Residency Project Pearls 2017

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Speakers have no conflicts of interest to discolse

Use of Clonidine as Adjunct Therapy in the Emergency Department for Alcohol Withdrawal

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Learning Objectives

1. Identify the risks of overuse of benzodiazepine therapy and its impact on patients with alcohol withdrawal
2. Describe the mechanism of action and rationale for use of clonidine as adjunctive therapy in alcohol withdrawal

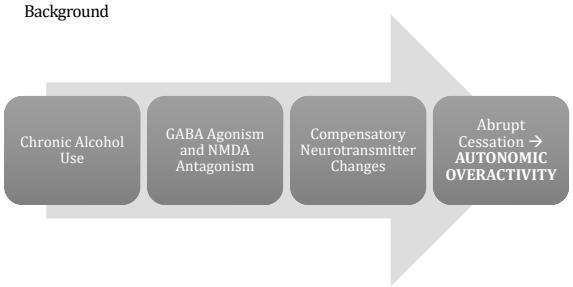
Alcohol Withdrawal Syndrome (AWS)

- Significant cause of morbidity and mortality
  - 17.9 million Americans have alcohol dependence
  - Up to 33% of intensive care unit (ICU) admissions are at risk of alcohol withdrawal

VanderWeide LA, et al. *J Intensive Care Med*. 2016;31(3):198-204.
Alcohol Use Statistics. National Institute of Health website. www.niaaa.nih.gov. Updated February 2017.

Alcohol Withdrawal Syndrome

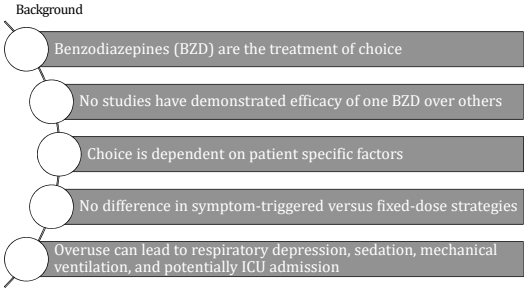
Background



Jesse S, et al. *Acta Neurol Scand*. 2017; 135:4-16.

Current Practice

Background



Jesse S, et al. *Acta Neurol Scand*. 2017; 135:4-16.

Which of the following is/are potential side effect(s) of benzodiazepines?

A. Respiratory depression
B. Hypertension
C. Sedation
D. A and C

Alpha-2 Agonists

Background

- Rationale for evaluation of use as adjunct therapy
- May be beneficial as adjunct therapy by decreasing the sympathetic surge, ultimately, decreasing BZD requirements

Manhem et al. *Alcohol Clin Exp Res.* 1985;9(3):238-243.

What is the proposed mechanism of action of clonidine in alcohol withdrawal?

A. Antagonism at NMDA receptors in the brain decreasing neuronal excitation
B. Agonist activity at alpha-2 receptors in the CNS decreasing autonomic over-activity
C. Agonist activity at GABA receptors augmenting benzodiazepine activity
D. Treatment of hypertension associated with alcohol withdrawal

Effect of Clonidine on Sympathetic Activity

- Randomized, double blind, parallel group trial in 20 patients who met defined criteria for chronic alcoholism who presented with AWS
- Intervention arms
  - Clomethiazole
  - Clonidine

Endpoints	Result
SBP/HR	Significantly lower in the clonidine group
Symptoms	No major differences between the groups in withdrawal intensity ratings
Plasma NE/Epi	Sustained fall in clonidine group

Manhem et al. *Alcohol Clin Exp Res.* 1985;9(3):238-243.

Adjunctive Dexmedetomidine for AWS

- Single center, retrospective, controlled, cohort study evaluating the impact of early dexmedetomidine (DEX) on critically ill patients with AWS
- Intervention arms
  - Standard alcohol withdrawal protocol
  - DEX plus alcohol withdrawal protocol

VanderWeide LA et al. *J Intensive Care Med.* 2016;31(3):198-204.

Adjunctive Dexmedetomidine for AWS

Endpoints	Result
Cumulative 12-hour BZD requirement change Post minus pre after DEX exposure	-20 mg vs -8.3 mg, p = 0.0455
Length of ICU stay	87 hours vs 54 hours, p = 0.23
Incidence of mechanical ventilation (MV)	8% vs 9%, p = 1.0
Duration of MV	31 hours vs 49 hours, p = 0.23

VanderWeide LA, et al. *J Intensive Care Med.* 2016;31(3):198-204.

