Significance of Respiratory Syncytial Virus (RSV) Infection in the 1st Year of Life

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Summary

Background: In this study we investigated the frequency, symptoms and predisposing factors of respiratory syncytial virus (RSV) infection during the 1st year of life in infants with obstructive airway disease in comparison with infants without airway disease.

Patients: We enrolled 216 infants in their 1st year of life, who were hospitalized because of obstructive airway disease. As an age- and sex-balanced control group, we examined 133 infants hospitalized for other reasons than airway disease.

Method: A deep pharyngeal swab was taken from all infants and immediately examined for the presence of RSV antigen by using an enzyme immunoassay (Directigen®). Patient data were surveyed by a questionnaire.

Results: The frequency of RSV infections among infants with obstructive airway disease (34.3%; n = 74) differed significantly from the control group (15%; n = 20; p < 0.01). The frequency of RSV-infected infants with obstructive airway disease decreased with age ranging from 39.1% in trimenon I to 29.0% in trimenon IV. This trend was not observed in the control group. With respect to clinical symptoms and risk factors, there were no differences between RSV-infected versus noninfected infants.

Conclusion: RSV is an important agent causing lower obstructive airway disease (34.3% of all patients). There are no specific symptoms that can be used for diagnosing RSV infection. In order to prevent other patients on the ward from contracting nosocomial RSV infection and in the light of therapeutic options, one should test newly admitted patients presenting with symptoms of an obstructive airway disease for RSV antigen. On a ward with high-risk patients, we would recommend the use of an RSV test for all new patients.

Introduction

Respiratory syncytial virus (RSV) is the most important agent for obstructive airway disease of the lower respiratory tract in the 1st year of life. RSV infections appear epidemically every year between December and April [1–3].

In adults and children above 2 years of age, RSV infection leads to trivial flu with cough, rhinorrhea and seldom fever. However, during the 1st year of life it will cause a major airway disease with cough, breathlessness, wheezing and signs of chest overinflation. This appears to be related to the declining protective maternal antibody levels accompanied by a lack in the infant's immune system. The infection leads to obstructive bronchitis, interstitial pneumonia, and bronchiolitis and frequently to the hospitalization of the patients. In children with other severe diseases like pulmonary dysplasia or vitium cordis, the illness will take a more serious course [1–7, 14].

The cytopathological changes in lower airways include not only loss of the ciliae, hydropical swelling and necrosis, but edema and inflammation-cell infiltration of the mucosa. All these changes lead to obstruction of the bronchial tubes [4, 8].

Regeneration can be reached in about 2 or 3 weeks. Sometimes morphological obstructive residuals or asthma can persist [2, 9, 10]. Therefore nosocomial infection with RSV should be avoided and a quick therapy should be administered.

This study was designed to investigate the frequency, symptoms and predisposing factors of RSV infection in the

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1st year of life in infants with obstructive airway disease in comparison with infants without airway disease.

Patients and Methods

In each of 17 different pediatric hospitals in Westphalia, we enrolled 15 children prospectively in our study between December 1993 and May 1994. We recruited 216 patients for our study, who fulfilled the inclusion criteria "hospitalization", "age between 29 and 365 days" and "illness of obstructive bronchitis, interstitial pneumonia, or bronchiolitis".

For comparison to our patient group we examined 133 healthy children during the same time in these 17 hospitals, who had no evidence of respiratory illness and who were hospitalized because of non-RSV-related diseases (enteritis, trauma). The age and sex distribution was approximated to the patient group by the matched-pairs technique.

Immediately after admission to the hospital and diagnosis of the disease, patients were examined for the presence of RSV antigen. We took a deep pharyngeal swab. Afterwards, antigens adhering to the swab were put in sterile NaCl solution. This solution was analyzed for the presence of RSV antigen by using a membrane-enzyme immunoassay (Directigen®, Becton Dickinson). This test was carried out as a bedside test in order to minimize the loss of viral material (90% within 2 h by examination by culture). The method of a nasal lavage would have been better than the deep pharyngeal swab, but in order to reduce the discomfort of the patients, we avoided nasal lavage (ethical reasons). However, by conducting the test at the bedside (minimum of time) we compensated for the loss of antigen [11].

