Rhinovirus C Infections are Associated with Treatment Failure in Preschool Children with Recurrent Wheezing


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Abstract

**Rationale:** Viral infections, most commonly rhinoviruses (RV), are the most frequent cause of respiratory tract illnesses (RTIs) and wheezing in preschool children. There are three RV species, A, B, and C, and RV-C has recently been associated with more severe RTIs in children. We assessed the relationships among viral etiology and illness severity in children enrolled in the Azithromycin for Preventing the Development of Upper Respiratory Tract Illness into Lower Respiratory Tract Symptoms (APRIL) study.

**Methods:** Nasal samples (n=1983) were collected at randomization and during RTIs from preschool-age children enrolled in APRIL, and were analyzed using PCR and partial sequencing to identify adenoviruses, coronaviruses, bocavirus, enterovirus, rhinoviruses (A, B, C), influenza, parainfluenza, respiratory syncytial virus and metapneumovirus. Relationships among viral etiology and illness severity were analyzed by discrete survival. Treatment failure was defined as need for systemic corticosteroids.

**Results:** Viruses were detected in 87% of RTIs that led to treatment failure (TF), 78% of non-TF RTIs, and 38% of non-RTI samples. RV-A (22%) and RV-C (25%) were most commonly detected during RTIs. During the APRIL study, RV-C was detected in 36% of TFs. Patients with RTIs induced by RV-C had significantly increased risk of TF (HR 1.8; p=0.01). Infections with RV-A (HR 1.6; p=0.02) or RV-B (HR 1.0; p=0.87) or other viruses (HR 1.8; p=0.10) did not significantly increase risk of TF.

**Conclusions:** RV-A and C were the most common viruses detected during RTIs in preschool aged children enrolled in the APRIL study. Infection with RV-C was associated with increased risk of treatment failure.

**Future Directions**

- Determine if RV-C dependent treatment failures are more likely during specific seasons.
- Determine if the benefit of azithromycin is rhinovirus species specific in preventing treatment failures.

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**Figure 1.** Viral detection rates were 38% of well-visit samples, 78% of respiratory tract illness samples (RTI), and 87% of treatment failure samples (TF).

**Figure 2.** Rhinovirus species detection by season during well-visit and respiratory tract illness (RTI).

**Figure 3.** Odds Ratio of a respiratory tract illness progressing to treatment failure.