Alpha-2 Agonist Comparison

Background

	Dexmedetomidine	Clonidine
Onset of action	5-10 minutes	30-60 minutes
Duration of action	60 minutes	4 to 6 hours
Cost	High	Low
Formulation	Intravenous	Oral, transdermal
NMH restrictions	Yes	No
Common adverse effects	Hypotension, bradycardia	Hypotension, rebound hypertension

Dexmedetomidine. Clinical Pharmacology [online database]. Tampa, FL: Gold Standard, Inc.; 2006.
Clonidine. Clinical Pharmacology [online database]. Tampa, FL: Gold Standard, Inc.; 2006.

Northwestern Memorial Hospital (NMH) Practice

Background

Alcohol withdrawal protocol	• No NMH protocol • Provider preference
Dexmedetomidine	• Restricted to mechanically ventilated patients • Indication is unaddressed by P&T committee
CIWA	• Rarely used in the ED • Lack of data • Time constraints

Study Rationale

- Gaps in literature
  - Clonidine was previously studied as monotherapy
  - Dexmedetomidine demonstrated BZD sparing effects
- Some ED physicians have begun using clonidine as an alternative to dexmedetomidine for adjunctive therapy
  - Rationale
    - ICU admission not required
    - Cost effective

Study Question

Does the administration of adjunctive clonidine in the emergency department for alcohol withdrawal decrease the benzodiazepine requirements?

Northwestern Memorial Hospital Chicago, Illinois

Feinberg and Galter Pavilions

Prentice Women's Hospital

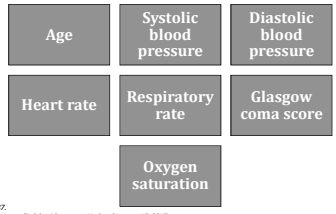
- 894-bed Academic Medical Center Hospital
- Primary teaching affiliate of Northwestern University Feinberg School of Medicine
- Calendar Year 2016
  –Inpatient Admissions: 43,933
  –Emergency Room Visits: 87,893

Study Design

- Single center, retrospective cohort study
  - Alcohol withdrawal patients admitted to NMH ED
  - Study arms
    - BZD monotherapy [control group]
    - BZD plus adjunctive clonidine [intervention group]
  - Matched at ratio of 3:1 based on rapid emergency medicine score
- Statistical analysis
  - Continuous data analyzed using T-test
  - Categorical data analyzed using Chi-Square test
  - All statistical analysis performed using IBM SPSS v 23

Rapid Emergency Medicine Score (REMS)

- Predictor of in-hospital mortality for nonsurgical patients in the emergency department
  - Derivative of the APACHE II



Olsson T, et al. *J Internal Med*. 2004;255:579-587.
Rapid Emergency Medicine Score Calculator. www.medicalalgorithms.com. Updated January 15, 2017.

Rapid Emergency Medicine Score (REMS)

REMS Score	In-Hospital Mortality
0-2	0%
3-5	1%
6-9	3%
10-11	4%
12-13	10%
14-15	17%
16-17	38%
18-19	45%
20-21	56%
22-23	66%
24-26	100%

Olsson T, et al. *J Internal Med*. 2004;255:579-587.

Study Population

- Inclusion Criteria
  - Patients 18 years or older who received at least 24 hours of BZD for alcohol withdrawal who present to the NMH emergency department
- Exclusion Criteria
  - Trauma
  - Primary diagnosis was not alcohol withdrawal
  - Discharged directly from the emergency department

Outcome Measures

Primary Endpoint

- 12 hour cumulative BZD requirements in lorazepam equivalents (LE)

Secondary Endpoints

- Total BZD requirements
- Admission to the ICU
- ICU and hospital days
- Hypotension

Lorazepam Equivalents

Benzodiazepine Conversions
1 mg oral lorazepam
0.25 mg oral clonazepam
0.5 mg oral alprazolam
0.5 mg intravenous lorazepam
5 mg intravenous diazepam
10 mg oral chlordiazepoxide

VanderWeide LA, et al. *J Intensive Care Med*. 2016;31(3):198-204.

