CPSP
CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

Respiratory syncytial virus (RSV) infections in paediatric transplant patients

PROTOCOLS

Principal investigator

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Background

The purpose of this study is to determine the severity of respiratory syncytial virus (RSV) infections in transplant recipients. RSV causes upper or lower respiratory tract infections in almost all children in the first two years of life, resulting in hospitalization for approximately 2%. It is increasingly recognized that the burden of lower respiratory tract disease from RSV extends to children two to five years of age, with about 0.4% being hospitalized annually with RSV-related respiratory disease.[1]

Children with prematurity, chronic lung disease (CLD) or immunodeficiency have markedly higher risks of hospitalization and intensive care stays with RSV infection. The magnitude of this increased risk has not been quantified in solid organ transplant (SOT) (liver, heart, lungs, kidneys, intestines) or hematopoietic stem cell transplant (HSCT) recipients. The literature describes almost universal hospitalization and a high rate of morbidity for children who develop a lower respiratory tract infection with RSV within one year post-transplant, but it is not clear if less severe cases occur and are not reported. A study of 122 HSCT recipients with weekly nasopharyngeal samples for the first 100 days post-transplant found five RSV infections, resulting in only one lower respiratory tract infection.[2] The bulk of the patients in this study, however, were adults who, although at risk for severe RSV disease post-transplant, are undoubtedly at much lower risk than young children. A medical decision analysis used markedly different estimates, presuming that about 20% of all paediatric HSCT recipients will be hospitalized with RSV infection within one year of the transplant with a 70% mortality rate.[3]

Quantifying the true risk of severe RSV infection for different types of transplants and different age groups at various times post-transplant has become an urgency of practical

importance, as there is now a monoclonal antibody (palivizumab) available for RSV prophylaxis. Serious adverse events are very rare with palivizumab and it prevents about half of RSV infections in children with congenital heart disease or CLD related to prematurity, and about 80% in children with prematurity and no CLD. However, it requires monthly injections throughout RSV season (typically five doses by intramuscular injection over the course of a year, with children weighing over 7 kg requiring multiple injections per dose) at a cost of approximately $1,400 per dose for a 7-kg child.

There is no published data on use of palivizumab in transplant recipients, yet a recent survey showed that about half of centres performing SOTs in the United States administer palivizumab, typically to children under 12 months of age but sometimes to children as old as four years.[4] An informal survey of Canadian centres suggests palivizumab is used primarily in children who have other major risk factors for severe RSV disease such as chronic lung disease. The objective of this study will be to collect data on morbidity associated with RSV infection in Canadian transplant recipients to establish potential costs and benefits of palivizumab.

Methods

Through the Canadian Paediatric Surveillance Program, over 2,500 paediatricians and paediatric subspecialists will be actively surveyed to identify new cases of RSV in transplant patients. Data on the number of SOTs and HSCTs from two years prior until the end of the study will be obtained from the Canadian Institute for Health Information and the C^{17} Research Network (a Canada-wide group of paediatric oncologists and hematologists researchers) for calculation of approximate RSV incidence rates.

Objectives

1) Estimate the incidence of RSV infections requiring hospitalization within two years following a SOT or HSCT.
2) Determine if the type of transplant alters the risk of hospitalization with RSV.
3) Describe the length of stay and need for intensive care for transplant patients admitted with RSV, and determine if the type of transplant or time since transplantation alters these factors.
4) Determine if children with infections from RSV within two years of a transplant are ever successfully managed as outpatients.

Case definition

Report all inpatients and outpatients less than 18 years of age who have:

- a laboratory-confirmed respiratory syncytial virus (RSV) infection

and

- received a solid organ transplantation (SOT) or a haematopoietic stem cell transplantation (HSCT) within the two previous years.

Duration

September 2010 to August 2013

Respiratory syncytial virus (RSV) infections in paediatric transplant patients (continued)

A three-year study is vital as the incidence of severe RSV infections can vary markedly from year to year. It is expected that the use of palivizumab in transplant recipients will increase as the study proceeds, as guidelines may become more permissive.

Expected number of cases

The number of SOT and HSCT patients admitted with RSV was three to the Hospital for Sick Children in 2009 and three to the Stollery Children's Hospital from 2003 to 2008 inclusively. Extrapolating from these numbers, two inpatients should be enrolled annually. In outpatients with RSV infections, the majority may be missed by the current methodology as routine testing is discouraged because of cost. The goal in looking at outpatients is primarily to determine if physicians ever knowingly manage known RSV infections in transplant recipients as outpatients. Five outpatients should be enrolled annually.

Ethical approval

University of Alberta Health Research Ethics Board

Analysis and publication

The investigators will analyse the data promptly and report any significant findings to the CPSP. Quarterly reports and an annual report will be distributed to all participants. Data will be presented as a scientific abstract at national and international meetings and submitted for publication to a peer-reviewed journal.

References

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3. Thomas NJ, Hollenbeak CS, Ceneviva GD, Geskey JM, Young MJ. Palivizumab prophylaxis to prevent respiratory syncytial virus mortality after pediatric bone marrow transplantation: a decision analysis model. *J Pediatr Hematol Oncol* 2007; 29: 227-32.
4. Michaels MG, Fonseca-Aten M, Green M, Charsha-May D, Friedman B et al. Respiratory syncytial virus prophylaxis: A survey of pediatric solid organ transplant centers. *Pediatr Transplant* 2009; 13(4): 451-6