



ABSTRACT

Introduction: The American Academy of Pediatrics recommends palivizumab prophylaxis for children born premature or with chronic lung disease to reduce the severity of respiratory syncytial virus (RSV) infection. The purpose of the current study is to examine palivizumab administration among children hospitalized with RSV infection.

Method: This is a retrospective medical record review at a tertiary care children's hospital. The study included children <2 years of age hospitalized between October 1, 2000, and April 1, 2001, with the diagnosis of RSV infection.

Results: The records of 264 children meeting inclusion criteria were reviewed. Forty children qualified for administration of palivizumab using American Academy of Pediatrics recommendations. Of these, 14 (35%) received palivizumab prior to admission. Palivizumab administration rate was not affected by age, race, or insurance coverage.

Discussion: Exact barriers to the administration of palivizumab remain unclear. The identification of high-risk children, prevention of RSV by use of palivizumab, and collaboration between hospital and community health care providers will help increase the use of palivizumab and decrease the incidence of RSV.

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Rate of Palivizumab Administration in Accordance With Current Recommendations Among Hospitalized Children



James A. Moynihan, MS, DO, FAAP,
Tommy Y. Kim, MD, FAAP,
Tammy Young, MSN, RN, FNP, &
Paul A. Checchia, MD, FAAP

Respiratory syncytial virus (RSV) infection constitutes the single greatest cause of lower respiratory infection among infants and children ([Centers for Disease Control and Prevention, 2001](#)). RSV is the leading cause of

James A. Moynihan is the Assistant Medical Director, Department of Emergency Medicine at Loma Linda University Medical Center & Children's Hospital, Department of Pediatric Emergency Medicine, Loma Linda, Calif.

Tommy Y. Kim is a Senior Fellow, Department of Emergency Medicine at Loma Linda University Medical Center & Children's Hospital, Loma Linda, Calif.

Tammy Young is a doctoral student (DrPH) at Loma Linda University, School of Public Health, Loma Linda, Calif. She is a staff nurse at Loma Linda University Medical Center & Children's Hospital, Pediatric Emergency Department, Loma Linda, Calif, and Chief Flight Nurse for JetWest International Medical Transportation, Van Nuys, Calif.

Paul A. Checchia is Director, Divisions of Critical Care Medicine and Cardiology, Washington University School of Medicine, St. Louis Children's Hospital, St. Louis, Mo.

Reprint requests: James A. Moynihan, DO, Loma Linda University Medical Center and Children's Hospital, Department of Emergency Medicine, 11234 Anderson St, Room A108, Loma Linda, CA 92354-2804; e-mail: jmoynihan@ahs.llumc.edu.

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lower respiratory infection among infants and children (Centers for Disease Control and Prevention, 2001). RSV is the leading cause of hospitalization in infants younger than 1 year (Leader & Kohlhasse, 2002) and the leading viral cause of death in infants (Thompson et al., 2003). Each year, more than 120,000 children are hospitalized in the United States for RSV-related illnesses (Shay et al., 1999). Children with the highest risk of serious complications from RSV infection include those with premature birth, chronic lung disease (CLD), also known as bronchopulmonary dysplasia, congenital heart disease, weight less than 5 kg, and T-cell immunodeficiency (Meissner et al., 1999). Infants born prematurely are the largest high-risk group, because they have an immature immune system, partial transfer of maternal antibodies, underdeveloped lungs, and low birth weight.

RSV is an enveloped, single-stranded RNA virus that uses two glycoproteins, G protein and F protein, to infect cells. The G protein attaches RSV to the host cell. The F protein fuses infected cells to healthy cells, allowing the virus to recognize, penetrate, and facilitate cell-to-cell transmission. Whereas the G protein is variable in makeup, the F protein is highly conserved and the target of treatment. Palivizumab (Synagis, MedImmune, Inc, Gaithersburg, MD) is a humanized monoclonal antibody produced by recombinant DNA technology. Palivizumab blocks the fusion of infected cells by binding to the F protein of RSV. Thus the virus cannot enter host cells and replicate, reducing viral activity and cell-to-cell transmission.

The IMpact RSV study group was formed to address the following question: Does palivizumab reduce the number of hospitalizations of infants at risk of serious RSV infection? The IMpact-RSV study group was a multicenter, multinational collaboration of 139 centers in the United States, the United Kingdom, and Canada. They performed the IMpact-RSV clinical trial, a phase III study to investigate the safety and effectiveness of palivizumab. It was a randomized, double-blind, placebo-controlled study enrolling 1502 children either born prematurely (<36 weeks) or with CLD. For every two infants receiving monthly intramuscular (the "IM" part of "IMpact") injections of palivizumab, one infant was selected

to receive an identical-appearing placebo, using a randomized system. The study showed a 55% reduction of RSV-related hospitalizations following prophylaxis with palivizumab of all children enrolled (IMpact RSV Study Group, 1998). After publication of these results, the American Academy of Pediatrics (AAP) developed recommendations for the use of palivizumab. The recommendations for prophylaxis include the following: (a) infants younger than 2 years who required medical therapy for CLD within 6 months before the anticipated RSV season; (b) infants born at ≤ 28 weeks' gestation who are ≤ 12 months old at the start of the RSV season; (c) infants born at 29 to 32 weeks who are ≤ 6 months old at the start of the RSV season; and (d) infants born at 32 to 35 weeks who are ≤ 6 months old at the start of the RSV season with two or more of the following risk factors: child care attendance, school-aged siblings, exposure to environmental air pollutants (eg, tobacco smoke in the home), congenital abnormalities of the airways, or severe neuromuscular disease (Committee on Infectious Diseases and Committee on Fetus and Newborn, 1998). The rate of compliance with these recommendations has not been determined.

