RSV Pneumonia in the Pediatric Intensive Care Unit

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Abstract

Objective: Respiratory syncytial virus (RSV) is the most common and fatal cause of bronchiolitis and severe pneumonia, especially in infants. Its morbidity and mortality are unpredictably high in critically ill patients. The aim of our study is to identify high-risk patients for early diagnosis and treatment of RSV pneumonia in the pediatric intensive care unit and to reduce hospitalizations and mortality. We want to emphasize the importance of vaccination and follow-up for the protection of other viral or bacterial pneumonia once again.

Material and Methods: We present 12 cases that were diagnosed as RSV pneumonia in our tertiary pediatric intensive care unit. Besides history, physical examination, and chest radiograph findings, patients were diagnosed with laboratory tests, such as complete blood count, c-reactive protein (CRP), and virus isolation with nasal smear samples. Demographic, clinical, and laboratory data were obtained from patients' medical files.

Results: Within 5 months of the study, 12 patients were diagnosed with RSV pneumonia. Risk factors were present in 11. Two of the patients were 35 weeks premature; others were born full-term, and none of them had received palivizumab prophylaxis. Except for a patient with a history of episodes of bronchiolitis, all of the patients had one or more risk factors for pneumonia. Nine of the patients (75%) were male, while 3 were female. Median age was 18.5 months (min: 2; max: 53 months). Five of our patients required mechanical ventilation. Two patients could not be separated from the ventilator; so, tracheostomy was performed and patients were discharged with home ventilation. One of the patients included in the study died.

Conclusion: We want to emphasize that RSV, seen especially in infants, is also an important factor in older children; it might be fatal, and pediatric intensive care admission might be necessary. Therefore, before determining medical therapy, underlying risk factors should be remembered.

(J Pediatr Inf 2014; 8: 12-7)

Keywords: Respiratory syncytial virus, risk factors, children

Received: 09.09.2013
Accepted: 23.01.2014

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DOI:10.5152/ced.2014.1587

Introduction

Respiratory Syncytial Virus (RSV), which is an enveloped RNA virus from paramyxovirus family, has taken on this particular name due to its tendency to generate sinsitiya in tissue cultures. Respiratory Syncytial Virus is a very contagious virus and is transmitted through human to human interaction or contaminated objects (1). Majority of children will have gone through the RSV infection in winter by the age of two. It is commonly known that it may cause lower respiratory tract infections such as bronchiolitis and pneumonia in all human beings especially in children aged less than 1. However, it is known that it may progress with a more serious clinical table and cause higher mortality rates in infants and high risk pediatric patients with suppressed immune system (2).

While Respiratory Syncytial Virus infection has some seasonal characteristics, it may cause epidemics in the months of November and April. It is known that Respiratory Syncytial Virus annually generate roughly 34 million episodic acute lower respiratory tract infections in children under the age of 5 and this finally results in 3,4 million hospitalizations all over the world. Moreover, it is estimated that there are approxi-

mately as many as 199000 RSV pneumonia-based pediatric mortalities every year (3). The RSV infection experienced in infancy may cause reactive airway disease in the future. As a result, there is higher risk of asthma and bronchiolitis (4).

Due to the fact that Respiratory Syncytial Virus is a prevalent and contagious virus, that it causes acute life threatening respiratory tract infections in infants and risky patients, that the main treatment should be supportive care and that there is no effective medical treatment, protection from the infection becomes all the more important. Being well-informed about the risk factors of RSV and quick onset of appropriate treatment and support are known to decrease mortality in those patients. It is the aim of this study to emphasize the clinical progression and complications patients hospitalized due to lower respiratory tract infections in the Pediatric Intensive Care Unit (PICU).

