Research Project IRB
Allison Baxterbeck MD, PGY-2
CRC Course
September 5, 2014

A. Study Purpose and Rationale

Patients who are admitted to the hospital with acute respiratory infections (ARI) are placed on isolation precautions in order to prevent transmission of infections within the hospital. Isolation precautions for ARI including influenza-like illnesses (ILI) include contact isolation (use of gowns and gloves) or droplet isolation (use of gown, gloves and masks). The type of precautions instituted varies by the type of virus, e.g., contact isolation for respiratory syncytial virus (RSV) and droplet isolation for influenza.

Diagnostic testing for respiratory viruses became widespread in the 1980s. The first widely used test was the viral culture. This test was both specific and sensitive; however, it had a slow turnaround time and required specialized laboratory equipment (8). Viral serologies produced faster results; however, they required 2 blood draws to measure a four-fold increase in antibody response over time. This method also takes days to result and is not very child-friendly. DFA provides rapid results but is far less sensitive than viral cultures and is only available for RSV and influenza. RT-PCR has been increasing in availability over the past 20 years. It is more sensitive than viral cultures, which had been the gold standard, and the results are available within hours (6). This method also allows for detection of viruses that are not commonly tested with the other methods, such as human metapneumovirus and coronavirus. Studies have shown that RT-PCR detects viruses at a higher rate than the other methods, which is not surprising since this test can detect many more strains than the other methods (4). It also detects higher rates of co-infections.

However, the clinical significance of the RT-PCR is not yet fully understood. Currently, there is conflicting evidence regarding the effect on length of stay, antibiotic use, chest x-ray use, and infection control (7). In an adult population, the RT-PCR has been found in increase diagnostic yield of viral testing and decrease chest x-ray use, but the same study found that it did not change antibiotic use or blood and urine diagnostic tests. However, another study found a significant decrease in length of stay by 1.2 days with the RT-PCR, a significant decrease in antibiotic use, and a significant decrease in hospital cost per day (9).

Patients are placed on isolation for ARIs based on symptomatology pending results from viral diagnostic studies. Until May 2012, viral diagnostic studies included the use of PCR for RSV and influenza virus, with a comprehensive viral panel follow-up if tests for RSV and influenza were negative. Beginning in May 2012, our hospital instituted a more extensive respiratory panel that uses real-time- polymerase chain reaction (RT-PCR) to test for 16 viral types and subtypes using a variety of gene targets for specific pathogens many of which haven't been tested for previously (e.g., human metapneumovirus and rhinovirus). Turnaround time for viral testing decreased from 1-5 days to hours. Testing is done 7 days a week. All testing both before and after the institution of RT-PCR viral testing is done on nasopharyngeal swab samples from patients with signs and symptoms of ARI. We are conducting this study in order to determine the effect of instituting RT-PCR

testing for viral respiratory pathogens on isolation days and resource utilization for children hospitalized with ARI. Our specific aims are to (1) compare the time spent on isolation precautions before and after institution of RT-PCR viral testing; (2) to compare the rates of chest x-ray utilization before and after institution of RT-PCR viral testing; and (3) to compare the rates of antibiotic use before and after institution of RT-PCR viral testing.

The hypothesis is that the following implementation of the RT-PCR respiratory viral testing, hospitalized patients will spend less time on isolation precautions, have lower rates of antibiotic use, and have lower rates of chest x-ray use.

B. Study Design and Statistical Analysis

We will conduct a retrospective pre-post intervention (i.e., institution of RT-PCR) study using existing data to assess the time spent on isolation for 2 years prior to the institution of RT-PCR viral testing versus 2 years after the initiation of RT-PCR testing for viral respiratory pathogens. Data will be collected using retrospective chart review for all 4 years in order to assure that the data collection strategies are done similarly in the pre- and post-intervention periods. We chose to include year-round data rather than data solely from traditional respiratory seasons (October-March) in order to capture data from months of maximal incidence of ARIs as well as throughout the rest of the year because we are seeing viruses beyond traditional respiratory seasons. We will obtain data from two New York Presbyterian campuses (Columbia and Cornell) since the RT-PCR intervention occurred at both campuses at the same time.

The primary outcome measure will be number of inpatient isolation days for patients admitted to the children's hospital who underwent diagnostic testing for a respiratory virus in the emergency department (ED) or within 48 hours of admission to the hospital. Hospital-acquired respiratory viral infections will be excluded from this analysis. The hours on isolation will be measured by using the date and time of the written isolation order, i.e., "isolation initiation" and date and time of the written order to discontinue isolation, i.e., "isolation discontinuation". The total patient admitted hours will be measured by using the date and time of the written admission order, i.e., "admission start" and the date and time of the written discharge order, i.e., "admission end".

We will use chi-squared to look for differences in categorical variables among the populations in the two time periods including gender and co-morbid conditions such as asthma. We will use a t –test to test for differences in continuous variables such as age. For the outcomes, we will use chi-squared to look for differences in rates of antibiotic use and chest x-ray use in the two groups. We will use Wilcoxon Rank Sum test to analyze the length of stay and length of time on isolation data, as this data does not follow a normal distribution. Although the majority of hospital stays were short (under 7 days), there were many prolonged hospital stays including several that lasted over one year.

A power analysis was conducted using a $p<0.05$ and a power of 80% to determine the necessary N to detect statistical significance. Based on this analysis, with the N of 4639 in our pre-RT PCR cohort and N of 4964 in our post- RT PCR cohort, we will be able to detect a change in rate of chest x-ray and antibiotic use of as small as 3%. Based on preliminary data using an unpaired t-test, we will be able to detect an effect size of 72 hours for length of stay and 63 hours for isolation time.

