Improving the Timing of Palivizumab Immunoprophylaxis: Can Local Respiratory Syncytial Virus (RSV) Diagnostic Testing Data Define the Season?

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ABSTRACT

Background: A maximum of 5 monthly doses of palivizumab is recommended for prophylaxis of severe RSV infection in high risk children during the "RSV season." Peak RSV activity varies annually and by geographical region. Inappropriate timing of palivizumab administration can result in unnecessary use of costly resources and/ or increase the risk of a RSV related hospitalization in high risk children. Historically, monthly palivizumab administrations were initiated on October 1st independent of local RSV prevalence at Children's Medical Center Dallas. During the 2011-12 RSV season, a multidisciplinary team (pharmacist, infectious diseases specialists, neonatologist, pediatrician and microbiologist) developed a policy for administering palivizumab during the RSV season as defined by the clinical RSV testing data from the Children's clinical virology laboratory. The objective of this study is to describe the clinical outcomes of the multidisciplinary approach to determine the onset and offset of RSV immunoprophylaxis.

Methods: A retrospective, observational review of electronic medical records was performed to evaluate the multidisciplinary intervention to determine palivizumab administrations based on clinical RSV data at CMCD. All patients who received ≥ 1 dose of palivizumab during the 2010-11 and 2011-12 RSV seasons were included. Demographic data including gestational age, birth weight, indication(s) for palivizumab, subsequent number of palivizumab doses per season and RSV-related hospitalizations during both RSV seasons were extracted and compared.

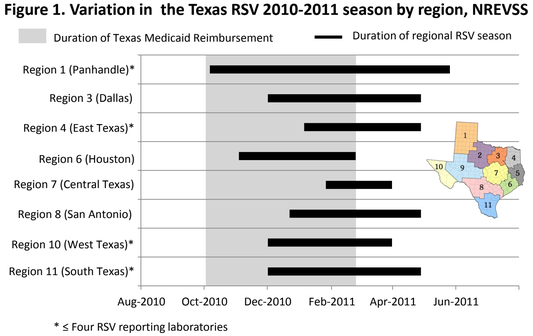
Results: During the 2010-11 and 2011-12 RSV seasons, 290 and 312 patients received palivizumab, respectively. Utilizing institutional surveillance of RSV prevalence in 2011-12, palivizumab immunoprophylaxis was initiated on November 2nd, approximately 1 month later than the previous season. Despite the later start date, there were no RSV related hospitalizations in patients meeting criteria for palivizumab before the onset of the 2011-12 RSV season. Even though there were fewer patients who received immunoprophylaxis in the 2010-11 season, there was not a significant difference in the percent of subsequent RSV related hospitalizations in patients receiving palivizumab in the succeeding 2011-12 season (4.1% vs. 3.5%). The number of patients who received >5 doses was reduced from 57 (19.7%) to 14 (4.5%) during the 2010-11 and 2011-12 seasons accounting for an estimated cost savings of ~$87,000

Conclusion: A multidisciplinary approach defining the RSV season using local RSV prevalence to determine timing of palivizumab immunoprophylaxis can be used to reduce the number of excessive doses administered to an individual patient.

BACKGROUND

- The National Respiratory and Enteric Virus Surveillance System (NREVSS) defines the RSV season as:
  - Onset: The first of 2 consecutive weeks during which the mean percentage of specimens testing positive is ≥10%.
  - Offset: The last of 2 consecutive weeks during which the mean percentage of positive specimens is ≤10%.
- The American Academy of Pediatrics recommends a maximum of 5 monthly doses of palivizumab per RSV season to high risk children.
- We have observed variation in the onset /offset of the RSV season by year and geographic location within Texas (Figure 1).
- Consistent with Texas Medicaid reimbursement, Children's Medical Center (CMC) had initiated annual RSV immunoprophylaxis ~October 1st, irrespective of the RSV prevalence in the community.

Figure 1. Variation in the Texas RSV 2010-2011 season by region, NREVSS



* ≤ Four RSV reporting laboratories

OBJECTIVE

- To determine if using real time surveillance of local laboratory RSV diagnostic testing data can be used to improve utilization of palivizumab administration to high risk children without increasing RSV-related hospitalizations

METHODS

Setting

- This quality improvement study was performed at CMC which is the fifth largest freestanding pediatric healthcare facility in the United States . The Children's virology laboratory performs ~12,000 respiratory viral tests annually on patients from all areas of North Texas.

Intervention

- For the 2011-2012 RSV season, a multidisciplinary committee (infectious diseases pharmacist, infectious disease specialists, neonatologist, pediatrician, and microbiologist) implemented a process to time palivizumab administrations during the months of peak RSV activity in the community.
- The onset of the RSV season with subsequent palivizumab administrations was declared when the prevalence of positive RSV tests performed in the CMC virology laboratory was projected to approach 10%. The offset of the RSV season was defined by NREVSS criteria.
- RSV testing was performed using rapid antigen (BD Directigen™ EZ RSV, Becton Dickinson and Company, Sparks, MC), direct fluorescent antibody (DFA), and polymerase chain reaction (PCR; xTag Respiratory Viral Panel [RVP], Luminex Corp. Austin, TX) tests .
- RSV prevalence was calculated as the total number of positive tests divided by the number of tests performed. Patient duplicates were not excluded.

Study Design

- Retrospective review of all patients who received at least one dose of palivizumab at CMC and/or at NICU discharge for infants born at Parkland Memorial Hospital during the 2010-11 and 2011-12 RSV seasons.
- Estimated cost savings were calculated and reflected only medication cost (average wholesale price) and not drug preparation or administration costs.

