Antimicrobial Stewardship Incorporating New Antimicrobials for Use against Multi-Drug Resistant *Pseudomonas aeruginosa* in Cystic Fibrosis

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BACKGROUND

- Cystic fibrosis (CF) is a life-limiting autosomal recessive disorder that affects approximately 80,000 people worldwide and at least 30,000 in the U.S[1]
- According to the Cystic Fibrosis Foundation Patient Registry 2018, nearly half of the registered patient population (45.3%) cultured positive for *Pseudomonas aeruginosa* (PA); of which, 28.3% were chronically infected with PA[1]
- Progressively worsening of lung function marked by a decrease in forced expiratory volume in 1 second (FEV_1) typically begins with recurrent PA infections in CF patients, and overtime eradication becomes very unlikely once PA mutate into mucoid variants[2]
- Chronic PA living in the CF lungs often develop to be multidrug-resistant (MDR) via various adaptation mechanisms and are associated increased morbidity and mortality[3,4]
- Ceftolozane/Tazobactam (C/T), a novel second generation beta-lactam plus beta-lactamase inhibitor effective against MDR-PA, was most recently approved by the FDA for hospital-acquired and ventilator-associated pneumonia[5]
- C/T has shown benefits over other standards of therapy in selected populations with MDR-PA infections; however, studies are lacking in CF population[6]
- Based on our previous single-center surveillance study (2017-2019), C/T was used in for CF exacerbation (11%) in a number of patients harboring MDR-PA, but clinical outcomes compared to other therapies were not assessed

OBJECTIVES

- To evaluate the current use and antimicrobial stewardship of C/T in CF patients with MDR-PA related pulmonary exacerbations (PEx)
- To compare clinical outcomes of C/T-based therapy to non-C/T based therapy

METHODS

Respiratory culture positive for MDR-PA from CF patients at Baylor St. Luke's Medical Center, Houston, TX (2016-2019)

C/T use in MDR-PA related PEx in CF patients was evaluated

Non-C/T based therapy for MDR-PA related in PEx in CF patients were included for controls

Descriptive and R studio (ggplot2) analysis were performed

RESULTS

Table 1. Baseline Demographic Characteristics

Baseline characteristics	C/T (n=18)	Controls (n=38)
Male, n (%)	7 (38.9)	19 (50.0)
Age (yrs)	27.7 ± 8.9	28.4 ± 9.8
Caucasian, n (%)	10 (55.6)	26 (68.4)
Weight (kg)	50.8 ± 10.7	56.3 ± 11.3
BMI, mean (kg/m^2)	19.5 ± 3.0	20.6 ± 3.5
F508 homozygous, n (%)	7 (38.9)	19 (50.0)
CFTR modulator therapy use, n (%)	6 (33.3)	7 (18.4)
Inhaled antibiotic use, n (%)	13 (72.2)	37 (97.4)

Table 2. Hospital and Antibiotics Courses

	C/T (n=18)	Controls (n=38)
Length of stay, mean (days)	20.5 ± 14.5	6.3 ± 2.5
ICU stay, n (%)	8 (44.4)	1 (2.6)
Days to infectious diseases consult since admission, mean (days)	3 ± 3.1	-
Monotherapy, n (%)	5 (27.8)	4 (10.5)
Dual therapy, n (%)	10 (55.6)	33 (86.8)
Aminoglycoside use, n (%)	10 (55.6)	19 (50)
Antibiotic duration, mean (days)	16.3 ± 8.7	13.9 ± 3.5

Figure 1. Baseline FEV_1

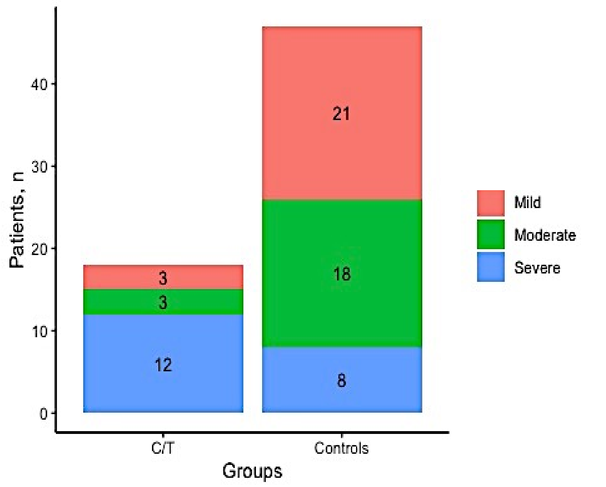
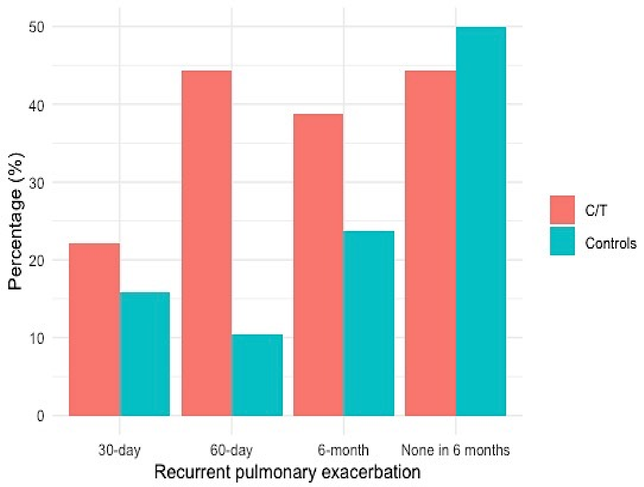


Figure 2. Recurrent PEx Episodes



CONCLUSIONS

- C/T was restricted to infectious diseases consult service and was reserved for the sickest group of CF patients with severe FEV_1
- The recurrent PEx rate was higher in the C/T group compared to the controls; however, the number of patients with no recurrent PEx episodes was similar between groups
- Given the devastating disease progression with MDR pathogens, new antibiotics with better clinical outcomes against chronic MDR-PA should be considered earlier in therapy for this population
- Larger studies are warranted to analyze cost-effectiveness and clinical outcomes with PEx leading to hospital admission

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