

CLINICAL STUDY

Prevention of Respiratory Syncytial Virus Infection Among Puerto Rican Infants

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Respiratory syncytial virus (RSV) is the leading cause of lower respiratory illness in children. Prevention of this infection is available with the use of intravenous immunoglobulin or an intramuscular humanized monoclonal antibody (palivizumab). Palivizumab has been available in Puerto Rico since 1999. The objective of this study was to follow-up infants who received RSV prophylaxis with palivizumab in Puerto Rico to assess its efficacy and safety. A total of 230 infants who received RSV prophylaxis during the 2000-2001 and 2001-2002 seasons were followed-up. Adverse events from injections were minimal including erythema (2%), fever (5%), pain (4%), and rash (2%). In none of the patients

prophylaxis was discontinued due to side effects. Forty-four infants (19%) had at least one respiratory hospitalization throughout the season, with RSV confirmed in seven (3%). Most hospitalizations occurred in the month of August when infants had received only one dose of palivizumab and on December, a peak month for RSV infections. Five infants (2.2%) required admission to an intensive care unit. In none of them, RSV was confirmed. This study confirms that monthly intramuscular administration of palivizumab is effective in preventing serious RSV infections in high risk infants.

Key words: Bronchiolitis, Chronic lung disease, Palivizumab, Prematurity, Respiratory syncytial virus

Respiratory syncytial virus (RSV) is the leading cause of lower respiratory illness in children (1). The risk of serious RSV illness is highest among those with prematurity, bronchopulmonary dysplasia (BPD), chronic lung disease (CLD), multiple congenital anomalies, and certain immunodeficiencies. Many of the children infected with RSV will require re-hospitalization and re-intubation for respiratory failure. A frequent and worrisome sequelae is the worsening lung disease, requiring increased support with supplemental oxygen, bronchodilators, and/or diuretics (2).

Prevention for this infection is available with the use of intravenous immunoglobulin (RSV-IGIV) or an

intramuscular humanized monoclonal antibody (palivizumab). Palivizumab is humanized by recombinant methods and has been found to be safe in monthly doses of 15 mg/kg. In 1998, the results of a multicenter, multinational, phase III trial (IMPact-RSV) to evaluate the safety and effectiveness of monthly administration of palivizumab as prophylaxis for serious RSV illness in high risk infants, were published (1). Palivizumab reduced the incidence of hospitalization due to RSV by 55%. After the IMPact study, the American Academy of Pediatrics Committee on Infectious Diseases and Committee on Fetus and Newborn published the recommendations for the use of palivizumab as RSV prophylaxis (3). The objective of this study was to follow-up infants who received RSV prophylaxis with palivizumab in Puerto Rico to assess the efficacy and safety of such therapy.

Methods

A group of infants who received RSV prophylaxis with palivizumab during the 2000-2001 and 2001-2002 seasons was followed-up. A questionnaire was filed by parents at clinics, by mail, or by telephone interview. Medical data was obtained from medical records. Descriptive statistics were obtained including means, median, frequency distribution, range, and standard deviation. Differences

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were assessed using t-test and Pearson's chi-square. The study was approved by the Institutional Review Board.

Results

Population characteristics. A total of 230 infants were followed, 129 females and 101 males. The mean gestational age was 30 weeks and mean birth weight was 1420 grams. Twenty-nine percent (29%) of the infants had bronchopulmonary dysplasia, defined as oxygen requirement at 28 days of age. Twenty-one percent (21%) had chronic lung disease, defined as oxygen requirement at 36 weeks post conceptional age. Eight infants (4%) required oxygen therapy at home after discharge from the neonatal intensive care unit. Sixty-nine percent (69%) of the infants had the government medical insurance.

Population outcome. All infants received a mean of four doses of palivizumab. Adverse events from injections were minimal including erythema (2%), fever (5%), pain (4%), and rash (2%). In none of the patients prophylaxis was discontinued due to side effects. Forty-four infants (19%) had at least one respiratory hospitalization throughout the season, with RSV confirmed in seven (3%). Main diagnoses on respiratory hospitalizations included bronchiolitis, pneumonia, and asthma. Most hospitalizations occurred in the month of August when infants had received only one dose of palivizumab and on December, a peak month for RSV infections (Figure 1).

