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Title: Epidemiology of Rhinovirus in pediatric patients with severe respiratory infections
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Study Purpose and Rationale

In the 1950s, Human Rhinovirus (HRV) was identified as the pathogen causing 'the common cold'. More recently HRVs have been reclassified into the Enterovirus genus (HEV) in the Picornaviridae family as they share many common features, including sense RNA genomes and partial nucleotide sequence identity. HRV and HEV are therefore commonly tested together via Polymerase Chain Reaction. Initial research showed HRV to grow best in cell cultures of 33 degrees Celsius, thus restricting it to the upper airways. However, there is now mounting evidence that HRV can also affect the lower respiratory tract, potentially causing severe respiratory disease in the pediatric population. In 1999 Papadopoulos et al demonstrated minimal differences in replication capacities at 33 and 37 degrees Celsius for eight different HRV strains. More recent studies have shown HRV to replicate in the lower respiratory tract with a few reported cases of histological changes both within the interstitium and in the alveoli. Pathological findings have included bronchiolitis obliterans with organizing pneumonia, interstitial pneumonitis, acute and chronic inflammation with fibrinopurulent alveolar debris, and hyperplasia and desquamation of alveolar cells. Now that there is growing evidence that HRV is a lower respiratory pathogen, studies have been carried out to investigate its pathogenesis and role in causing severe respiratory disease. Several studies suggest that HRV increases the incidence of secondary bacterial infection in pediatric patients, however it remains controversial as to whether HRV can cause severe respiratory disease in children as a sole pathogen. We will identify and characterize all children admitted to the Pediatric Intensive Care Unit at the Columbia University New York Presbyterian Hospital over the one year period from 12/01/14-12/1/15 who tested positive for HRV/HEV by the hospital clinical laboratory. From this we aim to investigate whether HRV, as a sole pathogen can cause severe respiratory disease in the pediatric population. The purpose of the study is to investigate whether Human Rhinovirus (HRV), as a single pathogen is associated with severe respiratory infections in pediatric patients. HRVs are antigenically diverse with over a hundred serotypes. This along with lack of epidemiological data to identify the most common circulating strains have resulted in difficulties to create a vaccine. The rationale behind this study is to determine if HRV is associated with severe respiratory infections in the pediatric population, and if so will warrant further research into its pathophysiology, epidemiology and development of preventative measures.

Study Design

The study is a retrospective observational medical chart review We will identify all children with nasopharyngeal specimens positive for HRV admitted over a year period from 12/1/2014 - 12/1/2015 to the Columbia University New York Presbyterian Hospital Pediatric Intensive Care Unit using NYPH Cohort Discovery. We will use the Electronic

Medical Records (EMR) to retrospectively gather data on general demographics, outcome, co-infections, co-morbidities, primary diagnosis, and laboratory data including white blood cells, C-reactive protein (CRP), blood gases, chest X-ray reports. The data will be entered into an Excel spreadsheet from which the data will be analyzed. We aim to identify all cases of respiratory disease in which HRV is the sole pathogen.

Statistical Procedures

We will use means or medians to characterize the cohorts demographics and vital signs and proportions of types of respiratory support, diagnoses and outcomes. We will also use means and medians to study laboratory values. After complete investigation of this cohort, we will further divide the cohort into those requiring prolonged respiratory support (>4 days) and compare them to those requiring a shortened duration of support (<2 days). We will compare different risk factors within both populations and potentially perform a logistic regression to look at all of the risk factors.

Location of Study

New York Presbyterian Hospital at Columbia University; CHONY PICU

Procedures

A. Analysis of Existing Data: yes
B. Audio or video recording of subjects: no
C. Biological Specimens: no
D. Cancer-related research: no
E. Drugs or Biologics: no
F. Future use of data: no
G. Genetic Research: no
H. Human embryos: no
I. Imaging or Radiation: no
J. Medical Devices: no
K. Surgical procedures: no
L. Survey/interview/questionnaire: no
M. Systematic observation of group behavior: no
N. Program Evaluation: no
O. Cognitive testing: no
P. Educational testing: no
Q. Non-invasive physical measures: no
R. Taste testing: no

Recruitment of Subjects

It will be a retrospective chart review. Study does not involve recruitment procedures.

Informed Consent of Subjects

This study qualifies for a waiver of consent as per 45CFR46.116(d) as the following criteria are met in this study (provide justification for EACH of these criteria):

(1)The research involves no more than minimal risk to the subjects. Provide justification: This is a retrospective chart review with no more than minimal risks to the subjects.