Baseline Characteristics

Results

	Intervention group (n=11)	Control group (n=33)	p-value
Age	50 (38-52)	47 (40-54)	0.62
Sex, male (n, %)	9 (82)	28 (85)	0.99
Weight (kg)	73 (67-78)	77 (69-89)	0.09
REMS	6 (3-10)	6 (3-8)	0.62
Maximum SBP	185 (143-206)	167 (146-194)	0.28
Maximum DBP	101 (92-119)	99 (81-109)	0.52
Maximum HR	132 (112-138)	120 (107-130)	0.32

Results reported in median (IQR) unless otherwise noted

Clonidine Use

Results

- Median cumulative clonidine in the ED
  - 100 mcg
  - Range: 100-300 mcg
- Continuation of clonidine after admission
  - 10/11 patients (91%)
- Median clonidine days
  - 3 days
  - Range: 1-4 days

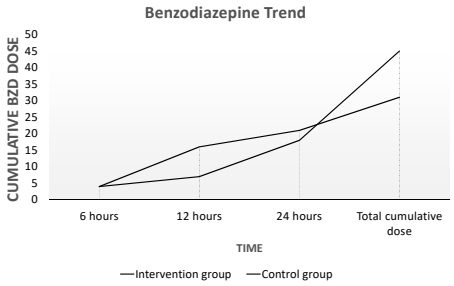
Benzodiazepine Requirements

Results

	Intervention group (n=11)	Control group (n=33)	p-value
12 hour cumulative BZD*	16 (3-19)	7 (4-13)	0.90
24 hour cumulative BZD	21 (16-30)	18 (11-34)	0.44
Total cumulative BZD	31 (21-48)	45 (26-71)	0.28

Results reported as milligrams of lorazepam equivalents in median (IQR)
*Primary outcome

Results



Secondary Endpoints

Results

	Intervention group (n=11)	Control group (n=33)	p-value
ICU admission (n, %)	5 (45)	14 (42)	0.99
ICU days	2 (2-3)	2 (2-5)	0.25
Hospital days	4 (3-5)	4 (4-8)	0.17
Hypotension (n, %)	0 (0)	3 (9)	0.56

Results reported as median (IQR) unless otherwise noted

Discussion

- Data did not show a statistical difference in 12 hour BZD requirements, but there may be a trend in decreased total BZD requirements

Difference in 12 hour BZD requirements

- 9 mg LE *higher* in the intervention group

Difference in total BZD requirements

- 14 mg LE *lower* in the intervention group

Discussion

- Clonidine continuation rate was higher than expected
  - No differences in rates of hypotension
  - Indicative that clonidine was well tolerated
  - ED management has downstream effects

Limitations

- Small sample size
  - Lack of statistical power
- Retrospective study
- Possible selection bias
- Limitations of REMS
- Included all patients who received clonidine regardless of how many doses he/she received

Conclusions

- Adjunctive clonidine was not associated with a reduction in 12 hour BZD requirements, total BZD requirements, ICU admission rates, or ICU/hospital days
- Clonidine was safe and well-tolerated
  - Clonidine did not result in higher rates of hypotension and was continued after admission in 90% of patients

Future Direction

- Submit manuscript for publication
- Further investigation in a prospective, randomized controlled trial
- Follow up evaluation to determine symptom mitigation and continuation rate of clonidine on discharge

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Role of proton pump inhibitor and recurrent *Clostridium difficile* infection

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Learning Objectives

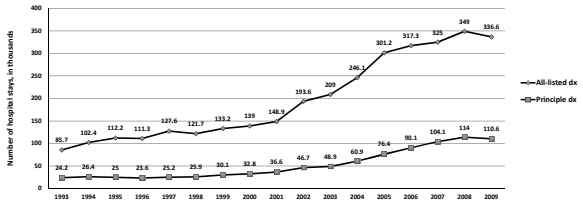
3. Identify risk factors associated with recurrent *Clostridium difficile* infection.
4. Recognize the role of proton pump inhibitor exposure in recurrent *Clostridium difficile* infection.

Edwards Hines, Jr. VA Hospital

- Located 12 miles west of downtown Chicago
- Offers primary, extended, and specialty care services
- Has 471 beds and 6 community based outpatient clinics
- Serves 59,000 Veterans

Urgent threat

Trends in hospital stays associated with *C. difficile* infection, 1993–2009



Adapted from Lucado J, et al. Agency for Healthcare Research and Quality, Rockville MD.

