Palivizumab Utilization and Compliance: Trends in Respiratory Syncytial Virus Prophylaxis in Florida

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Objectives To analyze adherence to guidelines to prevent respiratory syncytial virus hospitalization and to a monthly immunoprophylaxis schedule in the absence of prior authorization requirements.

Study design Among Florida Medicaid fee-for-service recipients 0 to 2 years of age from the 1998/1999 season through the 2004/2005 season with available birth certificates, we identified indications for palivizumab prophylaxis based on claims data. At least 4 doses of palivizumab in the 5 core season-months were considered full season coverage.

Results Of 302 101 children-seasons, 6089 were associated with 24 469 doses of palivizumab. In the 2004/2005 season, 73.6% of children with chronic lung disease received immunoprophylaxis, 67.6% children with gestational age <32 weeks, 37% with congenital heart disease, 26.4% with cystic fibrosis, and 19.4% with severe immunodeficiency. Multiple indications increased the likelihood for prophylaxis from 34.9% to 80.4%. Full season coverage was consistent across indications at approximately 70%. From the 1998/1999 season through the 2004/2005 season, 8038 doses were administered during 2051 children-seasons without any indication; mostly (69.6%) where premature children had exceeded the recommended age range for prophylaxis.

Conclusions High utilization rates were found in children with multiple indications, and compliance with a monthly schedule was consistently high. One third of doses were administered outside of guidelines, suggesting suboptimal utilization of resources in the absence of prior authorization. *(J Pediatr 2010;156:953-9)*.

Respiratory syncytial virus (RSV) is the most frequent cause of lower respiratory tract infections among infants and children. According to one estimate for the United States, RSV causes up to 120 000 hospitalizations annually for pneumonia or bronchiolitis among infants younger than 1 year of age,[1] whereas a more recent study reports an annual RSV hospitalization rate of 57 275 for children under the age of 5 years.[2] The same study estimated that 2.1 million children under the age of 5 years seek medical attention for RSV infections each year—3% of whom are hospitalized, 25% visit emergency departments, and 73% are treated in pediatric practices.

Although no vaccination is available for RSV, palivizumab (Synagis, MedImmune Inc., Gaithersburg, Maryland), a humanized monoclonal antibody, has been shown to prevent RSV-related hospitalizations,[3,4] albeit at significant cost. Five doses of palivizumab are necessary to protect 1 child throughout a 5-month RSV season at an average total wholesale price that can exceed $8000, depending on body weight.[5] These costs limit prophylaxis to children at greatest risk for infection, such as children with chronic lung disease (CLD), congenital heart disease (CHD), and certain preterm infants as recommended by the American Academy of Pediatrics (AAP) RSV prevention guideline from 2003.[6] Among the listed indications, strength of evidence for the effectiveness of palivizumab ranges from expert opinion to data from randomized clinical trials. Accordingly, the guideline's recommendations for indications that are not based on randomized clinical trials data are phrased more carefully (**Table I**; available at www.jpeds.com). Even though the strength of evidence is considered in guidelines development, it is unclear whether this is reflected in prescriber decision-making and palivizumab utilization rates.

Information about underutilization in children who should receive prophylaxis and overutilization in those not included in the guidelines is critical for third-party payers to target policy interventions. Knowledge about palivizumab utilization in the absence of prior authorization programs can help health plans to develop or refine their own reimbursement policies to ensure access for children who might benefit from immunoprophylaxis and restrict access where the RSV hospitalization risk is low. Furthermore, because gaps in palivizumab administration may lead to suboptimal effectiveness, knowledge about adherence to the monthly dosing schedule during the core season is important to ensure optimal protection. We sought to analyze

AAP	American Academy of Pediatrics
CF	Cystic fibrosis
CHD	Congenital heart disease
CI	Confidence interval
CLD	Chronic lung disease
GA	Gestational age
OR	Odds ratio
RSV	Respiratory syncytial virus

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longitudinal compliance with the 2003 AAP guidelines for RSV immunoprophylaxis with palivizumab in the Florida Medicaid population. We report the proportion of patients who recieved any palivizumab prophylaxis and the proportion with full compliance broken down by indication for prophylaxis during a single season. Further objectives were to investigate sociodemographic patient factors as determinants for immunoprophylaxis and to present the proportion of palivizumab recipients without indications according to guideline.