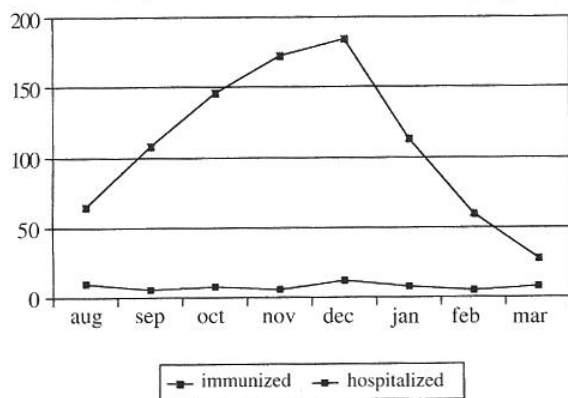


Figure 1. Number of infants Immunized each month and those of them who had hospitalizations for respiratory problems

Five infants (2.2%) required admission to an intensive care unit. In none of them RSV was confirmed.

Discussion

The respiratory syncytial virus is a serious threat to premature infants and those with CLD. These infections carry additional morbidity to infants born premature who

do not have a mature immune system. Unpublished data from community hospitals in Puerto Rico show a significant number of RSV-related admissions in infants less than two years old. RSV infections are seen in Puerto Rico throughout the year, with a peak incidence or season during the months of August through March.

Palivizumab has been available in Puerto Rico since 1999 but the prophylaxis rate is still low, with approximately 55% of infants with established criteria actually receiving the prophylaxis. Reasons for not receiving immunization include lack of awareness, of the indications for prophylaxis and the importance of preventing this serious infancy disease, among the medical community and the insurance companies. This study of Puerto Rican infants shows that monthly intramuscular administration of palivizumab is effective in preventing serious RSV infections at rates comparable to the Impact- RSV trial (Table I) with minimal adverse events. This was true even

Table 1. Outcome of infants immunized with palivizumab as compared to the IMpact trial

	Study Group N= 230	IMpact trial N= 1002
All patients	3.0%	4.8%
All premature <32 weeks	3.8%	5.8%
All infants with CLD	6.0%	7.9%

in the presence of high risk environments such as socio-economical disadvantage evidenced by the high number of families with the government health insurance. Efforts should be directed toward assuring that every infant who meets the criteria for prophylaxis, as recommended by the American Academy of Pediatrics, receives palivizumab throughout the RSV season.

Resumen

El virus respiratorio sincitial (VRS) es la causa principal de enfermedad del tracto respiratorio bajo en niños. Las medidas preventivas para esta infección están disponibles con el uso de inmunoglobulina intravenosa o un anticuerpo monoclonal humanizado intramuscular (palivizumab), el cual está disponible en Puerto Rico desde 1999. El objetivo de este estudio fue darle seguimiento a los niños que recibieron profilaxis para el VRS con palivizumab en Puerto Rico para determinar su eficacia y seguridad. Se le dió seguimiento a un total de 230 niños que recibieron profilaxis para VRS durante las temporadas 2000-2001 y 2001-2002. Los efectos adversos del medicamento intramuscular fueron mínimos: enrojecimiento (2%), fiebre (5%), dolor (4%), y erupción cutánea (2%). En ninguno de los pacientes se discontinuó

la profilaxis por efectos secundarios. Cuarenta y cuatro infantes (19%) tuvieron al menos una hospitalización por problemas respiratorios durante la temporada, con VRS confirmado en siete de ellos (3%). La mayor parte de las hospitalizaciones ocurrieron en el mes de agosto, cuando los infantes habían recibido solo una dosis de palivizumab y en diciembre, un mes pico para las infecciones por VRS. Cinco infantes (2.2%) requirieron admisión a una unidad de cuidado intensivo; en ninguno de ellos se confirmó el VRS. Este estudio demuestra que la administración mensual de palivizumab intramuscular es efectiva en prevenir infecciones serias de vías respiratorias por VRS en infantes de alto riesgo.

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