CONCISE COMMUNICATION

Safety of Palivizumab Stewardship in Conjunction with Infection Prevention and Control Strategies for Healthcare-Associated Respiratory Syncytial Virus Infections

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Transitioning from administration of monthly palivizumab to a single dose at discharge was associated with substantial pharmacy cost savings. With the concurrent adoption of private hospital rooms and visitor restriction policies, hospital-wide and neonatal intensive care unit healthcare-associated respiratory syncytial virus infections decreased following these changes.

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Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection in early childhood.[1,2] Monthly prophylaxis with palivizumab, a humanized monoclonal antibody, during the RSV season reduces hospitalization up to 55% in high-risk patients, including premature infants and those with congenital heart disease or chronic lung disease.[3] In 2003, the American Academy of Pediatrics (AAP) recommended that hospitalized infants eligible for prophylaxis during the RSV season receive their first dose 48–72 hours before discharge or promptly thereafter.[4] The AAP also recommends strict adherence to infection prevention and control practices as the primary strategy for reducing inpatient RSV transmission. However, many neonatal intensive care units (NICUs) continue to administer monthly RSV prophylaxis because of concerns about healthcare-associated RSV (HA-RSV) infection.[5] The purpose of this retrospective study was to describe the change in rates of HA-RSV over a 12-year period after changing from monthly inpatient palivizumab administration to administration at discharge in the setting of private hospital rooms and visitor restriction policies.

METHODS

This retrospective study was conducted at Children's Memorial Hospital (CMH) and Ann and Robert Lurie Children's Hospital of Chicago (LCH) between November 2007 and March 2017. From November 2007 to June 2012, patients were hospitalized at CMH, a 270-bed free-standing children's hospital with a 50-bed level III NICU. The CMH NICU contained 2 private isolation rooms and 6 shared bays with up to 8 neonates per bay. Approximately 50% of beds were in shared rooms in the remainder of the hospital. In June 2012, all patients were transferred to LCH, a new 288-bed free-standing children's hospital with all private rooms, including a 44-bed level III NICU. The NICUs at both hospitals admitted neonates from the community, including those with RSV. Both NICUs accepted approximately 500 transfers and 50 admissions from the community per year. Our institutional review board approved this study.

The primary study outcome was the incidence rate of NICU HA-RSV per 1,000 patient days. The secondary study outcome was the hospital-wide incidence rate of HA-RSV per 1,000 patient days. Additional data points for the 2011–2012 season and onwards included the number of palivizumab doses dispensed and pharmacy acquisition costs. Additionally, for patients receiving palivizumab from 2013 to 2017, the indications for palivizumab administration were retrieved from the electronic medical record.

Palivizumab Administration Policy

Prior to the 2011–2012 season, all patients meeting AAP criteria received monthly palivizumab 15 mg/kg intramuscularly during the RSV season (typically November through March), with a maximum of 5 doses.[4,6] In the 2011–2012 RSV season, a revised protocol was implemented at CMH where palivizumab was given monthly to patients in shared rooms and at discharge for patients in private rooms. After moving to all private rooms at LCH in 2012, the protocol was changed to administer the first dose up to seven days prior to discharge. Approval from the infectious diseases pharmacist was required for infants not meeting AAP criteria.[6,7]

Infection Prevention and Control Policy and HA-RSV Surveillance

At both hospitals, all patients presenting with respiratory symptoms or with documented RSV were placed under droplet and/or contact precautions, which require all persons to utilize appropriate hand hygiene and don masks, gloves, and gowns. At CMH, patients with respiratory viral symptoms or microbiologically confirmed RSV were cohorted or placed in a private room. At LCH, a new guest policy was implemented in the 2013–2014 viral season (January–April). Hospital wide, visitors were restricted to parents or guardians and no more than 2 additional guests ≥16 years old. Visitors with signs or symptoms of a respiratory illness were also restricted.

Surveillance for HA-RSV was performed as part of routine infection prevention and control activities. HA-RSV was defined as microbiologically confirmed RSV occurring >2

