10-1-2017

Retrospective Cohort Study of the Efficacy of Azithromycin Vs. Doxycycline as Part of Combination Therapy in Non-Intensive Care Unit Veterans Hospitalized with Community-Acquired Pneumonia

Justin Spivey

Heather Sirek
Mountain Home VA Healthcare System

Robert Wood
Mountain Home VA Healthcare System

Kalpit Devani
East Tennessee State University, DEVANI@etsu.edu

Billy Brooks
East Tennessee State University, brooksb1@etsu.edu

See next page for additional authors

Citation Information

Spivey, Justin; Sirek, Heather; Wood, Robert; Devani, Kalpit; Brooks, Billy; and Moorman, Jonathan. 2017. Retrospective Cohort Study of the Efficacy of Azithromycin Vs. Doxycycline as Part of Combination Therapy in Non-Intensive Care Unit Veterans Hospitalized with Community-Acquired Pneumonia. *Open Forum Infectious Diseases*. Vol.4 579-580. https://doi.org/10.1093/ofid/ofx163.1513

Retrospective Cohort Study of the Efficacy of Azithromycin Vs. Doxycycline as Part of Combination Therapy in Non-Intensive Care Unit Veterans Hospitalized with Community-Acquired Pneumonia

Creator(s)

Justin Spivey, Heather Sirek, Robert Wood, Kalpit Devani, Billy Brooks, and Jonathan Moorman

Background. Parainfluenza virus (PIV) is a significant cause of morbidity and mortality in children and the immunocompromised adult population, but its clinical manifestation, impact, and outcomes in hospitalized adults is not well studied.

Methods. Retrospectively, adults ≥ 18 years old admitted to Northwestern Memorial Hospital (Chicago, IL) or Prentice Women's Hospital (Chicago, IL) between August 1, 2009 and July 31, 2016 with a positive molecular test for PIV were included in the study. Epidemiologic, clinical, and outcomes data were retrospectively collected from the enterprise data warehouse and patient electronic health records after IRB approval.

Results. 550 adults with a positive molecular test for PIV were identified (see Table 1). Differences in seasonality, presentation (significant for cough, sputum), and outcomes of PIV serotype (-1, -2, and -3) were identified (see Table 2, Figure 1). At presentation, most patients had cough (88%), productive sputum (55%), fever (63%), and dyspnea (49%). 348 (63.3%) of patients were administered antibiotics with no confirmed bacterial infection. Patients given antibiotics had a longer length of hospital stay (6.9 d vs 3.2 d (P < 0.0001)). Presence of bacterial co-infections (P = 0.02), BMI (lower BMI associated with death, P = 0.01), dyspnea (P = 0.04) and various laboratory studies (ANC, ALC, Hematocrit, BUN, and AST) were associated with significant differences in outcome (see Table 3).

Conclusion. PIV infection results in significant morbidity in hospitalized adults. With improved diagnostic testing availability and knowledge of clinical manifestation, identification of PIV infections will improve. Future efforts should be directed at developing novel preventative and therapeutic approaches to PIV infection.

Figure 1. Monthly Prevalence of PIV by Serotype Over 7 Year Period.

Table 1. Patient Demographics of the 550 Enrolled Subjects

Characteristics	Mean Value
Female, n (%)	286 (52.0)
Immunocompetent°, n (%)	303 (55.1)
Age, mean (range)	60.4 (19-96) years
Hospital Stay, mean (range)	7.8 days (1 - 91)
Vitals, mean (range)	
BMI	28.3 (11.4 - 83.4) kg/m^2
Systolic BP	135.7 (60 - 249) mmHg
Diastolic BP	74.5 (41 - 136) mmHg
Temp	98.9 (85 - 104.3) F
Respiratory	20.1 (12 - 70) rpm
Pulse	96.1 (7 - 179) bpm
O_2 saturation	95.3 (24 - 100) %
Smoking	
History of, n (%)	238 (43.3)
Current use, n (%)	66 (12)
Average pack-year, mean (range)	26.3 (0 - 125)
Co-infection, n (%)	
Bacterial	90 (16.4)
Viral	43 (7.8)
Fungal	25 (4.5)
Presenting Symptoms, n (%)	
Cough	486 (88)
Sputum	346 (63)
Fever	303 (55)
Dyspnea	270 (49)
Fatigue	201 (37)
Rhinorrhea	149 (27)
Pharyngitis	146 (27)
Diarrhea	117 (21)
ICU Admission	
Admissions, n (%)	127 (23)
Length of stay, mean (range)	7.4 days (1 - 62)
Outcome (%)	
Home	471 (85.6)
Continuing care°°	51 (9.3)
Death	28 (5.1)

°Immune status was determined clinically with available patient data (e.g. hematologic malignancy/treatment, pharmacotherapy induced, CD4+ cell count < 500).

