## Palivizumab Prophylaxis: How to Compare Pre- and Post-Prophylaxis Eras?

To the Editor,

In a recent issue of Pediatric Pulmonology, Grimaldi et al. published their data on palivizumab prophylaxis in preterm infants with ≤30 weeks gestational age with no bronchopulmonary dysplasia.[1] In the Burgundy area with 12 hospitals, palivizumab was not in use for this patient group until 2002, but from the 2002–2003 respiratory syncytial viral (RSV) season onwards, palivizumab was given if the calendar age of the child was <6 months at the start of the season. The hospitalization rates for RSV bronchiolitis decreased from 14% (1999–2000 RSV season), 17% (2000–2001), and 10% (2001–2002) to 0% (2002–2003) and 2% (2003–2004). However, the annual numbers of hospitalized children were small, 3, 8, 5, 0, and 1, respectively. By the conventional chi-square test, $P$ value is <0.05 when analyzed per intention-to-treat and >0.05 when analyzed per completed protocol, and moving one patient in the era of prophylaxis or two patients in the era of non-prophylaxis from one group to another seems to cause marked changes in statistical significances.

The other problem in the article was the calculation of the number needed to treat (NNT) values when historical controls were used. Maybe, the use of NNT values should be restricted only to randomized-controlled trials. Furthermore, NNT values were calculated also for observational Scandinavian studies,[2,3] and in these calculations, palivizumab was proposed to produce a 55% relative risk reduction, as was observed in the Impact study.[4] The figures got by these calculations are only speculative. In addition to the social differences between different countries,[1] RSV infections seem to have different epidemiological patterns in different climates. In northern climates, there is an RSV epidemic every other year, usually from October to January, alternating with mild spring epidemics every other April to May.[5]

In the study from Burgundy,[1] no attempts were made to control confounding factors. At least the 12 attending hospitals and the 5 different RSV seasons are such confounders. In 2005–2006 during a severe epidemics, as many as 8% of all infants <6 months of age were hospitalized for RSV infections within a 3-month period in the Kuopio area in North-East Finland,[6] compared to only occasional cases 1 year earlier. One potential explanation for the improved figures in Burgundy may be the Hawthorne effect, since during palivizumab prophylaxis requiring repeated contacts with medical or nursing staff, the parents become more aware of the risks of getting an RSV infection. This must have been influenced to the behavior of the families.

Though the efficacy (can it work?) of palivizumab prophylaxis in preterm infants has been shown in the Impact study,[1] the effectiveness (does it work?) and efficiency (is it worth it?) of the use of palivizumab prophylaxis, not only the validity of the restricted palivizumab indications stressed by Grimaldi et al.,[1] should be assessed by population-based studies. Currently, palivizumab is used by different indications in different countries, and even in different areas within the same country. This is a challenge when reporting monitoring data on the efficiency of prophylaxis. To avoid publication bias, both positive and negative reports should be submitted and published. When the pre- and post-prophylaxis eras are compared, the interpretation of the results should be done with care and certain conservatism.

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## REFERENCE

1. Grimaldi M, Gouyon B, Sagot P, Quantin C, Huet F, Gouyon J-P. Palivizumab efficacy in preterm infants with gestational age ≤30 weeks without bronchopulmonary dysplasia. Pediatr Pulmonol 2007;42:189–192.
2. Naver L, Eriksson M, Ewald U, Linde A, Lindroth M, Schollin J. Appropriate prophylaxis with restrictive palivizumab regimen in pre-term children in Sweden. Acta Paediatr 2004;93:1470–1473.
3. Heikkinen T, Valkonen H, Lehtonen L, Vainionpää R, Ruuskanen O. High risk infants for respiratory syncytial virus infection: implications for palivizumab prophylaxis. Arch Dis Child Fetal neonatal Ed 2005;90:F64–F68.
4. The Impact-RSV study group. Palivizumab, a homogenized respiratory syncytial virus monoclonal antibody reduces hospitalization from respiratory syncytial virus infection in high-risk infants. Pediatrics 1998;102:531–537.
5. Waris M. Pattern of respiratory syncytial virus epidemics in Finland: two-year cycles with alternating prevalence of groups A and B. J Infect Dis 1991;163:464–469.
6. Korppi M, Hiltunen J. Pertussis is common in nonvaccinated infants hospitalized for respiratory syncytial virus infection. Pediatr Infect Dis J 2007;26:316–318.

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