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ORIGINAL

FREQUENCY OF RSV INFECTIONS IN PRETERM INFANTS AFTER MONOCLONAL ANTIBODY PROPHYLAXIS

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The aim: to investigate the frequency of RSV infections in preterm infants with 33-35 gestational weeks after the use of monoclonal antibody prophylaxis

Methods: The study involved preterm born children (33-35 gestation weeks) 1 to 5 years old who received palivizumab for prophylaxis of respiratory infections caused by RSV. 108 patients met inclusion criteria and were hospitalized at the University Clinical Center Tuzla, Clinic for Children's Diseases, Bosnia and Herzegovina in the period 26 September, 2013- 22 July, 2014. Detection of virus in serum of infected children was conducted at the Institute for Diagnostic, University Clinical Center Tuzla.

Results: During the time period of investigation there were 4095 live born infants, of which 6.7% (N 274) were preterm, of which 74.8% infants were between 33-35 weeks of gestation. Out of 205 preterm infants with gestational age 33-35 weeks, palivizumab immunoprophylaxis for RSV infections received 108 (52.6%) infants. Out of a total of 108 preterm infants with gestational age 33-35 weeks who received palivizumab immunoprophylaxis, RSV infection developed in 7 infants (6.5%). All the children with the RSV infection had at least one comorbidity, and the diagnosis confirmed were bronchopulmonary dysplasia/chronic pulmonary disease and congenital heart anomalies.

Conlusion: Our data suggest that palivizumab prophylaxis to late preterm infants results in lower incidence of RSV infectiones in analised group of infants.

INTRODUCTION

Since its isolation in 1965, respiratory syncytial virus (RSV) has been recognized as one of the major health issues in the world [1]. It is most common in infants 2-6 months old. Of all viruses, RSV has most commonly been reported to be the main cause of death [2]. Annually, RSV infections are causing 125.000 hospitalizations in the United States [3]. The main risk factors for severe RSV disease in children include prematurity, bronchopulmonary dysplasia/chronic pulmonary disease and congenital heart failure.

Due to the lack of effecive therapy for RSV infection, prophylactic use of monoclonal antibodies (palivizumab) has been shown as the best course of treatment both in the prevention of acute and chronic manifestations and complications of the disease [4]. Palivizumab blocks the fusion of the virus to the host epithelial cell [5].

The aim of this study is to investigate the frequency of RSV infections in preterm infants with 33-35 gestational weeks after the use of monoclonal antibody prophylaxis.

MATERIALS AND METHODS

It was conducted an observational study that included demographyc and clinical characteristics, as well as outcomes of children who received palivizumab. The study included infants and children 1-5 years of age, who were hospitalized at the University Clinical Center Tuzla, Clinic for Children's Diseases, Bosnia and Herzegovina in the period 26 September, 2013- 22 July, 2014.

The following are criteria for the inclusion: children born with gestational age between 33-35 weeks and that they received a monoclonal antibody for RSV infection prophylaxis. In the sudy were included 108 patients who met inclusion criteria. The prophylaxis was conducted at the University Clinical Center Tuzla, Clinic for Children's Diseases, during the mentioned period and according to the National guidance from the year 2009 established by the Bosnian Neonatal Society.

The study involved preterm born children (33-35 GA) under 5 years of age who received palivizumab for prophylaxis of respiratory infections caused by RSV, in a one-year period at the University Clinical Center Tuzla, Clinic for Children's

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Diseases, Bosnia and Herzegovina (BiH). Detection of virus in serum of infected children was conducted at the Institute for Diagnostic, University Clinical Center Tuzla. The prophylaxis was conducted at the Clinic for Children's Diseases Tuzla according to the National guidance from the year 2009 established by the Bosnian Neonatal Society.

The study was approved by the Ethical Committee of the University Clinical Center Tuzla, and a signed parental consent forms were obtained for each child involved in a study. This study brings sub-analysis of data from the PONI-A study. PONI-A multi-cantry, epidemiological study to identify predictors associated with RSV hospitalization in non-profilaxed, premature infants born between 33 weeks and 0 days and 35 weks and 6 days of gestation (Abbvi PONI 10101). Data analysis was done using standard descriptive statistics.