°°Continuing care includes nursing home, long-term acute care, hospice, and outside hospital.

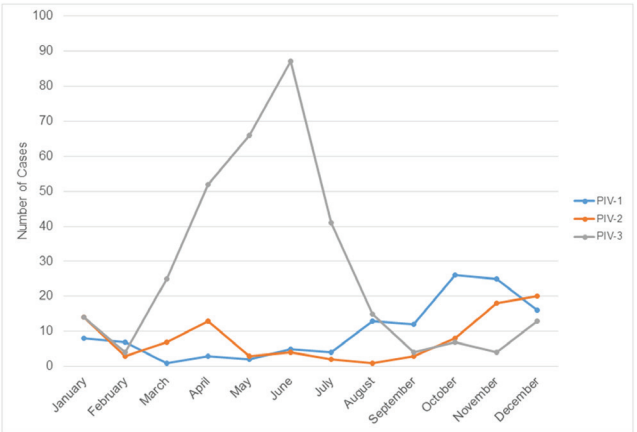


Table 2. Comparing PIV Serotypes in Hospitalized Adults

Characteristics	PIV-1	PIV-2	PIV-3	p value
Prevalence, n (%)	122 (22.2)	96 (17.5)	332 (60.4)	-
Age, years	59.7	57.2	61.5	0.08
Presenting Symptoms, %				
Cough	87.6	74.0	93.1	< 0.0001
Sputum	60.3	41.7	57.2	0.011
Fever	70.2	60.4	61.3	0.18
Dyspnea	45.5	47.9	51.1	0.55
Rhinorrhea	20.6	16.7	32.6	0.001
Clinical Course				
Hospital stay, days	8.88	7.9	7.2	0.37
Received Abx, %	81.1	71.9	81.3	0.11
ICU admissions, n (%)	26 (21.3)	26 (27.1)	78 (23.4)	0.58
ICU stay, days	10.1	9.2	5.9	0.131

Table 3. Mortality of PIV Infection in Hospitalized Adults

Characteristics	Mortality		p value
	Yes (n = 28)	No (n = 522)	
Age, mean	65.6 y	60.1 y	0.10
Immunocompromised, %	59.3	44.1	0.13
Clinical Course			
Hospital stay, mean	17.5 d	7.22 d	**0.004**
Received Abx, %	96.5	78.7	**< 0.0001**
Past Medical History, %			
Lung disease	25.9	32.7	0.44
CV disease	59.3	42.3	0.09
Malignancy	51.9	35.1	0.10
Presenting Symptoms, %			
Cough	73.1	89.5	0.08
Sputum	46.2	55.7	0.35
Fever	57.7	63.4	0.58
Dyspnea	69.2	48.3	**0.04**
Rhinorrhea	7.7	28.7	**0.001**
Smoking			
History of, n	45.8	44.1	0.87
Current use, n	13.3	18.9	0.56
Average pack-year, mean	31.8	26.0	0.38
Co-infection, %			
Bacterial	35.7	15.3	**0.04**
Viral	17.9	7.3	0.17
Fungal	17.9	3.8	0.06
Vitals, mean			
BMI	24.8	28.4	**0.01**
Systolic BP	126	136	0.08
Diastolic BP	75	69	0.06
Temp	98.3	98.9	0.11
Respiratory	23.9	19.9	0.08
Pulse	100.8	95.9	0.29
O_2 saturation	94.7	95.4	0.58
Labs, mean			
Absolute Neutrophil Count	8.55 k/L	5.7 k/L	**0.04**
Absolute Lymphocyte Count	0.77 k/L	1.4 k/L	**< 0.0001**
Hematocrit	32.7%	36.0%	**0.01**
Blood Urea Nitrogen	34.5 mg/dL	22.1 mg/dL	**0.01**
AST	54.4 U/L	35.4 U/L	**0.02**

Disclosures. **M. G. Ison**, Beckman Coulter: Grant Investigator, Research grant; Chimerix: Grant Investigator, Research grant; Gilead: Grant Investigator, Research grant