Risk factors

- Risk factors for the development of *Clostridium difficile* infection (CDI)
  - Non-CDI directed antibiotic exposure
  - Advanced age
  - Previous hospitalization
  - **Proton pump inhibitor (PPI)**
    - **Increased risk of CDI**
    - **Nosocomial and community setting**
- Recurrence
  - ~18% to 32% (first)
  - Subsequent recurrence rate ~40% to 60%

Garey KW, et al. J Hosp Infect. 2008;70(4):298-304.
Howell MD, et al. Arch Intern Med. 2010 May 10;170(9):784-90.
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Leong C, et al. Can J Hosp Pharm. 2013 Nov-Dec; 66(6): 361–8.

Mechanism

- Jump and colleagues
  - Vegetative form of *C. difficile* may shed into environment and remain viable on moist surfaces
  - Higher pH and survival of the vegetative form
- Hypothesis
  - Ingestion of the viable vegetative form
  - Possible contribution to CDI development due to elevated gastric pH

Jump RL, et al. Antimicrob Agents Chemother. 2007 Aug; 51(8): 2883–87.

Which of the following may be risk factor(s) for recurrent CDI?

A. Concomitant PPI use
B. Age <30
C. Receipt of antibiotics (non-CDI treatment)
D. A and C

What is one proposed mechanism between PPI and CDI recurrence?

A. Acid suppression by PPI leads to survival of vegetative form of *C. difficile*, which increases risk of CDI
B. PPI use may disrupt normal flora in the upper and lower GI tract
C. PPI use may increase inflammation, which increases risk of recurrent CDI
D. There is currently no hypothesized mechanism

Why is this important?

- Limited evidence exists as to how PPIs play a role in **recurrent CDI**
  - *Gastric acid suppression and outcomes in Clostridium difficile infection: a population-based study* (Khanna et al. 2012)
  - *Proton pump inhibitors and risk for recurrent Clostridium difficile infection among inpatients* (Freedberg et al. 2013)
  - *Epidemiology of Clostridium difficile infection and risk factors for unfavorable clinical outcomes: results of a hospital-based study in Barcelona, Spain* (Rodríguez-Pardo et al. 2013)

Literature review

Author	Design	Population	Relevant outcomes	Results
Khanna et al. 2012	Population based	n=385 Hospital and community patients, median age 67.5	CDI outcomes, recurrent CDI	Univariate: OR 0.75 (95% CI 0.47-1.19; p=0.22) Multivariate: OR 0.65 (95% CI 0.4-1.06; p=0.08)
Rodríguez-Pardo et al. 2013	Prospective surveillance	n=317 Inpatient from 15 hospitals, median age 72	Predictor of recurrent CDAD	Univariate: OR 1.99 (95% CI 1.043-3.81; p=0.035) Multivariate: OR 2.168 (95% CI 1.081-4.347; p=0.029)
Freedberg et al. 2013	Retrospective	n=894 Inpatient adult, mean age 64	Risk factors for recurrence within 15-90 days of initial positive test	Multivariate: HR 0.82 (95% CI 0.58-1.16)

Khanna S, et al. Mayo Clin Proc. 2012 Jul;87(7):636-42.
Freedberg DE, et al. Am J Gastroenterol. 2013 Nov;108(11):1794-801.
Rodríguez-Pardo D, et al. J Clin Microbiol. 2013 May;51(5):1465-73.

Study focus

- Role of proton pump inhibitor and recurrent *Clostridium difficile* infection
- Aim
  - To evaluate the association between PPI therapy and first recurrence of CDI

Study methods

- Retrospective, observational, single-center study
  - Approved by Hines VA Institutional Review Board
- All *C. difficile* PCR results electronically retrieved
  - July 1, 2012 to June 30, 2016
- PCR results were screened via electronic medical record
  - Included only the index CDI episode
  - Each patient was included only once
- Patients were stratified into PPI-exposure group and non PPI-exposure group
  - Further categorized based on CDI recurrence status