Material and Methods

Patients hospitalized in the Pediatric Intensive Care Unit of Ankara Child Health Hematology Onkology Education and Research Hospital throughout the whole RSV season (between1st of November-31st of March, 2013) with the diagnosis of bronchiolitis and pneumonia and RSV-positivity detected in their nasal wipe samples were included in the study. The samples taken from the patients were analyzed via the method of multiplex polymerase chain reaction (PCR) at the Virology Laboratory of Ankara Refik Saydam Sanitation Center. Information regarding demographic data inclusive of patients' age, weight and gender, the underlying chronic diseases and vital symptoms inclusive of fever as well as WBC (leukocyte count), CRP (C-reactive protein) and biochemistry values were scanned and recorded retrospectively onto a form. The reference values for CRP in our hospital were 0-0.8 mg/dL. Since it was reported that critical patients who had RSV-related lower respiratory infection may develop hyponatremia (5), the Sodium (Na) values of the patients were recorded. Hyponatremia was defined as <130 mmol/L. Fever was monitored by using a ready-to-use commercial tympanic thermometer that measured it tympanic membrane on the ear and measurements over 38°C were accepted as fever. Detection of another virus together with RSV on a viral panel through nasal wipe sample was defined as co-infection. Patients' date of admission to hospital, whether the patient needed respiratory support treatment (mechanic ventilation) and developing complications were recorded. As a risk group; those born under 35 weeks, those with bronchopulmonary dysplasia, congenital heart disease, neuromuscular diseases, those with a immunocompromised condition such as leukemia or bone marrow transplantation, those with congenital or acquired immune deficiency, also those infants under 6 months after the onset of RSV season, exposure to smoking, atopy history, malnutrition and those with low birth weight were determined (6).

Statistical analysis

Descriptive statistics were calculated by using SPSS 20 statistical package program. Approval was obtained from the ethical committee of our hospital on the 24.09.2013 for our study.

Result

Throughout the five-month duration of this study, a total of 12 patients diagnosed with RSV-related pneumonia were monitored in the 14-bed Pediatric Intensive Care Unit (PICU). While 11 of the patients had a risk factor, only one patient did not have it. While two of the patients were 35-week premature babies, the rest of the babies were born mature and none of them took palivizumab prophylaxis. Apart from one patient with a history of bronchiolitis attack, the rest of the patients had one or more risk factors. While 9 (75%) of the patients were male and 3 female, age-median value was 18.5 months (min: 2 months, max: 53 months).

While three patients who were admitted with a diagnosis of bronchiolitis at the Pediatric Infection ward were later transferred to PICU due to increase in breathing problems and decrease in saturation values, 9 patients were admitted to PICU directly from Pediatric Emergency. Seven patients had fever (58%) on admission to hospital. It was calculated that minimum hospitalization was 3 days; maximum 70 days; median 17 days; minimum intensive hospitalization 1 day; maximum 50 days; median 6.5 days. The CRP value of the patients on admission was minimum 0.1, maximum 5.2, median 2.75, white blood cell count (WBC) 11900/μL min: 5900, maximum 21100 and median 10350.

The biochemistry values of all the patients on admission were normal: Sodium value was; minimum 130, maximum 144; median 134.5 mg/dL. No hyponatremia developed in any of the patients. While only RSV was positive in the nasal wipe samples of 11 patients, one patient had HBoV (humanbocavirus) positivity together with RSV positivity. The patient who was RSV+HBoV positive was the one who was monitored with the diagnoses of mitochondrial cytopathy and epilepsy. A total of five patients needed mechanic ventilation. While four patients were intubated as soon as they were admitted to intensive care unit; one patient was intubated on the third day of admission to the unit. Duration of staying in the ventilator was minimum 10 days, maximum 50 day and median 21

days. Since they were not able to be detached from the ventilator, two patients were discharged with a home-type ventilator after opening a tracheostomy tube. In the follow-up of a patient who had bronchiolitis attack and did not have any other underlying risk factor, atelectasis developed in the lower right lobe. A patient who had to stay in intensive care unit for a total of four day due to breathing problem did not need ventilation. Of all the participant patients, only one patient (8%) died. Demographic data, duration of hospital stay, the need for mechanic ventilation (MV) and risk factors were all summarized in Table 1.

The 26 month-old male patient diagnosed with RSV pneumonia was followed up with a diagnosis of mitochondrial cytopathy and then died. Even though the CRP value of this patient was positive on admission, he had fever. The CRP value that was measured in the follow-up period after dropping of fever was checked again and it was seen that the value rose to 23 mg/dL. After the patient who initially had interstitial pneumonia findings in his chest radiography had deterioration in the follow-up and he later died after 22-day mechanic ventilator follow-up. In another case of a 25 month-old male patient diagnosed with infantile spasm and hypoxic ischemic encephalopathy (HIE) sequel, upon the resumption of fever and deterioration of clinical condition, the analyses of the CRP was performed: 1 mg/dL and WBC: 4900/µL and there was no positivity in the cultures. In the PZR analyses of the second nasal wipe, influenza virus (H1N1) was found to be positive. While there was initially no need for ventilatory support, the patient deteriorated following four weeks after the admission and needed mechanic ventilation for 21 days, and then a tracheostomy tube.

