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Abstract

Children who have been infected with Respiratory Syncytial Virus have a higher incidence of wheeze-associated clinic visits and hospitalizations compared to children without previous RSV exposure. The purpose of this study is to determine if palivizumab, an immunoglobulin injection used to prevent RSV infections, can decrease the incidence of recurrent wheezing in children. The review of literature will follow male and female children from infancy to age 13 who were treated with palivizumab and compare these children to patients with similar demographics that were not treated with palivizumab to determine if there is any difference in incidence of wheezing. The anticipated results are that patients treated with palivizumab will have a decreased incidence of recurrent wheeze. The findings may indicate that prevention of RSV with palivizumab will improve long-term health in children.

Introduction

Respiratory syncytial virus is a very common disorder seen in the pediatric population. RSV may lead to severe infections requiring admission to a pediatric intensive care unit, especially in children considered to be high-risk. Palivizumab is a humanized monoclonal antibody that was approved in the United States by the FDA in 1998 to prevent RSV infections. The purpose of this study is to determine if the incidence of recurrent wheezing can be decreased by preventing RSV infections with palivizumab.

Statement of the Problem

Currently only high-risk patients are receiving palivizumab due to the high cost associated with the injections. It is unknown if administration of palivizumab would be beneficial for patients that are not considered to be high-risk. Studies are needed to determine if palivizumab administration can prevent recurrent wheezing and the healthcare costs associated with wheeze related clinic visits and hospital admissions.

Research Question

- In patients treated with palivizumab, is there a statistical difference in recurrent wheeze when compared to children not given palivizumab?
- Are there long-term or even lifelong benefits to preventing RSV with palivizumab?

Literature Review

- RSV is the single most common cause of bronchiolitis
- 30-40% of patients hospitalized with an RSV infection will wheeze later in childhood, and RSV infection in infancy may be on important precursor to asthma (Hay et al., 2012)
- RSV bronchiolitis may interfere with normal lung development or immune maturation and subsequently cause recurrent episodes of wheezing (Blanken et al., 2013)
- In a non-randomized, observational, prospective study conducted by Yoshihara et al. (2013) recurrent wheeze was reported in 18.9% of the untreated group and only 6.4% of the palivizumab treated group (RR, 0.34 [95% CI, 0.19-0.60} P <0.001)
- When comparing a palivizumab treated group to a control group Simoes et al. (2007) determined the palivizumab treated group had a longer time to onset of recurrent wheeze (HR=0.46, 95% CI = 0.29 to 0.74) and also a decrease in physician diagnosed recurrent wheeze (HR = 0.36, 95% CI = 0.25 to 0.83)
- In a study conducted by Blanken et al. in 2013, there was a significant difference in recurrent wheeze in the treated group (11.2%) versus the placebo group (20.9%) (See Table 1)
- Stein et al. (1999) determined through a longitudinal report that the risk of infrequent and frequent wheezing decreased enough to become non-significant by the age of thirteen
- Sigurs (2002) conducted a cohort study which determined that at age 7.5 years 23% of patients with RSV were diagnosed with asthma, whereas only 2% of the control patients were diagnosed with asthma (See Table 2)

Discussion

- Palivizumab can decrease recurrent wheezing throughout childhood
- After correcting for variables such as daycare attendance, smoking in the home, furred pets in the home, number of people living in the home, etc., in patient groups, palivizumab groups were viewed to have a significant decrease in recurrent wheezing
- Reduction in recurrent wheeze remained statistically significant up to the age of thirteen
- Palivizumab administration can decrease clinic visits and hospital admissions during childhood and can improve quality of life

Table 1. Days with Wheezing in the First Year of Life

Variable	Palivizumab (N=214)			Placebo (N=215)			Absolute Reduction	RR Reduction (95% CI)
	Total Log Days	Total Symptom Days	Incidence per Day	Total Log Days	Total Symptom Days	Incidence per Day		
	no.		*%*	*no.*		*%*	*symptom days*	*%*
Days with wheezing								
First year of life	53,075	930	1.8	51,726	2,309	4.5	1,379	61 (56-65)
<2mo after prophylaxis	28,455	666	2.3	282,220	1,382	4.9	716	52 (46-59)
≥2mo after prophylaxis	24,620	264	1.1	23,506	927	3.9	663	73 (66-80)
During RSV season	26,176	646	2.5	26,081	1,348	5	702	52 (46-59)
Outside RSV season	26,899	284	1.1	25,645	961	3.7	677	73 (66-80)

The incidence of wheezing was calculated as the number of days with parent-reported airway symptoms divided by the number of log days during follow up. P <0.001 for all comparisons except P = 0.006 for the category of less than 2 months after the end of prophylaxis. (Blanken et al. 2013)

Table 2. Number (percentage) of Children with Bronchial Obstructive Symptoms in the Respiratory Syncytial Virus Group and the Control Group at age 7.5

Symptoms	RSV Group (n=47)	Control Group (n=93)	P-Value	RR	95% CI
Asthma					
Cumulative	14/47 (30%)	3/93 (3%)	<0.0001	9.23	2.79-30.55
Current	11/47 (23%)	2/92 (2%)	<0.001	10.88	2.51-47.11
Current Atopic	7/47 (9%)	1/93 (1%)	0.002	13.85	1.76-109.30
Recurrent Wheezing					
Cumulative	13/47 (28%)	10/93 (11%)	0.015	2.57	1.22-5.42
Current	6/47 (13%)	0/93 (0%)	<0.001	Not Calculable	
Any Wheezing					
Cumulative	32/47 (68%)	32/93 (34%)	<0.001	1.98	1.40-2.79
Current	18/47 (38%)	2/93 (2%)	<0.0001	17.81	4.31-73.54

"Current symptoms" means disease during the preceding year; "Current, atopic asthma" means asthma with allergic sensitisation. (Sigurs et al., 2002).

Applicability to Clinical Practice

- Palivizumab has limited FDA approval in the U.S. and is limited to high-risk infants only
- Premature infants <35wga or infants with chronic lung disease of prematurity should be offered palivizumab
- RSV prophylaxis with Synagis, palivizumab, is expensive and prior authorization for the antibody should be investigated prior to administration

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