The purpose of this study was to investigate the administration of palivizumab among qualified patients who were hospitalized with RSV infection at a single site serving Southern California. A secondary objective was to examine possible barriers to the administration of palivizumab.

METHODS

The Institutional Review Board approved this study. The medical records of admissions between the dates of October 1, 2000, and April 1, 2001 (RSV season) were queried for patients admitted with the diagnosis of RSV infection using ICD-9-CM coding. During this season, the RSV status of all children was determined before admission. Our hospital serves an area with a population base of 2.5 million persons, an estimated 300,000 of whom are younger than 15 years. The following information was obtained: age at admission to the hospital with the diagnosis of RSV disease; demographics; gestational age at birth; presence of CLD; institutional characteristics of the

discharge neonatal unit; insurance coverage; and history of palivizumab administration. For the purposes of this retrospective review, CLD was defined in accordance with the IMpact-RSV study group definition of bronchopulmonary dysplasia. If this information was not able to be obtained from the medical record, the parent or guardian listed on the admission information was telephoned and asked if their child received palivizumab to prevent RSV bronchiolitis. If the parent or guardian did not know if palivizumab was administered, it was presumed that the child did not receive the antibody.

Statistical analysis was performed with use of the statistical software SAS version 8 (SAS Institute, Inc, Cary, NC). Children were grouped into those who received palivizumab and those who did not receive palivizumab. Age, race, insurance coverage, and type of discharging newborn institution were compared with use of the Student *t* test. Statistical significance was determined as a *P* value < 0.05.

RESULTS

Administration Rates

During the season from October 1, 2000, to April 1, 2001, 264 children younger than 2 years were hospitalized with the diagnosis of RSV infection. Of these children, 40 qualified to receive palivizumab according to AAP guidelines. Fourteen of these patients (35%) had received at least one dose of palivizumab at the time of admission. No patient received respiratory syncytial virus immune globulin, RSV-IVIG.

The IMpact-RSV clinical trial excluded patients with the following conditions: life expectancy less than 6 months; active or recent RSV infection; known hepatic or renal dysfunction; seizure disorder; immunodeficiency; allergy to IgG products; receipt of RSV immune globulin within the past 3 months; previous receipt of palivizumab, other monoclonal antibodies, RSV vaccines, or other investigational agents; and children with congenital heart disease other than a patent ductus arteriosus or an uncomplicated septal defect (IMpact-RSV Study Group, 1998). A review of hospital data within our patient population failed to reveal any such contraindications to administration of palivizumab.

TABLE 1 Patient demographics representation and insurance status

Palivizumab	+	-
Mean age (mo)	7.6 ± 6.0*	9.3 ± 8.7*
Race		
Hispanic	9	11
African-American	2	5
White	3	5
Other	0	5
Insurance		
Medi-Cal/CCS	12	21
Private	2	5
Discharge neonatal unit		
Academic	10	10
Community	4	16

*Mean ± SD.

Population Characteristics

The factors examined are represented in Table 1. Statistical significance ($P < .05$) was not achieved when comparing any of the population characteristics examined. Mean age on admission to the hospital with RSV infection was similar between the group that received palivizumab and the group that did not receive it. Four self-described demographic groups were represented among the 40 qualifying patients: Hispanic; White; African-American; and other. This is representative of the population demographics of the hospital catchment area. There was no significant difference between the group that received palivizumab and the group that did not receive it in regard to demographic representation.

Insurance coverage did not affect the rate of palivizumab administration. Overall, the incidence of private insurance within the qualifying patient population was low (7 of 40; 17.5%). The incidence of private insurance was similar between patients with regard to palivizumab administration.

Discharge institutions ranged from large academic children’s hospitals to community hospitals. Infants qualifying to receive palivizumab were identified or failed to be identified in both academic medical centers and community hospitals. Some institutions provided the first palivizumab dose at discharge from the neonatal intensive care unit, whereas others instructed the patient’s parents or guardian to follow up shortly afterward on an outpatient basis.

In 27 of 40 charts, the medical records could not initially verify

palivizumab administration. The parents or guardians of all but seven patients were found. Those whose children did not receive palivizumab volunteered that they did not have any knowledge of the product. Because of our study design, the cases that could not be confirmed were classified as not receiving palivizumab.

There was a low rate of administration of palivizumab in accordance with AAP recommendations among our study population.