1983. Retrospective Cohort Study of the Efficacy of Azithromycin Vs. Doxycycline as Part of Combination Therapy in Non-Intensive Care Unit Veterans Hospitalized with Community-Acquired Pneumonia

Justin Spivey, PharmD, BCPS[1,2]; Heather Sirek, PharmD[1]; Robert Wood, PharmD, BCPS[1,2]; Kalpit Devani, MD[3]; Billy Brooks, DrPH, MPH[4] and Jonathan Moorman, MD, PhD, FACP[1,3,5]; [1]Mountain Home VA Healthcare System, Mountain Home, Tennessee, [2]East Tennessee State University, College of Pharmacy, Johnson City, Tennessee, [3]East Tennessee State University, James H. Quillen College of Medicine, Johnson City, Tennessee, [4]East Tennessee State University, College of Public Health, Johnson City, Tennessee, [5]East Tennessee State University, James H. Quillen College of Medicine, Center of Excellence in Inflammation, Infectious Diseases, and Immunity, Johnson City, Tennessee

Session: 233. Clinical: Respiratory Track

Saturday, October 7, 2017: 12:30 PM

Background. The IDSA Community-Acquired Pneumonia (CAP) Guideline recommends ceftriaxone in combination with doxycycline as an alternative to combination therapy with ceftriaxone and azithromycin for non-intensive care unit (ICU) patients hospitalized with CAP. This is an attractive alternative regimen due to recent concerns of increased cardiovascular risk associated with azithromycin. The objective of this study was to compare the clinical outcomes of azithromycin and doxycycline each in combination with ceftriaxone for non-ICU Veterans hospitalized with CAP.

Methods. This retrospective cohort study included Veterans with pneumonia admitted to the VA MidSouth Healthcare Network from January 2007 to January 2015

who received ceftriaxone plus either azithromycin or doxycycline within 48 hours of admission. Demographics, modified CURB-65, Charleston Comorbidity Index (CCI), antimicrobials received, and microbiology data were obtained. A composite outcome was used to assess clinical failure and included either broadened antimicrobial coverage during index hospitalization, mortality, readmission, or emergency department visit within 30 days. Univariate and multivariate logistic regression were performed to identify risk factors associated with clinical outcomes.

Results. 3788 patients met inclusion criteria: 3711 in the azithromycin group and 77 in the doxycycline group. These were well-matched according to CAP severity and comorbidities. There was no statistical difference in the composite outcome between the azithromycin and doxycycline groups (44.3% vs 51.9%, $P = 0.18$). Multivariate analysis identified positive blood culture (OR 5.81, 95% CI 2.69–12.55), CURB-65 [2 vs 0] (OR 1.24, 95% CI 1.05–1.47), CURB-65 [≥3 vs 0] (OR 2.4, 95% CI 1.22–4.71) and CCI (OR 1.1, 95% CI 1.06–1.14) as risk factors for the composite outcome. Receipt of doxycycline was not associated with components of the composite outcome in secondary analyses.

Conclusion. Doxycycline was not associated with a statistical difference in the composite outcome for non-ICU Veterans hospitalized for CAP compared with azithromycin. These data offer support for the inclusion of doxycycline as an alternative regimen in current IDSA recommendations.

Disclosures. **All authors:** No reported disclosures.

1984. Co-circulation of Rhinovirus A and C during the EV-D68 Epidemic Period

Amy Callear, MPH[1]; Sydney Foote, BS[1]; Hannah E Segaloff, MPH[1]; Duane Newton, PhD[2]; Nicole S. Stroufe, MD[3]; Helena Wang-Flores, DO[3]; Terri Stillwell, MD[4]; Marc Hershenson, MD[3] and Emily T. Martin, MPH, PhD[1]; [1]Epidemiology, University of Michigan School of Public Health, Ann Arbor, Michigan, [2]University of Michigan Health Systems, Ann Arbor, Michigan, [3]Michigan Medicine, Ann Arbor, Michigan, [4]Department of Pediatics, Michigan Medicine, Ann Arbor, Michigan

