INTRODUCTION

Respiratory syncytial virus (RSV) is the leading cause of hospitalization for respiratory infection in children (1). Monthly intramuscular injections of palivizumab (Synagis®, MedImmune Inc.), a monoclonal antibody, reduce RSV-related hospitalizations in high-risk infants with prematurity, chronic lung disease or heart disease(2). Alaska Native infants from the Yukon Kuskokwim (YK) Delta region of Alaska experience extremely high rates of RSV hospitalization, 156 per 1000 infants < 1 year (3). RSV hospitalization rates among high-risk YK premature infants decreased after palivizumab use; however, compliance with monthly palivizumab was low (4).

The YK Delta encompasses 75,000 square miles of coastal wetlands and tundra, and the population of ~30,000 is comprised primarily of Yup’ik Eskimos (85%) who live in 52 villages, and the regional town. Villages are connected only by airplane, boat and snow machine, and no roads connect the region to the remainder of the state. The YK Delta Regional Hospital (YKDRH), a 50-bed primary care facility, is the only hospital in the region. Primary health care in the village clinics is provided by certified Community Health Aides (CHAs). These non-licensed providers receive standardized training and
act on standing orders and phone communication with YKDRH physicians.

During 1998-2003, palivizumab recipients received palivizumab doses either at YKDRH (requiring a plane flight from the village) or by a nurse traveling to the village. Adverse weather and scheduling problems resulted in low compliance. During the 2003-2004, YKDRH conducted a pilot project to train CHAs to administer palivizumab in villages.

MATERIAL AND METHODS

In 2003, 22 CHAs (representing 20 of the 52 YK villages) received a 4-day training on RSV and palivizumab reconstitution and administration at YKDRH. Villages selected for the intervention had children eligible for palivizumab and CHAs who were trained to administer intramuscular injections. The YKDRH pediatric nurse case manager maintained a database of palivizumab recipients with administration and due dates. Before a child’s due date, the nurse contacted the CHA for the current weight and YKDRH pharmacy shipped the palivizumab to the village clinic. At the village clinic visit, the CHA reviewed the dose by phone with the pediatrician, and the dose was reconstituted and administered. Children in non-pilot villages, in general, were flown to YKDRH for palivizumab doses.

We used the American Academy of Pediatrics criteria to select children eligible for palivizumab (5) at the start of the RSV season: infants < 12 months old with gestational age < 28 weeks; infants < 6 months of age with gestational age 29-32 weeks; infants < 6 months of age with gestational age 33-35 weeks and 2 other risk factors; children < 2 years of age with chronic lung disease requiring daily medication; and children < 2 years of age with...
significant heart disease. The only contraindication to palivizumab is history of severe prior reaction to palivizumab.

Applying the methodology of Mullins et al (6) the median RSV season onset week in YK Delta during 1994-2004 was October 14-20 and median offset was May 19-25. The median RSV season duration in YK Delta was 31 weeks versus 15 weeks for the US. Because of the prolonged RSV season, palivizumab was administered between October 1 and May 31.

We evaluated patient compliance by comparing the actual number of injections administered with the projected numbers, based on month of first dose. For example, a patient initiating palivizumab prophylaxis in January could anticipate receiving a total of 5 injections. We also calculated the proportion of “protected days” during the RSV season. “Protected days” were defined as those ≤ 32 days after palivizumab administration, whereas “unprotected days” were days during the RSV season before the first palivizumab dose or >32 days after an injection. The recommended monthly administration time period was determined based on pharmacodynamic data. In this population, recommendations are to administer palivizumab 28-32 days apart, so we chose 32 days as a reasonable window within which children should receive their dose if compliant with palivizumab.

RESULTS

111 YK Delta children received ≥ 1 injection of palivizumab during the 1998-2001 seasons, and 68 children received ≥ 1 injection during 2003-2004. Patient criteria for palivizumab prophylaxis in 1998-2001 and 2003-2004 were, respectively, gestational age ≤ 32 weeks gestation (30% vs. 25%), gestational age 33-35 weeks (42% vs. 48%), chronic lung disease (23% vs. 9%), heart disease (4% vs. 9%), and other (1% vs. 9%).

During the 2003-2004 RSV season, 90.4% of projected palivizumab doses were administered compared with 74.0% during 1998-2001. Palivizumab recipients were protected during 85.1% of the RSV season days in the 2003-2004 season compared with 67.3% of the days during the 1998-2001 seasons. The increase in proportion of protected days from 1998-2001 to 2003-2004 was larger in pilot project villages (68.6% to 86.4%) than in non-project villages or regional town (76.4% to 82.2%, p< 0.01). During the 2003-2004 season 8% (n = 31) of palivizumab injections were received in Anchorage during the birth hospitalization or specialty clinic visits, 41% (n = 166) were received at YKDRH, and 51% (n = 207) were received in village clinics.

DISCUSSION

A targeted training program led to village-based administration of palivizumab which improved compliance. Having CHAs administer palivizumab eliminated the monthly plane trip to YKDRH. This resulted in a savings of time and money, and reduced risks associated with travel in small aircraft. Because of the high RSV hospitalization rates we estimated that treatment of 4 children from YK Delta would result in prevention of one RSV hospitalization (4). While the cost of palivizumab is high, the cost savings, reduc-
tion in RSV hospitalization and prevention of morbidity make this a reasonable prevention modality. In 2004-2005 the pilot project was expanded to other YK villages with palivizumab recipients. Ongoing surveillance of RSV-related and other respiratory hospitalizations in the YK Delta will evaluate the effect of palivizumab and other prevention and treatment modalities (4).

Since pilot villages were not randomly selected, unmeasured confounding factors could affect our comparison in 2003-2004 between pilot project villages and non-pilot project villages. However, we measured compliance before (1998-2001) and after (2003-4) project initiation, and in pilot project villages we saw an increase in compliance of 18% versus 6% in non-pilot project villages.

Golombek (7) also reported improved compliance when RSV prophylaxis was administered closer to home. In-home RSV prophylaxis was associated with lower RSV hospitalization rates than office-based prophylaxis (7), and parent satisfaction was high. In an increasingly complex health care system, patients prefer to receive care close to home.

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