Discussion

Respiratory Syncytial Virus that causes annual epidemics especially winter and spring seasons are common all over the world (2, 7). While epidemics are prevalent generally in November and April, they reach their peak levels in January and February (8-10). Respiratory Syncytial Virus is generally transmitted through direct contact (11), it is rare for the virus to infect though droplets since the virus gets inactivated in aerosol. However, giant aerosol droplets may cause infection. After contact with infected secretions or contaminated objects, the virus initiates the infection after inoculated nasopharyngeal or ocular mucosa virus (12). Infection generally causes bronchiolitis and pneumonia table in children under 1 year old (2, 4). In patients with a risk of lower respiratory tract infection and elderly patients, the disease occurs as lower respiratory tract infection such as bronchiolitis and pneumonia (13).

The patients, who have risk factors for lower respiratory tract infection, also have the risk in terms of RSV pneumonia. While premature babies, those with an underlying chronic pulmonary disease or reactive airway disease such as bronchopulmonary dysplasia and cystic fibrosis, those with congenital heart disease, immune deficiency and immunosuppression conditions constitute the major risk factors, down syndrome, infants under 6 months, expose to smoking, atopy history, malnutrition and low birth weight, male gender, low socioeconomic conditions and crowded living environments are the additional risk factors (3, 14).

There is a strong relationship between especially reactive airway disease and RSV infections (15). The patients with asthma have a greater risk of RSV infection. Besides, it was reported that even though the infection was not a series one, in babies who had RSV infection before, it might cause recurrent and persistent respiratory tract symptoms such as coughing and wheezing (16). The risk factors mentioned above were present in all patients expect one (Table 1). In patients followed up with asthma, RSV-related pneumonia did not progress slowly and there was no MV need in any of the patients.

Even though the disease lasts for a short time and usually heals on its own, especially in infants with high risks and suppressed immunity, hospitalization may be needed and it causes significant levels of morbidity and mortality. While mortality rate in RSV-related infections was 0.5% in the previous studies, it was reported that it can be 3% and over in cases with risk factors (17). In some other studies, on the other hand, depending on some certain risk factors, it was found that mortality could be as high as 15% (18). Besides, it was also revealed that the pace of mortality in pediatric patients with heavy immune deficiency could vary between 12 to 55% (19, 20). Almost all of our cases were immune-suppressed. However, RSV progressed infection in one infant without any risk factor; however, it did not require any intensive care, and so we can conclude that RSV infection can be serious especially in infants. Despite the low number cases in our study, the mortality rate in our study (8%) was compatible with the rate in the literature.

It is thought that serious infection, intensive care admission and the need for ventilation in our patients might be related with an underlying primer disease and/or co-infection or the secondary additional infections. Bronchiolitis patients with the association of RSV+HBoV and with only RSV or only HBoV in a study conducted by Midulla et al. (21), they found that in patients with RSV+HBoV the duration of hospital stay and clinic risk scores were apparently higher. Similarly, even though HBoV in children generally progressed as upper respiratory tract infection, they also found that co-infection frequently progressed together with the complications such as asthma and pneumonia and might progress seriously

Table 1. Summary of the patients

No	Gendr.	Age(Mon.)	Hospt. Dur.(day)	MV (day)	Risk factor	Follow-up
1	M	12	16	_	35 week premature birth Serious pulmonary stenos Exposure to smoking	Transfer to ward after 9-day stay in the PICU
2	F	50	3	_	Follow-up with Asthma bronchiole diagnosis	Transfer to ward after 1-day stay in the PICU
3	F	53	3	_	Low birth weight Follow-up with Asthma bronchiole diagnosis	Transfer to ward after 1-day stay in the PICU
4	F	48	21	_	Cerebral palsy, epilepsy Exposure to smoking	Transfer to ward after 3-day stay in the PICU
5	M	2	10	_	35 week premature birth Congenital CMV infection (elongated hepatitis +, no organ involvement)	Transfer to ward after 1-day stay in the PICU
6	M	4	11	_	Low birth weight	Transfer to ward after 1-day stay in the PICU
7	M	2	52	50	Werdnig-Hofman Exposure to smoking	Discharge dependent on home mechanical ventilation after50-day stay
8	M	25	70	21	Infantile Spasm+HIE-sequelae	Discharge dependent on home mechanical ventilation after 50-day stay
9 stay	M	2	21	10	SCID	Transfer to ward after 13-day in the PICU
10	M	26	50	22	Mitochondrial cytopathy+Epilepsy	Secondary bacterial infection, septic shock, exitus
11	M	11	10	-	Single bronchiolitis attack	Transfer to ward after 4-day stay in the PICU
12	M	36	18	3	CP+MMR+Epilepsy+recurring bronchiolitis	Transfer to ward after 18-day stay in the PICU

MV: mechanic ventilation; CMV: cytomegalovirus; SCID: severe combined immune deficiency; MMR: motor mental retardation; CP: cerebral palsy; M: male; F: female

enough to require hospitalization (22). The fact that clinic symptoms progressed seriously in our co-infection patient (RSV+HBoV association) supported this result. Besides, additional secondary influenza virus infection- related (H1N1) deterioration in clinical table and elongation of intensive care unit-stay also supported what was mentioned above.