Study methods – key definitions

- Recurrent CDI
  - CDI diagnosis within 8 weeks after clinical cure of previous initial CDI episode
- Clinical cure
  - Resolution of signs and symptoms of initial CDI and maintenance of resolution for the duration of therapy
  - No further treatment for CDI as of the second day after the end of course of therapy
- PPI exposure
  - Receipt of PPI therapy for at least 48 hours after initial CDI diagnosis and prior to first recurrent episode

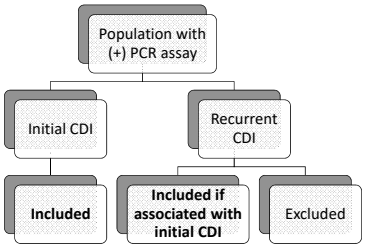
Rodríguez-Pardo D, et al. J Clin Microbiol. 2013 May;51(5):1465-73.
Louie TJ, et al. N Engl J Med. 2011 Feb 3;364(5):422-31.

Study methods

Primary outcome	Secondary outcome
Impact of PPI therapy on proportion of recurrent CDI	Impact of age, PPI exposure, and antibiotic use on proportion of recurrent CDI

Inclusion	Main exclusion
Adult patients ≥18 years of age	In-hospital mortality prior to clinical cure of initial CDI episode
Positive *C. difficile* PCR	CDI treated at outside institution and/or insufficient documentation through available electronic record
	CDI not treated

Study methods



Study analyses

- A minimum of 206 unique patients are required to detect a difference of 25% with 80% power
  - Two-sided alpha level of 0.05 for statistical significance
- Descriptive statistical analyses conducted using Epi Info™ (version 7.2.1)
- Univariate analyses
  - Continuous variables: Students t-test or Wilcoxon rank sum test
  - Dichotomous variables: Chi-square, Fisher's exact test, or McNemar's test

Freedberg DE, et al. Am J Gastroenterol. 2013 Nov;108(11):1794-801.
Khanna S, et al. Mayo Clin Proc. 2012 Jul;87(7):636-42.
McFarland LV, et al. Am J Gastroenterol. 2002 Jul;97(7):1769-75.
Rodriguez-Pardo D, et al. J Clin Microbiol. 2013 May;51(5):1465-73.

Patient level data

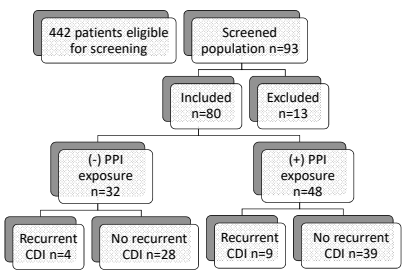
- Age
- Gender
- Race
- Height
- Weight
- Serum creatinine
- Admission date
- Admission-from location
- Admission-to location
- Discharge date
- Discharge-to location
- Location at positive PCR
- CDI onset location
- **Hospital length of stay (LOS)**
- Prior antibiotics exposure
- **Modified Charlson Comorbidity Index (M-CCI)[1]**
- Date of CDI clinical resolution
- Time to recurrence (from resolution)
- Initial CDI treatment
- Duration of CDI therapy (DOT)
- Hepatic dysfunction
- **PPI therapy (dose, indication, route)**
- PPI duration of therapy
- Concurrent acid suppression therapy
- Time from first PPI dose to recurrent CDI
- Immunosuppression status
- Surgical history related to GI
- In-hospital mortality
- Time to mortality

[1]Removed peptic ulcer disease

Results

- Together, 578 valid, positive PCR results were available during the study period
  - July 1, 2012 to June 30, 2016
- 442 unique patients were eligible for screening
- 80 patients included thus far
  - Pending further data collection
- 13 patients excluded
  - In-hospital all cause mortality prior to clinical cure (n=6)
  - CDI treated at outside institution and/or insufficient documentation through available electronic record (n=5)
  - Other reasons (n=2)

Results



Baseline characteristics

Demographics	Patients (n=80)
Age in years, mean ± SD[1] (range)	68.4 ± 12.0 (35, 98)
Male gender, n (%)	78 (97.5)
Race/ethnicity, n (%)	
White	62 (77.5)
Black	16 (20.0)
Unknown[2]	2 (2.5)
M-CCI, mean (SD)	3.0 (2.2)
PPI exposure, n (%)	48 (60.0)
Prior antibiotics exposure, n (%)	63 (79.8)
CDI onset location, n (%)	
Community	38 (47.5)
Residential	42 (52.5)