Methods

Our sample consisted of Florida Medicaid fee-for-service recipients under 2 years of age. This analysis concentrated on the core months of the RSV season from October through February and covered 7 seasons from 1998/1999 through 2004/2005. To ensure that every subject had the chance to receive a full course of palivizumab, participants had to be continuously eligible between September and February to be included in the respective season. We restricted age to a minimum of 30 days on October 1 and a maximum of 2 years at the end of February. Subjects had to be in ambulatory care during September because inpatient claims data provide no information about medication utilization, which was necessary for the identification of guideline-supported indications for palivizumab prophylaxis. The unit of analysis was children-season, and 1 child could contribute up to 2 children-seasons. To achieve valid estimates on gestational age, we matched Medicaid recipient data to birth certificates.

Season Definition

RSV seasons in Florida differ from the rest of the country, resulting in earlier onset and longer duration.[7] As a consequence, seasonal palivizumab utilization can exceed the 5 doses per child, as are generally recommended for the northern hemisphere.[6] Seasons differ even within the state, with longer seasons in the south compared with the north.[8] To use a time period that is applicable to the whole state, we defined a core season from October through February to include months that consistently have shown high infection rates across the study period according to the Centers for Disease Control and Prevention's National Respiratory and Enteric Virus Surveillance System and the Florida Department of Heath RSV Surveillance System.[9,10]

Indications

We grouped risk factors for RSV infections according to AAP guidelines into 6 palivizumab indications, which are detailed in **Table I** (available at www.jpeds.com). This classification considered age restrictions for immunoprophylaxis such as a maximum age at season onset of 12 months for infants born before or during 28 weeks' gestational age (GA). As a consequence, a prematurely born child with CLD would have multiple indications in the first year of life but only 1 indication, CLD, in the second year.

The guideline from 2003 added the CHD indication as a modification from the previous guideline published in 1998.[11] To facilitate longitudinal comparisons, we applied the definitions from the 2003 guideline to the entire time period. International Classification of Diseases–Clinical Modification Version 9 codes of inpatient and outpatient claims were used in conjunction with drug claims (for CLD and CHD) to identify children with current indications for palivizumab.

Utilization and Compliance

Using National Drug Codes and procedure codes, we identified palivizumab claims for each season and assigned recipients into categories according to their number of claims in 1 season. Two claims had to be at least 20 days apart to ensure that single doses that were associated with multiple claims (for more than 1 vial) only were counted once. Because the nature of our data set did not allow for assessment of drug utilization during hospital stays, we imputed 1 dose of palivizumab for each hospital stay if the patient had another claim for palivizumab at some point in the season but not between admission and 30 days after discharge.

We calculated the proportion of fully compliant users as the proportion of patients with at least 4 doses during 1 season divided by the number of palivizumab users, that is, children who received at least 1 dose. Although a 5-month season would require 5 doses of palivizumab for a high-risk patient, we accepted 4 doses as full coverage to allow for minor delays in palivizumab administration.

For the most recent season in our study period, the 2004/2005 season, we calculated unadjusted exposure odds ratios for subjects with indication to determine predictors for immunoprophylaxis. Also for 2004/2005, we provide additional detail on the level of single indications. Within indications, we used conditional logistic regression to calculate the likelihood of receiving immunoprophylaxis associated with the presence of a second indication, adjusting for patient demographics (sex, age, race, Medicaid district, type of eligibility, and rural versus urban location).

Data were analyzed using SAS 9.1.3 (SAS Institute, Cary, North Carolina), graphs were created in Microsoft Office Excel 2003 (Microsoft Corporation, Redmond, Washington), and Epi Info 3.3.2 (Centers for Disease Control and Prevention, Atlanta, Georgia) was used to calculate odds ratios and 95% confidence intervals. The institutional review boards of the University of Florida and the Florida Department of Health approved the study protocol.

Results

After excluding patients without available birth certificates and applying our seasonal eligibility criteria, our sample consisted of 302 101 children-seasons. Among these, 6089 were associated with 24 469 doses of palivizumab during the seasons 1998/1999 through 2004/2005.