Patient data were surveyed by a questionnaire by the doctors in charge. This questionnaire included the following parameters: age, sex, present weight, birthweight, symptoms, period of hospitalization and therapy. Results of x-ray examinations were included if this examination had been carried out (because of ethical aspects of an additional x-ray). Risk factors like cigarette smoking by the patient's parents were inquired about. In the control group, we used the same questionnaire for patient characteristics. Moreover, we asked for the cause of clinical treatment, immunosuppressive therapy and illness before and after hospital stay.

The statistical analysis was carried out by dividing the children into four trimena. The statistical significance of a possible correlation was investigated by the chi-square and the Mann-Whitney-Wilcoxon test.

Results

74 of the 216 patients examined in our study with obstructive bronchitis, interstitial pneumonia or bronchiolitis were RSV positive (34.3%) and 142 were RSV negative. In our control group of hospitalized children without respiratory disease, 20 patients were RSV positive (15%) and 113 were RSV negative. The difference between the two groups is statistically significant ($p < 0.01$) (Figure 1).

In the patient group with respiratory illness, 69 children were between 29 and 90 days of age (32.9%), 73 children 91-180 days (22.8%), 43 children 181–270 days (19.9%), and 31 children 271–365 days of age (14.4%) (corresponding to trimenon I–IV). Age distribution of the control group was adjusted to that of the patient group. With increasing age, the percentage of RSV-positive patients declined in the patient group, whereas the percentage of RSV-positive children in the control group remained constant (trimenon I: 39.1%/9.3%, trimenon II: 34.2%/18.6%, trimenon III: 30.2%/17.9%, trimenon IV: 29.0%/15.8%).

In the different diagnoses double designations were possible. 96.7% (n = 195) were diagnosed as having obstructive bronchitis, 27.2% (n = 53) interstitial pneumonia and 9.4% (n = 18) as bronchiolitis. The percentage of RSV-positive patients was highest among those with bronchiolitis (61.1%), followed by obstructive bronchitis (34.6%) and interstitial pneumonia (30.2%). The result is significant for patients with bronchiolitis ($p < 0.01$) and with obstructive bronchitis ($p = 0.05$), but not for patients with interstitial pneumonia ($p = 0.4$) (Figure 2).

Symptoms in the RSV-positive and negative group were similar. No child died in our study.

More boys (62.2%) than girls (37.8%) were hospitalized because of an illness of the respiratory system. Among
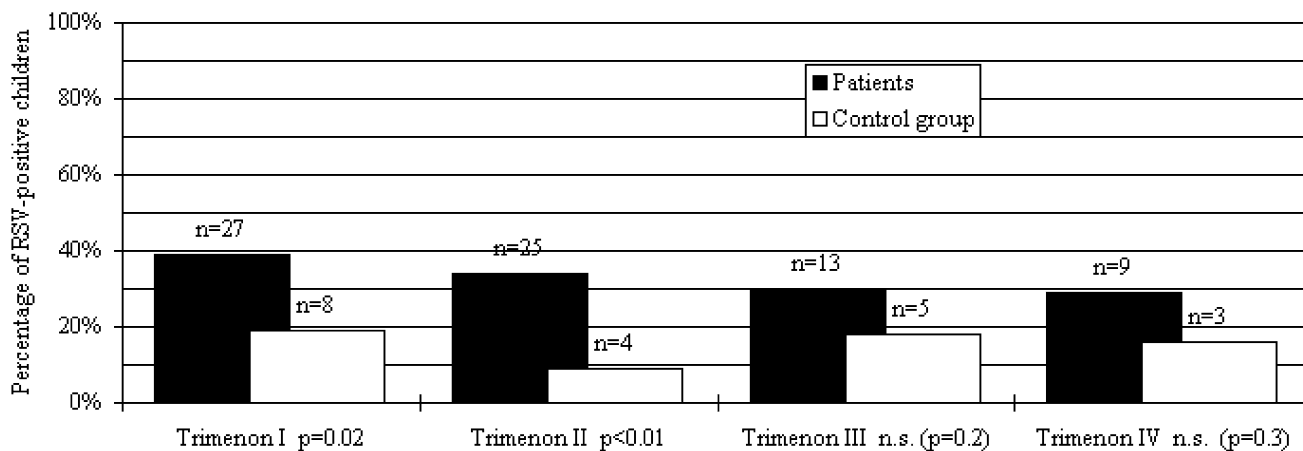

Figure 1
RSV-positive patients divided by age in comparison to the control group without airway disease and the significance of the difference.

boys the percentage of RSV-positive patients was 35.6% and among girls 32.1% (not significant).