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects

Provide justification: This is a retrospective chart review with minimal risks to the subjects and will not adversely affect the rights or welfare of the subjects.

(3) The research could not practicably be carried out without the waiver or alteration

Provide justification: To obtain accurate epidemiological data all patients with positive HRV testing during the one year period will need to be included in the analysis. Obtaining consent from each subject would not be feasible and would preclude the research from taking place.

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation Provide justification: This is a retrospective chart review with minimal risks to the subjects. To obtain accurate epidemiological data all patients with positive HRV testing during the one year period will need tobe included in the analysis. The subjects will not be provided information after participation.

Confidentiality of Subjects

All data will remain confidential. Retrospective data will be entered directly into Excel database that will be password protected on an encrypted computer that has been approved by Columbia University IT Department. Data will be kept confidential on a password protected computer that has been approved by Columbia University. Data analysis will be performed on a Columbia University computer in compliance with security policies in place by Columbia University.

Potential Risks

There is a potential of data theft. All study data will be stored on password-protected, encrypted computers to help minimize this per Columbia University protocol.

Potential Benefits

If we can identify Human Rhinovirus (HRV) as the sole pathogen in children with severe respiratory infection requiring ICU admission, it will add to the current evolving evidence that HRV is less benign than initially thought. This would warrant further research in to its pathogenesis and the development of preventative measures.

Alternatives

To not perform the study or to perform a prospective study.

Data and Safety Monitoring

NA

Subjects

A. Target Enrollment: 55
B. Population Gender: 50% Female, 50% Male
C. Population Age: 0-7: 65%; 8-17: 35%; 18-65: 0%; >65: 0%
D. Population Race: American Indian / Alaskan Native: 0%; Native Hawaiian or Other Pacific Islander: 0%; Black or African American: 25%; White: 45%, More than One Race: 0%, Non-specific: 30%
E. Population Ethnicity: Hispanic or Latino: 30%; Not Hispanic or Latino: 70%; Non-specific: 0%

Child Involvement:
There is no physical risk to the study subjects for participating in this study as we will be reviewing data from medical charts in a retrospective manner.

Parental Permission:

No parental permission will be obtained because the involvement of children in this research meets the criteria for a complete waiver of consent (45 CFR 46.116(d)), which is requested in the "Recruitment and Informed Consent" section.

REFERENCES

- Papadopolous, NG. Sanderson, G. Johnston, SL. Rhinoviruses replicate effectively at lower airway temperatures. J Med Virol. 1999 May; 58(1) 100-4.
- Jacobs, SE. Lamson, DM. St. George, K. Walkh, T. Human Rhinoviruses. Clin Microbiol Rev. 2013 Jan; 26(1): 135-162.
- Heymann, PW. Platts-Mills, TA. Johnston, SL. Role of viral infections, atopy and antiviral immunity in the etiology of wheezing exacerbations among children and young adults. Pediatr Infect Dis J. 2005;24(11 Suppl):S217.
- Winther, B. Gwaltney, JM Jr. Mygind, N. Hendley, JO. Viral-induced rhinitis. Am J Rhinol. 1998;12(1):17.
- Papadopoulos, NG. Bates, PJ. Bardin, PG. Papi, A. Leir, SH. Fraenkel, DJ. Meyer, J. Lackie, PM. Sanderson, G. Holgate, ST. Johnston, SL. Rhinoviruses infect the lower airways. J Infect Dis. 2000;181(6):1875.
- Gern JE, Galagan DM, Jarjour NN, Dick EC, Busse WW. 1997. Detection of rhinovirus RNA in lower airway cells during experimentally induced infection. Am. J. Respir. Crit. Care Med. 155:1159–1161.
- Blair HT, Greenberg SB, Stevens PM, Bilunos PA, Couch RB. 1976. Effects of rhinovirus infection of pulmonary function of healthy human volunteers. Am. Rev. Respir. Dis. 114:95–102.

- Malcolm E, Arruda E, Hayden FG, Kaiser L. 2001. Clinical features of patients with acute respiratory illness and rhinovirus in their bronchoalveolar lavages. J. Clin. Virol. 21:9–16.
- Imakita M, Shiraki K, Yutani C, Ishibashi-Ueda H. 2000. Pneumonia caused by rhinovirus. Clin. Infect. Dis. 30:611–612.