Session: 233. Clinical: Respiratory Track

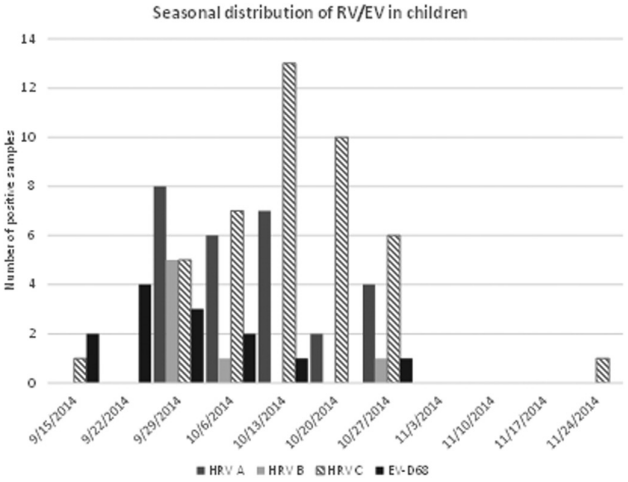
Saturday, October 7, 2017: 12:30 PM

Background. The beginning of the 2014–2015 respiratory season in the United States was marked by reports of a re-emergent subtype of enterovirus (EV-D68). Documented EV-D68 was associated with severe asthma exacerbations and neurologic effects; however rapid assays in clinical use detect rhinovirus/enterovirus more broadly. The objective of our study was to determine the prevalence of EV-D68 as well as non-EV-D68 rhinovirus and enterovirus subtypes during the epidemic period.

Methods. Residual nasal swab specimens were obtained from the University of Michigan clinical microbiology laboratory for children and adults presenting for care due to acute respiratory symptoms from September to November 2014. Specimens were restricted to those testing positive for "Rhinovirus / Enterovirus" (RV/EV+) by the FilmArray Respiratory Virus Panel (Biofire Diagnostics). Specimens were tested to identify EV-D68 by real-time RT-PCR and serotype was determined for non-EV-D68 specimens through amplification and Sanger sequencing of a segment of the 5' non-coding region using previously published assays.

Results. A total of 159 patients with acute respiratory illness were included with RV/EV+ nasal swab specimens collected from September to November 2014. Sixty-four percent (n = 101) of patients were children. Unexpectedly, only 20 RV/EV+ specimens were the EV-D68 subtype, with 13 detections in children (13%) and 7 in adults (12%). Rhinovirus A was the most frequently identified group among adults (n = 23; 40%); rhinovirus C was the most frequently identified in children (n = 43; 43%) (Figure). In the children, 13 different serotypes of rhinovirus-C and 21 different serotypes of group A were identified.

Conclusion. We found rhinovirus C to be a major contributor to rhinovirus-associated hospitalizations in children during the time of the EV-D68 epidemic period in the United States. These data demonstrate that local determinations of the burden of EV-D68 require the use of subtype-specific assays. In addition, our results add to the growing evidence of the important role of rhinovirus group C in severe acute respiratory infections.



Disclosures. **E. T. Martin**, Pfizer: Scientific Advisor, Research grant; Merck: Scientific Advisor, Research grant; Multiparty Group For Advice on Science: Scientific Advisor, Research grant

1985. Epidemiology and Outcomes of Mild-Moderate Immunosuppressed (MMI) Patients with Pneumonia

Deeter Neumann, PharmD[1]; Tejal Gandhi, MD[2]; Scott Flanders, MD[3]; Anna Conlon, PhD[4]; Anurag Malani, MD, FIDSA[5] and Jerod Nagel, PharmD, BCPS[1]; [1]Michigan Medicine, Ann Arbor, Michigan, [2]Internal Medicine, Division of Infectious Diseases, Michigan Medicine, Ann Arbor, Michigan, [3]Internal Medicine, University of Michigan, Ann Arbor, Michigan, [4]University of Michigan Health System, Ann Arbor, Michigan, [5]Saint Joseph Mercy Health System, Ann Arbor, Michigan

Session: 233. Clinical: Respiratory Track

Saturday, October 7, 2017: 12:30 PM

Background. The current ATS/IDSA pneumonia guidelines lacks a concise definition of immunosuppression, which causes significant heterogeneity in antibiotic use for patients with MMI. Furthermore, the impact of mild-moderate immune suppression on pneumonia severity, incidence of multi-drug resistant (MDR) pathogens, disease course and clinical outcomes has not been well described.