Data Collection

- Patients were identified using the electronic medical record as having received palivizumab in the inpatient or outpatient settings from September 2010 to June 2012.
- Medical record review:
  - Demographics, indication(s), microbiologic data administration dates and total number of palivizumab doses per RSV season
  - RSV-related encounter was defined as any patient who had a laboratory confirmed test for RSV and visited either the CMC emergency department or was admitted to CMC.
  - RSV-related mortality

Statistical Analysis

- Statistical testing of subgroups was performed using the Wilcoxon Rank Sum test for continuous data, and Chi-square test or Fisher's Exact test for categorical data, as appropriate to the variable's distribution. A p-value <0.05 was considered to be statistically significant.

RESULTS

Table 1. Patient demographics

	2010-2011	2011-2012
No. of patients	290	312
Male, n (%)	143 (49)	171 (55)
Race/ethnicity, n (%)		
African American	72 (25)	68 (22)
Caucasian	61 (21)	69 (22)
Hispanic	144 (50)	146 (47)
Other	13 (5)	29 (9)
Mean birth weight (grams), mean ± SD	1867 ± 1056	1904 ± 1088
Gestational age (weeks), mean ± SD	32 ± 6	32 ± 6
Palivizumab indication, n (%) *		
<29 weeks gestation + <12 months	73 (25)	70 (22)
29-<32 weeks gestation + <6 months	38 (13)	43 (14)
32-<35 weeks gestation + <3 months and risk factor	8 (3)	5 (2)
Chronic lung disease	20 (7)	37 (12)
Hemodynamically significant congenital heart disease	98 (34)	107 (34)
Neuromuscular disease or congenital airway abnormality	7 (2)	6 (2)
Immunodeficiency	5 (1.7)	0 (0)
Cystic fibrosis	0 (0)	0 (0)
>1 AAP indication	35 (12)	36 (12)
Other	6 (2)	8 (3)

*Indications based on recommendations by the American Academy of Pediatrics (AAP, Red Book)

Figure 2. RSV prevalence from CMC laboratory testing vs NREVSS, 2010-2012

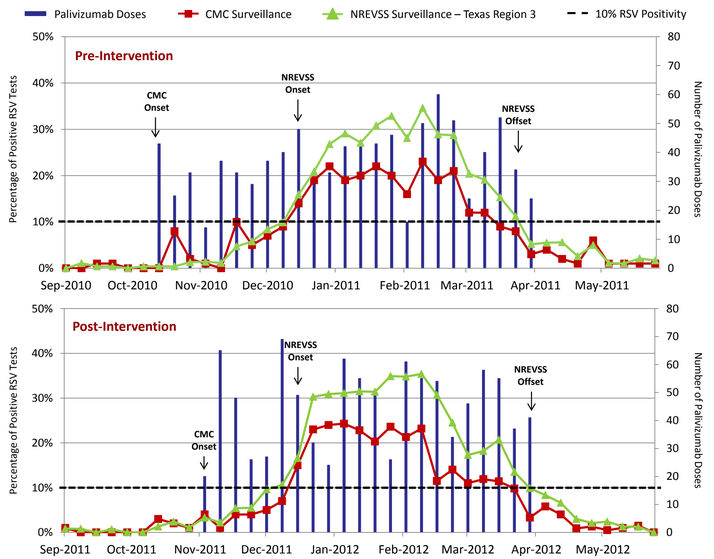
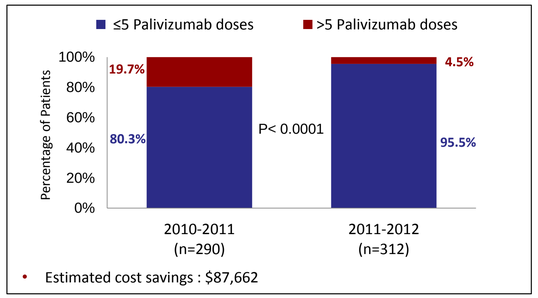


Table 2. Palivizumab doses and RSV-related morbidity & mortality

	2010-2011	2011-2012	P-value
Declared RSV season onset (CMC)	October 1	November 2	-
Declared RSV season offset (CMC)	March 31	March 30	-
No. of patients	290	312	-
No. of administered doses	957	1030	-
Doses per patient, mean ± SD	3.3 (± 2)	3.3 (± 2)	0.89
No. of patients receiving > 5 doses	57	14	<0.0001
Estimated cost of additional doses	$116,194	$28,532	-
RSV-related hospital encounters, n (%)	23 (8)	24 (8)	0.86
ICU admission, n	4	6	
Non-ICU admission, n	17	17	
Emergency department, n	2	1	
RSV-related mortality, n (%)	0 (0)	1* (0.3)	0.77

*Death secondary to congenital heart disease and MRSA sepsis after two palivizumab doses

Figure 3. Cumulative palivizumab doses per RSV season, 2010 – 2012



- Estimated cost savings : $87,662

CONCLUSION

- Utilizing prospective real time RSV surveillance from a large clinical virology laboratory to predict the onset of the RSV season was an effective means to reduce hospital costs by decreasing the number of patients who received >5 palivizumab doses.
- Projecting the true onset of the RSV season remains challenging due to the unpredictable variation of weekly RSV prevalence.
- Continuous evaluation at CMC and implementation at other institutions across the country are needed to validate our approach.

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