2630. Treatment of RSV Lower Respiratory Tract Infection in Two Immunocompromised Children with Polyclonal Immunoglobulin Containing Standardized Levels of Neutralizing Anti-RSV Antibody

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Session: 271. Pediatric Respiratory Viral Infections
Saturday, October 5, 2019: 12:15 PM

Background: Respiratory syncytial virus (RSV) can cause severe lower respiratory tract infection (LRTI) in immunocompromised children. There is no standard effective treatment, though ribavirin (inhaled or oral), pooled human intravenous immunoglobulin (IVIG), and monoclonal anti-RSV antibody (palivizumab) have been described. RI-002 (ADMA Biologics Inc.) is a pooled human polyclonal IVIG that contains standardized levels of neutralizing anti-RSV antibodies. It was recently FDA-approved for prophylaxis in primary immunodeficiency patients and has been used as compassionate treatment for RSV LRTI in stem cell transplant patients.

Methods: Two children with T-cell lymphoblastic lymphoma, both undergoing delayed intensification chemotherapy, were diagnosed with RSV LRTI. They were both treated with RI-002 under an emergency FDA Investigational New Drug protocol.

Results: Patient 1, a 4-year-old boy, was admitted with fever, neutropenia and nasal congestion, and diagnosed with RSV infection on hospital day (HD) 5. On HD17, he was intubated for respiratory failure. IVIG, palivizumab, and daily oral ribavirin were administered. On HD18, he required high frequency oscillator ventilation, nitric oxide, and paralysis. He was given RI-002 (1.5 g/kg on HD20 and 0.75 g/kg on HD22). He was placed on veno-venous extracorporeal membrane oxygenation (ECMO) on HD23. RSV PCR crossing point (Cp) values trended higher, but remained positive (table). On HD33, RI-002 was re-dosed (0.75 g/kg). Pulmonary compliance and chest CTs improved (figure). On HD52, ECMO support was discontinued. He was discharged on HD88, and currently requires no respiratory support. Patient 2, a 5-year-old boy, was admitted with fever, neutropenia, nasal congestion, cough, and stridor and diagnosed with RSV infection (HD1). He required nasal cannula oxygen. IVIG and daily oral ribavirin were administered. He was given RI-002 (1.5 g/kg on HD3 and 0.75 g/kg on HD5). By HD5, he was afebrile; oxygen was discontinued. He was discharged HD6.

Conclusion: Human polyclonal IVIG containing standardized levels of neutralizing anti-RSV antibodies may be useful in the treatment of RSV LRTI in immunocompromised children. Future studies on the role of RI-002 in treatment of RSV infection in immunocompromised children are warranted.

Figure: Serial Axial Chest CT Images for Patient 1 in Relation to First Dose of RI-002 Treatment

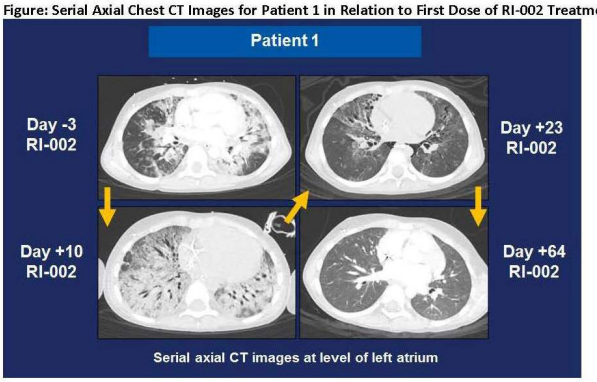

Table: Microbiology data and PCR Crossing Point (Cp) Values from Patient 1

Hospital Day (HD)	RI-002 treatment	Specimen type	RSV PCR Result	RSV PCR Cp*	Viral Culture
HD5		NP swab	Positive	n/a	n/a
HD10		BAL	Positive	21.1	RSV positive
HD17		BAL	Positive	23.2	RSV positive
HD20	1.5g/kg				
HD22	0.75g/kg				
HD24		BAL	Positive	29	No growth
HD29		NP swab	Negative	n/a	n/a
HD29		ETT aspirate	Positive	33.8	No growth
HD33		ETT aspirate	Positive	35.7	No growth
HD34	0.75g/kg				
HD36		ETT aspirate	Negative	n/a	No growth
HD37		NP swab	Negative	n/a	n/a

*PCR Cp values are a semi-quantitative determination of strength of positivity
NP, nasopharyngeal; BAL, bronchoalveolar lavage; ETT, endotracheal; n/a, not available; Cp, crossing point

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2631. Influenza-Associated Intensive Care Unit Hospitalizations and Deaths in Children, During 2010–2019 in Greece

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Session: 271. Pediatric Respiratory Viral Infections
Saturday, October 5, 2019: 12:15 PM

Background: The clinico-epidemiological characteristics of children with severe influenza-related intensive care unit (ICU) admissions in Greece during 2010–2019 are described.