[1]Standard deviation
[2]Patient declined to answer

Results

Demographics	No PPI exposure (n=32)	PPI exposure (n=48)	P value
Age, mean ± SD	67.6 ± 13.2	67.0 ± 11.2	0.6619
Male gender, n (%)	31 (96.9)	47 (97.9)	-
Race/ethnicity, n (%)			-
White	26 (81.3)	36 (75.0)	-
m-CCI, mean ± SD	2.4 ± 1.9	3.5 ± 2.4	0.0506
Prior antibiotics exposure, n (%)	24 (77.4)	39 (81.3)	0.7767
Recurrence CDI, n (%)	4 (12.5)	9 (18.8)	0.5471
Community onset, n (%)	17 (53.1)	21 (34.8)	0.4951
Admit to hospital	11 (34.4)	16 (33.3)	0.4910
Initial CDI treatment, n (%)			**0.0206**
Metronidazole PO	28 (87.5)	30 (62.5)	-
Vancomycin PO	4 (12.5)	18 (37.5)	-
DOT in days, mean ± SD	15.5 ± 8.3	15.7 ± 6.7	0.6159
DOT, n (%)			-
14 days or less	24 (75.0)	36 (75.0)	-
>14 days	8 (25.0)	12 (25.0)	-
Hospital LOS, mean ± SD	24.2 ± 33.1	36.9 ± 66.7	-

Subgroup analyses

- Stratification by the following dichotomous variables and test for association between PPI use and CDI recurrence
  - PPI dose exposure (high dose vs. low dose)
  - Surgical history
  - Immunosuppression
  - DOT for CDI (≤14 days vs. >14 days)
  - CDI directed treatment
  - Admission from location
  - Age
  - Prior antibiotic exposure
  - Race/ethnicity
- Considered statistical significance if p values <0.10

Discussion

- Preliminary data revealed no association between PPI use and recurrent CDI
- Limitation
  - Mostly white, elderly male patients
  - Hospital length of stay is highly variable across groups
    - Likely due to extended rehabilitation stay

Moving forward…

- Pending data
- Evaluate the relationship between PPI exposure and first recurrent CDI
- Assess the duration of PPI therapy and its relationship with recurrent CDI
- Evaluate other potential risk factors for recurrent CDI

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  - Jeffrey Wieczorkiewicz, PharmD, BCPS
- Co-investigator
  - Katie Suda, PharmD, MS

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Hospital Readmission Rates for Patients Treated with Ceftriaxone and Azithromycin Versus Levofloxacin for Community Acquired Pneumonia

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Learning Objectives

5. Identify adverse effects of fluoroquinolones which are less prevalent in ceftriaxone and azithromycin.
6. Discuss resistance considerations when comparing empiric treatment of CAP for inpatients.

Community Acquired Pneumonia (CAP)

- Pneumonia is the primary reason for severe sepsis and infectious death in US[1]
  - *Streptococcus pneumoniae*
    - 75% acute presentations of CAP
- Inpatient non-ICU treatment[2]
  - Respiratory fluoroquinolone
  - Beta-lactam plus a macrolide
  - Both options show efficacy
  - Limited data of preferred regimen[2-6]

1. Blackford MG, et al. *Pharmacotherapy: A Pathophysiologic Approach, 9e*
2. IDSA/ATS Consensus Guidelines on the Management of CAP in Adults
3. Frank E, et al. Clin Ther. 2002 Aug;24(8):1292-308
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Levofloxacin and Azithromycin Plus Ceftriaxone in Moderate to Severe CAP[3]

- Open-label, randomized
  - Levofloxacin 500 mg PO/IV
  - Azithromycin 500 mg PO and ceftriaxone 1 g IV
  - At least 10 days of therapy
- 110 patients in FQ group vs 114 patients in combination
  - 94.1% FQ vs 92.3% combo clinical success rate
  - 89.5% FQ vs 92.3% combo microbiologic eradication
  - 5.3% FQ vs 9.3% combo ADE
- Levofloxacin is at least as effective as combination for CAP

3. Frank E, et al. Clin Ther. 2002 Aug;24(8):1292-308

Fluoroquinolones (FQ)

