Understanding the New Palivizumab Guidelines

Allan S. Lieberthal, MD, FAAP

In the August 2014 issue of Pediatrics the AAP published new guidelines for the use of palivizumab (Synagis™) that makes significant changes from previous policy statements and the current Red Book. The purpose of this article is to briefly review the major changes.[1,2]

While RSV is present in 76% of bronchiolitis patients, human rhinovirus is present in 39% of patients. Other viruses found in bronchiolitis are influenza, coronavirus, human metapneumovirus, and parainfluenza. Co-infection with more than 1 virus is common. Most of the literature focuses on RSV.[3]

There have been only 2 randomized controlled trials of palivizumab, both done by the manufacturer for licensing purposes. The first is the IMpact-RSV trial conducted during the 1996-1997 RSV season. This randomized, placebo-controlled, double-blind trial involved 1501 infants and young children born preterm (at or before 35 weeks' gestation), some of whom had chronic lung disease (CLD) of prematurity.[4] The IMpact-RSV trial demonstrated a RSV hospitalization rate of 10.6% in the placebo arm and 4.8% among high-risk infants who received prophylaxis, a reduction of 5.8% in RSV hospitalizations (P <.001). Patients in this study were less than 36 week gestation, As a result, the FDA licensed Synagis™.

The second randomized, double-blind, placebo-controlled trial conducted from 1998-2002 enrolled 1287 children with hemodynamically significant congenital heart disease (CHD).[5] This cardiac trial evaluated both the safety and efficacy of palivizumab prophylaxis and demonstrated an RSV hospitalization rate of 9.7% in the placebo arm and 5.3% among recipients of palivizumab prophylaxis, a reduction in the RSV hospitalization rate of 4.4% (P <.003).[4]

All studies since then have been observational and epidemiological. However these studies have consistently shown a decrease in hospitalizations due to bronchiolitis. They have also studied the infants at greatest risk of hospitalization. The new guidelines are based on this extensive body of literature.

The most important, and controversial, recommendation is that palivizumab prophylaxis may be administered to infants born before 29 weeks, 0 days' gestation who are younger than 12 months at the start of the RSV season.[6] This is a significant change from the 2009 Red Book statement that palivizumab should be given to premature infants less than 32 weeks gestation.[7] This is based on several studies showing little statistical difference between premature infants ≥29 weeks gestation and those later pre-term infants

Epidemiologic studies[8,9,10] consistently show the greatest increase in hospitalization rates in children <29 weeks gestation; 2-4 times higher than later preterm infants as shown in Table 1.

Table 1[8]: Average RSV Hospitalization Rates Among Children Younger Than 24 Months (2000-2005)[a]

Children <24 mos.	N[a]	RSV Hospitalization Rate/1000	95% CI
All infants regardless of gestational age	559[b]	5.2	4.8-5.7
All term infants (≥37 wk gestation)	479	5.3	4.9-5.8
All preterm infants (<37 wk gestation	56	4.6	3.4-5.8
≥35 wk gestation	494	5.1	4.7-5.5
32-34 wk gestation	23	6.9	4.3-10.1
29 -31 wk gestation	6	6.3	2.0-12.4
<29 wk gestation	12	19.3	8.4-23.0
All very preterm (<30 wk gestation)	15	18.7	10.0-30.0

a. Among 2149 enrolled hospitalized children from a birth cohort of 132 085 children.

b. The total of 559 children hospitalized with RSV includes 24 whose gestational age could not be verified.

c. Personal communication, Geoffrey A. Weinberg, MD.