Regarding the predisposing factors, no differences between RSV-positive and negative children were observed.

Discussion

RSV is the most important cause of obstructive airway disease in the 1st year of life. According to previous studies, 34.3% of all obstructive airway diseases are caused by RSV [1, 6]. It is the predominant pathogen of bronchiolitis (60% in our study) [1].

Whereas the distribution of age in our control group remained at a constant level in all age-groups, it reached a peak in 2 to 6 months in our patient group. This supports the hypothesis that in the first 6 months of life there is a predisposing factor for the outbreak of RSV diseases, such as immunodeficiency and not a high exposition to the virus.

The symptoms were similar with RSV-positive and negative patients. This proves that the right patients were included in the study. Moreover, it shows the inability to diagnose RSV infection on the basis of symptoms. It is necessary to use laboratory methods. Thus one should use an RSV test like the enzyme-immunoassay for all new patients with obstructive airway disease in the 1st year of life in order to arrive at the correct diagnosis. Reliable and quick results can be obtained by a bedside test (attaining the best results because there is no loss of viral material [11]). With the correct diagnosis very ill patients can be treated specifically with ribavirin or hyperimmune sera [12, 13, 15, 16].

On the other hand, one can protect other patients from getting nosocomial RSV infection on the ward. 30% of all hospitalized RSV diseases are acquired nosocomially [17]. *Madge* et al. could reduce all nosocomially acquired RSV infections to 3% by cohort-nursing and the use of gowns and gloves [18, 19]. Thus it is possible to reduce nosocomial RSV infections from 30 to 3% by carrying out a simple RSV test. On intensive care wards with high-risk patients (bronchopulmonary dysplasia, vitium cordis, intensive care treatment) it is necessary to avoid this kind of infection, especially because of severe courses of RSV infections. Our study shows that 15% of all healthy children in the 1st year of life are colonized with RSV. Accordingly, on wards with high-risk patients, all new patients should be tested for the presence of RSV in order to avoid a dangerous infection of other patients.

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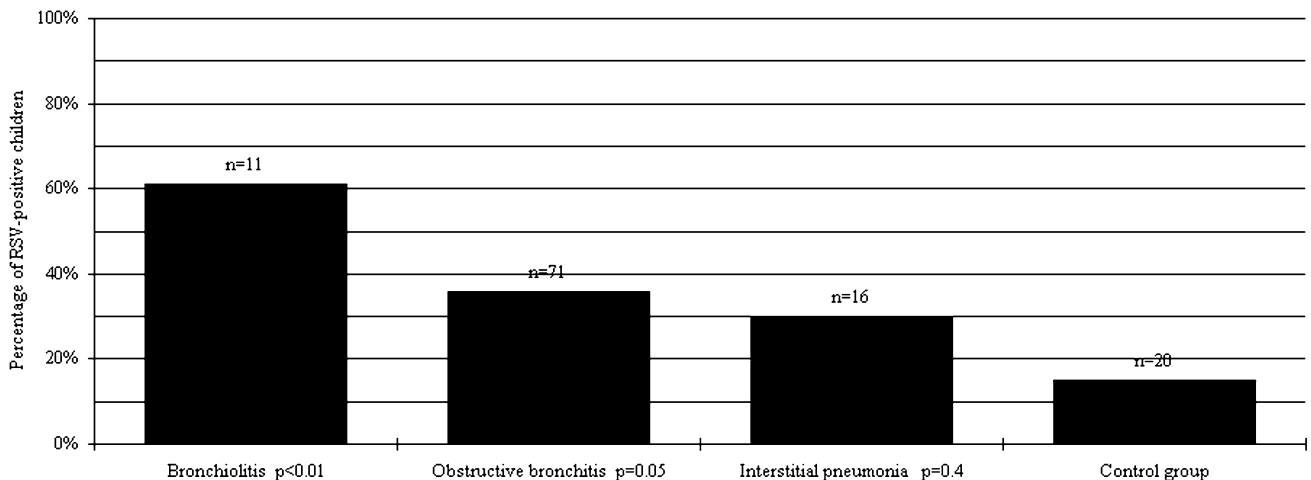3. Sinnott JT, Gilchrist L, Ellis L: Respiratory syncytial virus. Infect Control Hosp Epidemiol 1988; 9: 465–468.

Figure 2
RSV-positive patients with airway disease and their diagnosis in comparison to the control group without airway disease. Significance of the correlation between diagnosis and RSV result.

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