- Black Box Warning[7]
  - Tendonitis
  - Tendon rupture
  - Peripheral neuropathy
  - CNS
    - Hallucinations
    - Dizziness
    - Confusion
- FDA Strengthens Warning
  - July 2016
  - Fluoroquinolones reserved for patients with no other treatment choices
    - Acute bacterial sinusitis
    - Acute exacerbation of chronic bronchitis
    - Uncomplicated urinary tract infection
  - Risks may outweigh benefits

7. U.S. Food and Drug Administration. Fluoroquinolone Antibacterial Drugs: Drug Safety Communication

Fluoroquinolones (FQ)

- *Clostridium difficile*
  - Cephalosporins, FQ, and clindamycin
  - FQ resistant strain outbreaks[8]
    - 12 hospitals in Quebec
    - Patients with CDI were more likely to have received a FQ or cephalosporin
    - *C. difficile* strain resistant to FQ determined responsible for outbreak
- *Streptococcus pneumoniae*[9]
  - 1988 to 1997
    - FQ prescriptions on the rise
    - Pneumococci reduced susceptibility to FQ
      - 0% in 1993
      - 1.7% in 1997 and 1998.
      - Strains associated with penicillin resistance

2. IDSA/ATS Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults
8. Loo, Vivian G., et al. NEJM 353.23 (2005): 2442-2449
9. Chen, Danny K., et al. NEJM 341.4 (1999): 233-239

Purpose

- To determine if the combination ceftriaxone and azithromycin is superior to levofloxacin in treatment of CAP in non-ICU patients based on readmission rates

Endpoints

- Primary
  - All cause 30 day readmission rates
    - Planned admissions or emergency department
- Secondary
  - Length of stay
  - 30 day mortality
  - Total inpatient treatment length
  - *C. difficile* infection development
  - Outpatient treatment length
  - Outpatient treatment choice
  - Adverse effects

Study Setting

- OSF Saint Francis Medical Center, Peoria, IL
  - 629 beds
- OSF Saint Anthony Medical Center, Rockford, IL
  - 254 beds

Methods

- Retrospective chart review
  - Hospital quality metric program
- Multi-center
- IRB approval
  - University Illinois College of Medicine Peoria
  - OSF St. Francis and St. Anthony Medical Centers
- Intention to Treat
- Superiority
  - Historical data

Inclusion Criteria

- Admitted to:
  - OSF Saint Anthony Medical Center
  - OSF Saint Francis Medical Center
- Community acquired pneumonia DRG
  - 193, 194, 195
- 18 years and older
- Received at least 48 hours of therapy
  - Ceftriaxone and azithromycin
  - Levofloxacin

Exclusion Criteria

- ICU admissions
- Less than 18 years or greater than 88 years
- Pregnant women
- Prisoners
- Received non-study antibiotics within first 48 hours
- Received both study arms within first 48 hours

Exclusion Criteria

- Immunocompromised patients
  - Transplant patients on immunosuppressive therapy
  - Chemotherapy administration within 90 days
  - Greater than 30 days of high dose steroids
  - HIV with a CD4 count of less than 350.
- COPD and related DRGs
  - Potential misdiagnosed code
- IV antibiotics or 5 days of antibiotics in past 90 days

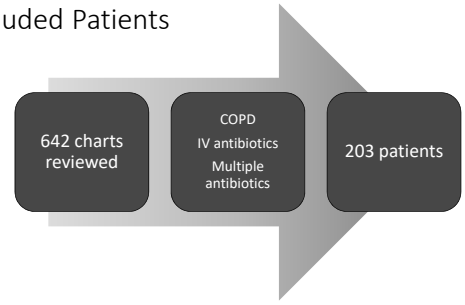
Data Collection

- Retrospective Chart Review
- Hospital quality metrics program
  - Develop patient population
  - Facility inclusion
  - Simple pneumonia DRG
    - 193, 194, 195
    - Exclude non-CAP isolations
      - *Pseudomonas, Staphylococcus aureus,* viral, TB, etc.
    - Exclude DRGs indicating COPD
  - June 2014 – September 2016
  - Azithromycin and levofloxacin products
    - Separate patient lists