Methods. This multicenter observational cohort study included non-ICU patients diagnosed with pneumonia within 48 hours of admission from 10 hospitals between November 2015 and November 2016. MMI patients were defined as asplenic; HIV with CD4 count ≥200; non-neutropenic leukemic or solid malignancy receiving treatment in the previous 30 days; kidney transplant >1 year ago without rejection; receiving ≥15 mg/day prednisone for ≥30 days, TNF-alpha inhibitor, azathioprine or methotrexate use. All cause 30-day mortality, pneumonia severity, hospital length of stay (LOS), pneumonia readmissions, MDR pathogen (resistant to levofloxacin or ceftriaxone), and time to clinical stability were compared between MMI and immunocompetent patients.

Results. A total of 2,505 patients with pneumonia were included and 274 (11%) were classified as MMI. Similar rates of respiratory and blood cultures were obtained between MMI and immunocompetent groups (88.7% vs. 85.1%, $P > 0.05$), but the MMI group demonstrated a higher rate of culture positivity (19% vs. 15.5%, $P = 0.013$). There was no difference in culture positivity with traditional CAP pathogens between groups (5.5% vs. 5.2%, $P > 0.05$), but MMI patients had higher incidence of MDR pathogens (72.4% vs. 39.5%, $P = 0.002$). MMI patients presented with more severe disease (PSI of 115.6 vs. 87.2, $P < 0.001$), had higher mortality rates (7.7% vs. 2.1%, $P < 0.001$), and longer LOS (5.4 vs. 4.7 days, $P < 0.001$). However, time to clinical stability (2.6 vs. 2.64 days, $P = 0.79$) and recurrent pneumonia rates (34.8 vs. 33.8%, $P = 0.89$) were similar.

Conclusion. MMI patients with pneumonia have a higher incidence of MDR pathogens. and culture positivity. MMI patients also have a higher mortality rate and longer LOS. Antibiotic regimens which extend coverage beyond traditional CAP pathogens may be needed in MMI patients, but broader coverage could be more targeted if risk factors for MDR pathogens in this population were identified.

Disclosures. **J. Nagel**, Merck: Grant Investigator, Research grant

1986. Incidence and Organism Specific Mortality Associated with Healthcare Associated Pneumonia Over a Six Year Period

Gina Maki, D.O.[1]; Yuan Xin, MPH[1]; Nikhath Zeeshan, MD[1]; Anthony Harris, MD[2]; Steven J. Lawrence, MD, MSc[3]; Andrew Masica, MD, MSCI[4]; Lois Lamerato, PhD[5] and Marcus Zervos, MD[1]; [1]Infectious Diseases, Henry Ford Health System, Detroit, Michigan, [2]University of Maryland, Baltimore, Maryland, [3]Infectious Diseases, Washington University School of Medicine, St. Louis, Missouri, [4]Baylor Scott & White Health, Dallas, Texas, [5]Henry Ford Health System, Detroit, Michigan

Session: 233. Clinical: Respiratory Track

Saturday, October 7, 2017: 12:30 PM

Background. Healthcare-associated pneumonia (HCAP) is a common and potentially life threatening illness. Pneumonia is one of the most common causes of healthcare associated infections. The purpose of our study was to investigate in a large multicenter cohort over a several year period, the association of specific organisms with patient mortality in HCAP patients.

Methods. This is a retrospective multicenter analysis of patients over 18 years of age hospitalized with HCAP over a 6-year period from 2008 to 2013 from 4 large healthcare institutions. Patients were identified by electronic medical record review. HCAP was defined by inclusion of patients with a discharge diagnosis of pneumonia by ICD-9 code plus associated antibiotic use in the initial 24 hours. Patients were considered to have HCAP if initial antimicrobial use included one of the following: cefepime, doripenem, meropenem, imipenem, or piperacillin-tazobactam, in combination with vancomycin or linezolid.

Results. There were 16084 patients. *Staphylococcus aureus* was the most common organism isolated in 368 patients and had 15.0% mortality at 30 days. *Pseudomonas aeruginosa* was isolated in 359 patients and had 24.2% mortality at 30 days. *Acinetobacter baumannii* was isolated in 200 patients, and accounted for 34.0% mortality. *Escherichia coli* was isolated in 89 patients with 24.7% mortality. *Klebsiella pneumoniae* was isolated in 99 patients with 27.3% mortality. Commensal bacteria were isolated or positive cultures with no speciation occurred in 5214 of patients with 22.8% mortality at 30 days. The remaining patients did not have organisms identified in the blood or sputum.