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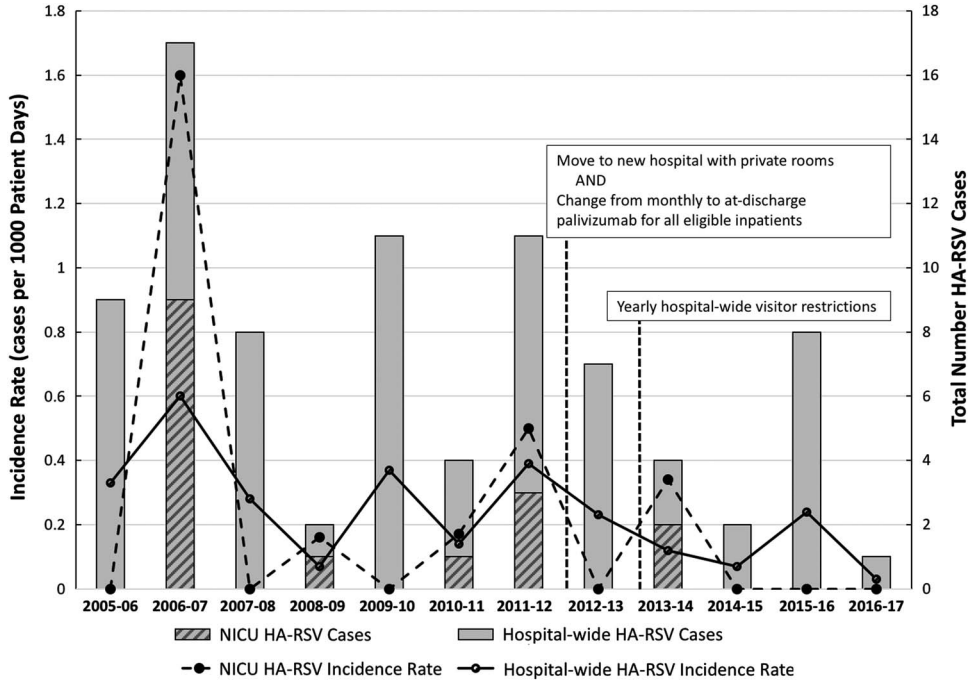

FIGURE 1. Neonatal intensive care unit (NICU) and hospital-wide healthcare-associated respiratory syncytial virus (HA-RSV) cases and incidence rate over a 12-year period.

hospital days after admission in a patient known to be RSV negative initially or without signs or symptoms of respiratory infection at the time of admission. HA-RSV was also diagnosed in patients readmitted within 2 days of previous hospital discharge who had microbiologically confirmed RSV but without respiratory symptoms at the time of previous discharge.

Prior to 2012, the microbiology laboratory at CMH and LCH performed RSV testing using a rapid antigen assay (either Directigen RSV, Becton Dickinson, Franklin Lakes, NJ or RSV NOW, Binax, Scarborough, ME) directly from nasopharyngeal specimens. Starting in 2012, only molecular-based polymerase chain reaction assays were used to detect RSV (FilmArray Respiratory Patel, bioMérieux, Salt Lake City, UT and Verigene, Nanosphere, Northbrook, IL).

Statistical Analysis

The NICU HA-RSV and hospital-wide HA-RSV incidence rates were compared between the monthly (2005–2012) and at-discharge (2012–2017) palivizumab administration periods using Poisson regression conducted with SAS version 9.2 software for Windows (SAS Institute, Cary, NC).

RESULTS

Compared to the 7-year period (2005–2012) of monthly palivizumab administration, the NICU HA-RSV incidence rate (Figure 1) in the subsequent 5-year period (2012–2017) of palivizumab administration prior to discharge declined from 0.34 to 0.07 cases per 1,000 patient days ($P = .01$). The hospital-wide HA-RSV incidence rate (Figure 1) declined from 0.31 to 0.14 cases per 1,000 patient days ($P < .01$). Since starting administration at discharge, no HA-RSV cases occurred in infants who would have received palivizumab with the previous policy. There were no deaths in patients acquiring HA-RSV.

When comparing the 2012–2017 period to the preceding 2 years, the mean annual number of palivizumab doses dispensed decreased by 59% (227 to 92 doses). The mean acquisition cost per season from 2012 to 2017 was $194,515, a 37% reduction when compared to the preceding 2 years, despite a 25% increase in the drug cost of palivizumab from 2011 to 2017. The cumulative cost savings over 5 years, accounting for inflation, were more than $750,000.

There was a clear shift in palivizumab indications. When comparing the 2013–2014 season to 2016–2017, the number of doses given to premature infants and those with chronic lung disease decreased by 22% (36 to 28 doses) and 55% (22 to 10 doses), respectively, whereas doses given to infants with congenital heart disease doubled (26 to 52 doses). There were only 4 occurrences in which AAP indications were not met during this period.

DISCUSSION

Although data supporting the AAP recommendation of palivizumab administration at discharge remain limited, 1 report documented no increase in HA-RSV 1 year after discontinuation of monthly inpatient administration.[8] Our study

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also confirmed no increase in HA-RSV, but over a longer period, which limited the influence of interseason variation. In addition, we conducted a separate analysis for NICU HA-RSV and showed a reduction in HA-RSV in this vulnerable group. Importantly, there were no major complications or deaths attributed to HA-RSV, and no patients who acquired HA-RSV would have qualified for palivizumab, further supporting the limited benefit of monthly inpatient administration.

Our study had several limitations. Although this study did not address subsequent RSV-related hospitalization, a retrospective study of 207 neonates showed hospitalization rates for RSV did not differ significantly between those who received monthly dosing and those who received 1 dose prior to discharge.[9] Our study and statistical analyses also did not assess the individual effects of palivizumab administration, change in RSV testing, patient cohorting, and visitor restriction policies. Lastly, our calculation of cost savings did not consider reduction in other supplies and labor cost.

In summary, we demonstrated a decrease in HA-RSV in the setting of visitor restriction and strict infection prevention and control while administering palivizumab at discharge only, supporting current AAP recommendations.

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