It was reported that inappropriate antidiuretic hormone release-related hyponatremia (ADH) developed in patients who had RSV-related lower respiratory tract infection, especially in those who needed mechanic ventilation (5).

None of our patients had hyponatremia and/or inappropriate ADH syndrome finding; it did not develop in the follow-up either. The fact that there was no hyponatremia might be related to the fact that the maintenance fluid given to all patients in routine practice in our unit was ½ SF hypertonic fluid.

Since the virus is transmitted through direct contact, it is primarily vital to care about hand hygiene and other hygienic conditions in order to be protected from RSV infections. Precautions such as isolating RSV-infected patients from other patients are recommended (23). Hand hygiene and hygienic rules, and droplet isolation of the patients are implemented in our unit. The fact that it did not infect other patients during the follow-up in our clinic also supported it.

The main treatment of RSV-related lower respiratory tract infections is supportive care. Patients may be in need of oxygen or respiratory support. In the hospitalized cases, bronchodilators, corticosteroids, antiviral agents (ribavirin) and combined treatments might be given (24). American Pediatrics Academy does not recommend routine use of ribavirin and states that it should be saved for immunosuppressed patients who have serious RSV infection (25). There are contradictory results in the literature in patients using ribavirin in the treatment due to RSV infection regarding its capacity of providing reduction in the duration of intensive care unit-stay or the need for mechanic ventilators (26). In vitro effect of inhaled ribavirin is better. Because of the potential toxic effects to the health personnel due to inhalation and the fact that it has

no clearly proven effect on mortality and high costs, it should be used only in selected cases under the recommendations of a pediatric infection expert (25). Ribavirin was not used in the treatment of our patients.

In selected patients, monoclonal RSV antibody (palivizumab) and RSV-specific intravenous immunoglobulin passive prophylaxis may be used as well (27). While RSV prophylaxis reduces the frequency and seriousness of RSV infection, it also reduces the recurring wheezing episodes in non-atopic children in the long run (28). It was proved in the literature that palivizumab was safe and effective in premature infants. It is especially used in premature infants under 32 weeks and/or those with active chronic lung disease (29). In preterms under 35 weeks, on the other hand, American Pediatrics Academy recommends palivizumab prophylaxis in the presence of at least two factors such as neuromuscular disease and airway congenital anomaly (25). However, for older children and patients in other risk groups, there is no sufficient information in terms of reliability and cost-effectiveness. None of our patients took prophylaxis.

Presence of RSV in all age groups and intensive care hospitalizations especially in infants and patients with additional risks and the need for mechanic ventilation due to the underlying diseases cause great deal of economic losses. Therefore, vaccination studies have expedited in recent years; however, there is still no commonly approved routine vaccine. Due to the fact that RSV infections cause a great deal of morbidity and mortality in risky cases, there is a need for new vaccine studies (30).

Conclusion

It should be born in mind that RSV is a major pneumonia agent especially in infants; however, it can be seen in older children with underlying risk factors, and it may proceed seriously enough to require intensive care and finally that it may even result in mortality. We are of the opinion that the use of prophylaxis by the high risk groups may result in decreasing hospitalization and admission of ICU and this will eventually reduce pecuniary losses and intangible damages.

Ethics Committe Approval: Ethics committee approval was received for this study from the ethics committee of Ankara Child Health Hematology and Oncology Education and Research Hospital/24.09.2013-030.

Informed Consent: Written informed consent was not obtained from patients due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - G.A.; Design - G.A.; Supervision - H.T.; Funding - G.A.; Materials - G.A.; Data Collection and/or Processing - G.A., M.U.Y.; Analysis and/or Interpretation - G.A.; Literature Review - G.A., Ş.Ş.; Writing - G.A., Ş.Ş ; Critical Review - H.T., A.Ö.P.; Other - G.A.

Conflict of Interest: There are no conflicts of interest between authors in connection with this paper.

Financial Disclosure: No financial support and no institutional departmental funds is used for the study.

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