RESULTS

During the time period of investigation there were 4095 live born infants, of which 6.7% (N 274) were preterm, of which 74.8% infants were between 33-35 weeks of gestation (Table1).

Table 1. The number of live born infants according to gestational age in period of investigation.

Gestational age	Number of live born infants	%
≤ 32	12	4.3%
Total 33 do 35	205	74.8%
Total <37	57	20.9
Total	274	100%

Out of 205 preterm infants with gestational age 33-35 weeks, palivizumab immunoprophylaxis for RSV infections received 108 (52.6%) infants. The demographyc characteristics of the examined infants are presented in Table 2.

Table 2. Birth weight, gestational age and Apgar score of investigated infants

Characteristics	Mean (S.D.)
Birth weight	2230±382.1 (1260-3400)
Gestational age (weeks)	33.6±0.447 (33-35)
Apgar score 1st minute	7.35±1.837 (1-10)
Apgar score 5th minute	8±1.233 (1-10)

Out of a total of 108 preterm infants with gestational age 33-35 weeks who received palivizumab immunoprophylaxis, RSV infection developed in 7 infants (6.5%).

All the children with the RSV infection had at least one comorbidity, and the diagnosis confirmed were bronchopulmonary dysplasia/chronic pulmonary disease and congenital heart anomalies (Table3).

Table 3. Comorbidity in children with RSV infection

		GN	n	%	GN±SD
BPD/CPD*			3	42.8	33±1.5
CHA**			2	28.6	34.6±1.3
other	congenital diaphragmatic hernia		1	14.3	
	agenesis of lung				
	neuromuscular diseases		1		
	cystic fibrosis		1		

BPD/HPB* bronchopulmonary dysplasia/chronic pulmonary disease
CHA**congenital heart anomaly

DISCUSSION

In our study, the frequency of RSV infections in infants with 33-35 gestational weeks was 6.5%. The average lifespan ranged 1-3 years of life at the time of infection. RSV infection developed in all infants, and they were hospitalized 23±1.5 hospital days. All infants with RSV infection had at least one comorbidity, while the most common confirmed diagnosis were bronchopulmonary displasia/ chronic pulmonary disease and congenital heart anomalies.

Prophylaxis with palivizumab to late preterm infants is still a matter of concern since this

drug is too expensive to be used for the entire population of late preterm infants. The costeffectiveness of the use of palivizumab in the latepreterm has been analyzed by several studies to identify environmental or individual risk factors for severe RSV infection. An attempt was made to use risk scores derived from the risk factors to detect the subjects for whom the administration of palivizumab could be effective in reducing RSV-related mortality and morbidity [6].

By the age of 2 years, almost all children have an RSV infection with a common reinfection [7], with morbidity and mortality significantly increased in preterm infants compared to term infants [8]. Up to now, researchers identified extrinsic and intrinsic risk factors for RSV-associated hospitalizations in early preterm infants: multiple gestations [9], extremely low birth weight and/or gestational age [10], intrauterine growth restriction, chronic lung disease of prematurity lack of prenatal care, neonatal complications such as intraventricular hemorrhage, necrotizing enterocolitis, mechanical ventilation, bacteremia, lower levels of maternal education , and low parental socioeconomic status. Because of these reasons, and proven efficacy and safety in preterm children (≤35 weeks of gestation) palivizumab is used for the prevention of severe RSV low respiratory tract infectiones (LRTI) requiring hospitalization in children at high risk for the disease, although indications and recommendations regarding the target population in need for immunoprophylaxis had changed significantly from time of first registration till now restricting its use [11].

IMPACT palivizumab study has shown its efficacy in reduction of hospitalization days up to 55% [12]. Study of Simoes at al. [13] has demonstrated efficacy of palivizumab in reduction of the rate of RSV hospitalization in premature infants with chronic lung disease 78%- 80%; but the clinical efficacy of palivizumab has been shown in several secondary aspects: reduction in the total number of RSV hospital days, reduction in the number of RSV days with increased oxygen requirement, reduction in the number of RSV hospital days with a moderate or severe respiratory tract illness, and reduction in frequency and duration of intensive care unit stay.

Our data suggest that palivizumab prophylaxis to late preterm infants results in lower incidence of RSV infections in analised group of infants.

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