Methods: All laboratory-confirmed influenza cases (real-time PCR), in children 0–16 years old, admitted to Pediatric ICUs throughout the country, are reported using a mandatory notification system to the National Public Health Organization of Greece. Case fatality rates (CFR) were analyzed according to age and presence of comorbidities.

Results: From October 2010 to April 2019, 131 influenza cases [7.2/100,000 children, 65 (49.6%) girls] with PICUs admissions were recorded. The majority of cases (n = 78; 60%) occurred in the age group 0–4 years-old [31 (24%) children were < 12 months-old]. Sixty-five (49.6%) children had underlying comorbidities (22 neurological disease, 12 congenital syndromes, 7 cancer, 5 chronic respiratory, 19 other). The most common diagnosis was febrile ARDS and 67 (51.14%) had severe pneumonia (40% viral, 7% bacterial). Seventy-five (57.2%) children required invasive ventilation. Influenza A accounted for 102 (77.86%) of cases; out of 86 (84.31%) subtyped, 68 (79%) were AH1N1pdm09, and 18 (21%) were AH3N2. Influenza B accounted for 29 (22.13%) of cases. All children received oseltamivir. Median length of stay was 10 days (range 1–90). A total of 32 deaths was recorded (CFR 24.4%, total rate: 1.76/100,000 children); 13 (40.1%) deaths occurred in children with no known co-morbidity. Mortality rates were higher in children aged > 4 years (18/53, 33.9% vs. 14/78, 17.9%, P = 0.04) while there was a trend for children with comorbidities (19/65, 29.2% vs. 13/66, 19.69%, P = 0.1). Only 4% of children were previously immunized against influenza.

Conclusion: AH1N1pdm09 accounted for the vast majority of severe cases and influenza associated deaths in children in Greece over the last 10 years. Severe disease occurred also in children with no comorbitidies. Longitudinal clinico-epidemiological data should be considered in shaping the national immunization program.

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2632. Cord Blood Vitamin D and Maternal Vaccination Status Associated with Decreased Laboratory Confirmed Influenza Infections in Infants

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Session: 271. Pediatric Respiratory Viral Infections
Saturday, October 5, 2019: 12:15 PM

Background: Maternal influenza vaccination has been demonstrated to reduce influenza infections in infants. Influenza infections generally peak during the winter season, and several studies support the association between low levels of vitamin D during winter months and an increase in respiratory infections, including influenza. We examined the effects of vitamin D and maternal influenza vaccination status on laboratory confirmed influenza infections in infants less than 6 months of age.

Methods: Pregnant Bangladeshi mothers were randomized to receive influenza vaccine or pneumococcal vaccine as part of the Mother's Gift study. Mothers reported breastfeeding frequency, along with episodes of infant respiratory illness with fever, every week for the first 6 months of life. If a respiratory illness with fever was reported, nasal swabs were obtained from the infant and tested with a commercial rapid influenza test. Infants with confirmed influenza disease were matched with four controls by birth month and sex, for a total of 84 controls. We measured 25-hydroxyvitamin D levels from cord blood in all cases and controls. A conditional logistic regression was performed to test the effect of vitamin D on the odds of laboratory confirmed influenza while controlling for birth weight, gestational age, crowding, number of siblings, and socioeconomic status score.

Results: A total of 21 infants had laboratory confirmed influenza disease. There were no significant differences in birth weight, crowding, family size, gestational age, socioeconomic status score, infant gender, and smokers in the home between cases and controls (Table 1). Frequency of maternal influenza vaccine was lower in cases when compared with controls (23.81% vs. 58.33%). Serum vitamin D was lower in cases than in controls (8.73 ± 3.34 vs. 10.67 ± 4.08, Table 2).

Conclusion: Both vitamin D levels and maternal vaccination status have medically relevant, and statistically significant, independent effects on the odds of infants contracting influenza. Although the vitamin D levels in the infants at birth were low, there was a significant association of lower levels at birth with an increased risk of influenza virus infection. Further study with a larger sample-size is needed to explore these effects.