Study Procedure

Data collection for all four years (pre-RT PCR cohort: 2010-2012, post-RT PCR cohort: 2012-2014) will be collected using retrospective chart review. We are using retrospective chart review for all data collection in order to assure similar data collection strategies for all time periods. We will obtain data from two New York Presbyterian campuses (Columbia and Cornell) since the RT-PCR intervention occurred at both campuses at the same time.

We will obtain the following data from the clinical data warehouse for all 4 periods. The data to be collected will include the following:

- Demographic information: name, medical record number, gender, date of birth, insurance status, patient language, race/ethnicity
- Hospital stay information: date of admission, date of discharge, room number, date of transfer to another floor (if applicable), time of transfer to another floor
- Viral testing information: date/time viral test ordered, viral test results, date/time viral test results reported in electronic health record
- Isolation information: Isolation type, isolation order name, date/time isolation order initiated, date/time isolation order discontinued
- Clinical information: Discharge primary diagnosis, discharge secondary diagnosis
- Antibiotic utilization: Calendar days during which patient received antibiotics
- Chest x-ray utilization: whether or not patient received chest x-ray during admission

C. Study Drugs

None

D. Medical Device

None

E. Study Questionnaires

None

F. Study Subjects

Inclusion criteria are patients who

- Are 0-18 years of age
- Are admitted to the hospital from the emergency department
- Underwent diagnostic testing for a viral respiratory pathogen either in the emergency room prior to admission or within the first day of admission to the hospital

Exclusion criteria are patients who

- Are admitted from another facility or clinic and bypass the emergency department

G. Recruitment of Subjects

Since this is a retrospective review of the electronic medical record and researchers will have no contact with patients, no recruitment materials will be used.

H. Confidentiality of Study Data

Data collected using the data abstraction form and data obtained via the clinical data warehouse will be stored in a password protected Excel spreadsheet on a password protected computer kept in a locked office. This data will be accessible only by study personnel. Paper data abstraction tools will be kept in a locked cabinet in a locked office for 5 years. Once all data is collected, identifying data will be removed from the data set prior to data being analyzed.

I. Potential Conflict of Interest

None

J. Location of Study

NYP-Columbia and Cornell

K. Potential Risks

The risks for subjects in this study are loss of confidentiality. All identifying data that is collected will be used only to link clinical data found in the electronic health record with microbiology data. Once data collection is complete, identifying data will be removed from the data set prior to data being analyzed.

L. Potential Benefits

There are no direct benefits to subjects that participate in this study. However, potential benefits that may come from this study are potentially decreasing patients placed on inappropriate isolation.

M. Alternative Therapies

None

N. Compensation of Subjects

None

O. Costs to Subjects

None

P. Minors as Research Subjects

Because this is a retrospective study, this research will not provide any direct benefit to subjects that are enrolled. However, this research will benefit children who are hospitalized in the future because it will show how real-time polymerase chain reaction viral testing for respiratory pathogens changes how patients are placed on isolation and which types of viruses cause patients to be hospitalized. This information is only available in the context of this research.

We will be applying for a waiver for documentation of informed consent and assent. This is a retrospective chart review of the data that has already been collected and is stored in the electronic medical record. The study is minimal risk for the subject as viral testing will be done in accordance with standard of care in both time periods that will be studied. The waiver will not adversely affect the rights and welfare of the subjects. Subject identifiers will be used during the data collection to link data from two data sources: 1) microbiology lab that will provide a list of patients seen during the study periods who had respiratory viral testing that originated from the emergency department or within a patient's first day of admission to the hospital; and 2) a retrospective chart review (via manual chart review and data obtained from the clinical data warehouse) of already collected information stored in the electronic medical record. Subject identifiers are necessary to be able to link data from these two sources. Once all data is collected and linked, subject identifiers will be removed from the database and the database will be de-identified. Additionally, because this is a retrospective chart review with no contact between the researchers and subjects, this study could not practicably be carried out without a waiver.

Q. Radiation or Radioactive Substances

None

References:

1. Chapin. Multiplex PCR for detection of respiratory viruses: Can the laboratory performing a respiratory viral panel (RVP) assay trigger better patient care and clinical outcomes? Clinical Biochemistry (2011) vol 44 pp. 496-7.

2. Litwin and Bosley. Seasonality and prevalence of respiratory pathogens detected by multiplex PCR at a tertiary care medical center. Arch Virol (2014) vol. 159 pp. 65-72.

3. Mansbach et al. Prospective, multicenter study of viral etiology and hospital length-of-stay in children with severe bronchiolitis. Arch Pediatr Adolesc Med. (2012) vol. 166 (8) pp. 700-706.

4. McGrath et al. Detection of respiratory coinfections in pediatric patients using a small volume polymerase chain reaction array respiratory panel: More evidence for combined droplet and contact isolation. American Journal of Infection Control (2013) vol. 41 pp. 868-73.

5. Mills et al. Rapid testing for respiratory syncytial virus in a paediatric emergency department: benefits for infection control and bed management. Journal of Hospital Infection (2011) vol. 77 pp. 248-51.

6. Rhedin et al. Clinical Utility of PCR for Common Viruses in Acute Respiratory Illness. Pediatrics (2014) vol. 133 pp. 538-545.

7. Rodriguez da Silva et al. Severe lower respiratory tract infection in infants and toddlers from a non-affluent population: viral etiology and co-detection as risk factors. BMC Infectious Diseases (2013) vol. 13 (41) pp. 1-8.

8. Wishaupt et al. PCR testing for Paediatric Acute Respiratory Tract Infections. Paediatric Respiratory Reviews (2014) pp. 1-6.

9. Woo et al. Cost-Effectiveness of Rapid Diagnosis of Viral Respiratory Tract Infections in Pediatric Patients. Journal of Clinical Microbiology (1997) pp. 1579-1581.