DISCUSSION

There was a low rate of administration of palivizumab in accordance with AAP recommendations among our study population. This low rate occurred independently of the factors examined: age, race, or insurance coverage. Our finding of a palivizumab administration rate of 35% among all qualifying, hospitalized children is consistent with a previous study that examined only pediatric intensive care unit admissions. The previous study

found that 30% (27 of 89) of children admitted to the pediatric intensive care unit for RSV complications qualified to receive palivizumab under current AAP recommendations (Buckingham, Quasney, Bush, & DeVincenzo, 2001).

One interesting finding was the difference in academic versus community-based hospital discharges. In the academic settings, 50% (10 of 20) of qualified children received palivizumab, whereas in the community setting only 20% (4 of 16) of qualified children received the antibody prior to discharge. Further studies are needed to determine if compliance with monthly palivizumab injections improves and serious illness reduces if palivizumab is received prior to neonatal discharge.

Barriers to palivizumab administration within our study population could not be clearly identified. We sought to examine some of the more commonly implicated factors such as age, race, type of discharging neonatal institution, and insurance coverage. The low rate of compliance found among our demographic sample suggests that there may be a more profound effect among higher risk infants with chronic medical conditions. If palivizumab administration is viewed as an immunization, low immunization rates among underinsured, minority populations have been reported previously (Alessandrini, Shaw, Bilker, Schwarz, & Bell, 2001). Additionally, numerous studies have found that patients who are of lower socioeconomic status receive fewer medical services (Lieu & Smith, 1994; McManus & Newacheck, 1993; Newacheck, Stoddard, & McManus, 1993; Newacheck & Halfon, 1986).

Whereas most insurance companies have acknowledged the AAP guidelines, authorization for palivizumab is frequently requested to confirm that the patient is high risk. The definition of “high-risk” varies within the insurance industry. Although investigating the policies of individual insurance companies was beyond the scope of this study, 85% (34 of 40) of patients were fully covered for palivizumab administration under Medi-Cal and/or California Children’s Services (CCS).

The phone interviews with the parents or guardians of these children revealed an interesting anecdotal factor. It does not appear that parental consent or insurance parameters were a hin-

drance toward appropriate administration of palivizumab. Rather, information was not disseminated from the medical community to the families in this patient population.

There is increasing evidence that palivizumab immunoprophylaxis therapy decreases the risk of RSV infection of high-risk infants and toddlers. The impact on this population's health is a top priority. RSV infection can be devastating and life threatening to premature infants and children younger than 2 years with CLD. One promising approach is for medical providers to recognize infants and toddlers at risk for RSV infection and refer them for recommended treatment.

Advanced practice nurses and case managers (CMs) play a key role in the management of this high-risk population. Pediatric nurse practitioners (PNPs) are well positioned to create partnerships between children, family members, and the community to maximize health care outcomes for children with special health care needs (Lindeke, Krajccek, & Patterson, 2001). PNPs must be knowledgeable of the AAP recommendations for administration of the antibody in the acute and primary care settings to identify infants at risk for RSV infection.

CMs working with high-risk infants also should be aware of the benefits of prophylactic therapy and should ensure that therapy is given on a monthly schedule during the season to promote optimal outcomes for this population (Deming, 2002). CMs are involved in the initial referral process and the comprehensive follow up of high-risk infants and toddlers.

It is important that PNPs and CMs identify community agencies that administer palivizumab, such as physician's offices, home health agencies, hospitals, clinics, and public health departments to arrange for delivery of care. Authorization from insurance companies or other funding sources is important to establish prior to administration of the antibody because of the high cost of palivizumab. Cost-containment issues are important to recognize, as well as nursing knowledge of administration of the antibody.

Pediatric nurses have the knowledge, experience, and opportunity to educate parents and guardians about RSV and why their child is at risk for development of the RSV infection. Nurses need

to reiterate the need for meticulous handwashing and explain why it is important to prevent the spread of RSV infection. Nurses also can inform parents of specific symptoms to be aware of (mild to severe) that are associated with RSV and remind parents to avoid exposure of their infant or toddler to others who have cough and cold symptoms. Once their child has been referred for palivizumab treatment, nurses must stress the importance of adhering to the monthly antibody injections during RSV season to protect the child.

The retrospective design of this study limited our ability to determine the reasons for the failure to administer palivizumab. Future areas of prospective investigation could include eluci-

It does not appear that parental consent or insurance parameters were a hindrance toward appropriate administration of palivizumab.

ating a clearer understanding of provider compliance with the AAP guidelines for the administration of palivizumab and potential barriers to the administration of palivizumab.

CONCLUSION

High-risk infants admitted to our hospital have a low rate of administration of palivizumab. Although the benefit of administering palivizumab to a wider pediatric population remains a question, the AAP has recommended specific guidelines for the high-risk population. Our data suggest that these recommendations are not being followed. The causes appear multifactorial. Possible remedies include education of parents of high-risk infants at the time of initial neonatal hospital discharge. Further efforts to improve palivizumab usage in the high-risk population through education should be promoted

among the medical caregivers and families of medically fragile children.

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