 12	8	10 (1–298)
Length of ICU stay, days	4 (0–76)	3 (0–298)	6 (1–62)	9, 12	5	4 (0–298)
Mortality	1 (1.9%)	0	0	0	0	1 (0.8%)
Mechanical ventilation	19 (36%)	12 (26%)	24 (100%)*	1	1* (100%)	57 (45%)
Intubation time, days	5.5 (1–76)	6.5 (0–298)	4 (0–50)	6	4	5 (0–298)
Nitric oxide	7 (13%)	3 (7%)	2 (9%)	1	0	13 (10%)
RSS on admission	8 (3–9)	8 (3–9)	7 (6–9)	8, NA	9	8 (3–9)
RSS before intubation or CPAP	8 (2–9)	8.5 (5–9)	7 (5–9)	NA	9	8 (2–9)
Highest oxygenation index	7.5 (1.4–28.6)	5.0 (2.6–14.4)	6.1 (1.7–14.4)	NA	NA	6.0 (1.4–28.6)
Antibiotics	29 (54%)	31 (67%)	23 (96%)	2 (100%)	1 (100%)	86 (68%)

NA, not applicable or no data; RSS, respiratory severity score (minimal score: 0, maximal score: 9).
*According to the study design, pneumonia was only diagnosed in intubated patients, thus leaving 100% of intubated patients in groups 3 and 5.
Results are given as median (range) or number (%). Some upper ranges for length of stay and ventilation are quite high, because a few patients were cared for and ventilated for other reasons after resolution of their RSV infection.

Table 2 Bacteria isolated in tracheal aspirates and blood specimens from infants with RSV bronchiolitis and bacterial co-infections

	Bacterial pneumonia*		Bacterial sepsis†	
Isolate	Community acquired	Nosocomial	Community acquired	Nosocomial
Haemophilus influenzae	8	9		
Moraxella catarrhalis	6	6		
Streptococcus pneumoniae	5	4	2	
Streptococcus pyogenes				1
Staphylococcus aureus	3	5		
Pseudomonas aeruginosa				1

*n = 25 infants, 15 tracheal aspirates with >1 microorganism (maximum 3 microorganisms).
†n = 3 infants, 1 blood culture with 2 microorganisms (*Streptococcus pyogenes* and *Pseudomonas*).

our study, the numbers for bacterial co-infections may be a conservative estimate as: (1) for methodological reasons, a diagnosis of bacterial pneumonia was only made in intubated patients; and (2) there were infants already on antibiotics when cultures were taken, thus preventing possible bacterial infections from being diagnosed. Bacterial co-infection does not add specific symptoms to the clinical signs already present in RSV bronchiolitis. Therefore, a diagnosis of bacterial pneumonia was only attempted in cases where a tracheal aspirate was available for microbiological investigation. The inconstant relation between the timing of cultures and start of antibiotic treatments is an important limitation in this retrospective study.

The presence of concomitant bacterial pneumonia did not aggravate the clinical course in our sample (table 1: group 3 *v* groups 1 and 2). Furthermore, the clinical parameters did not differ between SIRS negative and SIRS positive patients (without concomitant bacterial infections). Obviously, the presence of systemic inflammation as well as bacterial pneumonia (if treated correctly) does not influence the hospital course in infants with severe RSV bronchiolitis. The clinical course might be rather influenced by RSV specific consequences such as apnoea and lung disease.

No previous study assessed bacterial co-infections in the subgroup of infants with severe RSV bronchiolitis—that is, in infants admitted to the ICU. Furthermore, the diagnostic criteria for bacterial infections were very vague.[3 4] We diagnosed bacterial pneumonia and sepsis specifically as we used rigorous criteria.

According to our data, almost half of the patients were initially unnecessarily treated with antibiotics. However, in intubated RSV patients the number of unnecessarily treated patients was lower due to the high proportion of bacterial pneumonia. A high percentage of infants with RSV bronchiolitis are given antibiotics at ICU admission,[5] usually on the basis of clinical signs, such as fever, young age, ''ill looking'' appearance, respiratory deterioration, or laboratory parameters (leucocytosis, C reactive protein).[5] Antibiotics are of no benefit in RSV bronchiolitis.[6 7] It has been suggested that in infants admitted for acute lower respiratory tract infections, routine antibiotic treatment is not indicated, even if pulmonary consolidations are present.[6] However, in these studies, infants on mechanical ventilation[6] or with supposed sepsis[7] were excluded from analysis.

In infants with RSV bronchiolitis severe enough to require ICU admission, bacterial pneumonia (community acquired or nosocomial) is a frequent complication in the subgroup of patients who need to be mechanically ventilated. As clinical signs such as SIRS symptoms are not helpful in identifying these patients, tracheal aspirates have to be investigated microbiologically on a routine basis in order to restrict antibiotic use to the infants in real need of it.

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ARCHIVIST

Dilated cardiomyopathy: immunosuppressive treatment and long term outcome

Patients with dilated cardiomyopathy (DCM) have a large, poorly contractile, left ventricle. The causes of DCM are unknown but viral infection and/or autoimmunity are the favourite suggestions. Endomyocardial biopsy (EMB) studies have suggested two types of DCM; those with mononuclear infiltration of the myocardium (myocarditis) and those with only fibrosis (cardiomyopathy). With conventional non-immunosuppressive, treatment the outlook for these children has been poor with reported survival rates of 40–75% at 1 year and 37–47% at 5 years. Children, but not adults, with myocardial fibrosis tend to do worse than those with myocarditis and there is evidence that immunosuppressive treatment may be more effective in patients with myocarditis. Researchers in Rome (Maria G Gagliardi and colleagues. *Heart* 2004;**90**:1167–71) have reported a long-term observational study. Between March 1986 and December 2001 a total of 114 children (mean age 3 years 1 month, range <1 month to 19 years 9 months) were referred to the department with recent onset DCM and congestive heart failure. Heart defects and metabolic causes of DCM were excluded and all had EMB. The histological classification was: acute florid myocarditis (35), borderline myocarditis (35), and non-inflammatory cardiomyopathy (44). Children in the two myocarditis groups were treated with prednisone and cyclosporine in addition to conventional treatment whereas those with cardiomyopathy received only conventional treatment. The actuarial probability of event-free survival at 1 year was 0.96 in the myocarditis groups and 0.61 in the cardiomyopathy group. The probabilities of event-free survival at 13 years were 0.83 and 0.32. No patient in the acute florid myocarditis group died. Six in the borderline myocarditis group and three in the cardiomyopathy group died without heart transplant. Heart transplantation was performed in 32 patients; one with acute myocarditis, four with borderline myocarditis, and 27 with cardiomyopathy. Ten of the 27 died after transplantation. Complete recovery of cardiac function occurred in 79%, 64%, and 36% of survivors in the three groups respectively. Three factors predicted poor outcome: reduced left ventricular ejection fraction, increased left ventricular end diastolic volume, and non-inflammatory histology. Serial biopsies often showed resolution of the inflammatory changes in the children with myocarditis.

The children treated with immunosuppression in this series appeared to do better than children in previously reported series not given immunosuppression. The authors of this paper believe that a randomised trial might be unethical.