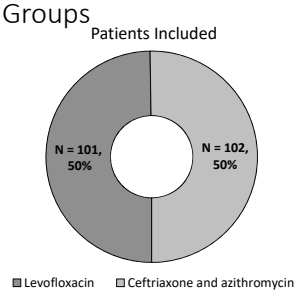
Statistical Analysis

- Chi-square test for categorical values and binary outcomes
- T-test for age comparison within each group
- Wilcoxon rank-sum test for continuous outcomes

Excluded Patients



Treatment Groups



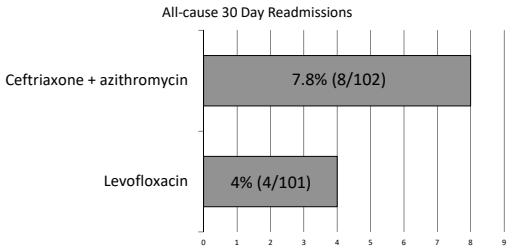
Patient Demographics

Variables	Total N = 203 (%)	Ceftriaxone Azithromycin N = 102 (%)	Levofloxacin N = 101 (%)	P value
Age (Mean ± SD)	67 ± 18.2	67.5 ± 19.0	66.5 ± 17.5	0.687 [T]
Sex				0.234[C]
Female	96 (47.3)	44 (43.1)	52 (51.5)	
Male	107 (52.7)	58 (56.9)	49 (48.5)	
CHF				0.021[C]
No	157 (77.3)	72 (70.6)	85 (84.2)	
Yes	46 (22.7)	30 (29.4)	16 (15.8)	
Diabetes				0.431[C]
No	132 (65.0)	69 (67.6)	63 (62.4)	
Yes	71 (35.0)	33 (32.4)	38 (37.6)	

[T]t-test
[C]Chi-square test

Primary Outcome

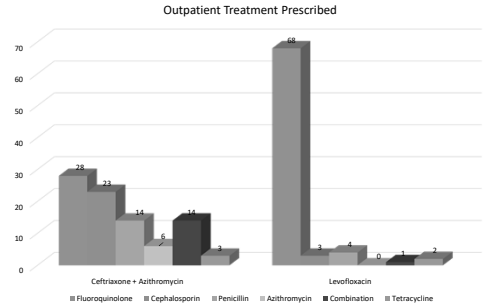
- P value
  - 0.241



Secondary Outcomes

Secondary Outcome	Ceftriaxone + Azithromycin N = 102 (%)	Levofloxacin N = 101 (%)	P Value
Length of Stay	3 (1 – 10) days	3 (1 – 10) days	0.255[W]
Outpatient Treatment Length	5 (0 – 14) days	4 (0 – 23) days	0.350[W]
Total Inpatient Treatment Length Mean	4 (1 – 9) days	3 (1 – 12) days	0.973[W]
C. Difficile Infection	1 (1)	1 (1)	1.000[C]
30 Day Mortality	1 (1)	2 (2)	0.432[C]
Adverse Effects	2 (2)	3 (3)	0.683[C]

[W] Wilcoxon rank-sum
[C]Chi-square test



Discussion

- Statistical power was not met
  - 203 of ~650 estimated patients
  - Based on estimated readmission rates
- No difference observed
- CHF patients
  - Follow-up
  - Azithromycin
- Cannot support one therapy as preference
  - Clinical factors of patient
  - Adverse effects
  - Spectrum of activity

Limitations

- Study did not meet power
  - Determined during chart review process
  - Overestimated readmission rates
- Retrospective chart review
- Narrow population
  - Many exclusion factors
  - Intention to increase external validity
  - Limited patients included

Future Directions

- Future study including patients with COPD
  - Additional data points of medication allergies, sputum cultures, *Streptococcus pneumoniae* urine antigen, and blood cultures
  - Increased patient population beyond June 2014
- Further studies to determine preference of levofloxacin or ceftriaxone with azithromycin for initial CAP treatment

Which of the following organisms is the most common cause of CAP and has been associated with increased rates of fluoroquinolone resistance?

A. Streptococcus pneumoniae
B. Haemophilus influenzae
C. Legionella species
D. Mycoplasma pneumoniae

Which of the following is a concerning side effect for fluoroquinolones which is not a black box warning?

A. Tendonitis
B. Clostridium difficile infection
C. Peripheral neuropathy
D. Hallucinations

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Questions for Speakers?