

**2275. Novel Therapeutic Options for the Treatment of Multi-Drug-Resistant *Achromobacter* Respiratory Infections**

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**Background.** Respiratory infection due to *Achromobacter* species has been increasingly more common, especially in patients with cystic fibrosis (CF). Recurrent infections in these patients contribute to significant morbidity and mortality as well as lead to repeated antibiotic exposures with subsequent development of multi-drug-resistant (MDR) pathogens. Several recently approved antimicrobials target MDR Gram-negative pathogens, but none are FDA approved for MDR *Achromobacter* respiratory infections and lack susceptibility breakpoint recommendations.

**Methods.** This retrospective analysis evaluated hospitalized patients with MDR *Achromobacter* respiratory infections from August 2017 to March 2019 at AdventHealth Orlando, a 2,885-bed healthcare system including 8 campuses across Central Florida. The purpose of this descriptive study was to examine novel therapeutic agents for the treatment of respiratory infections due to MDR *Achromobacter*.

**Results.** MDR *Achromobacter* was isolated in 36 respiratory cultures from 18 unique patients. *A. xylosoxidans* (61%) and *A. denitrificans* (22%) were the most frequently isolated species. Mean patient age was 40 years, 56% were female, and 67% had CF. Treatment indications included CF exacerbation (38%), pneumonia (35%), post-lung transplant infection (16%), and other (11%). Twenty-four infections were polymicrobial (67%) and 23 infections included MDR pathogens. Minimum inhibitory concentrations (MIC) of the antibiotics used for treatment were available for 70% of cases. Of the 18 patients with isolated MDR *Achromobacter* organisms, 72% had MIC changes with 69% exhibiting higher MICs on subsequent testing. Novel agents were used in 63% of cases (Table 1) for an average duration of 10 days. Eravacycline was the most frequently used monotherapy agent (5/6 cases) and the most utilized novel antibiotic (21%). All-cause readmission rates at 30 days was 33%; 92% was due to infection. Inpatient all-cause mortality was 11%.

**Conclusion.** Antibiotics available to treat MDR *Achromobacter* infections are limited and lack standard susceptibility breakpoint recommendations. Based on this evaluation, novel agents, such as eravacycline or meropenem/vaborbactam, may be viable treatment options for patients with MDR *Achromobacter* respiratory infections.

**Table 1: Novel Antibiotics Used in the Treatment of MDR *Achromobacter***

Drug	# of Treatment regimens	Mean Days of Therapy	Lowest MIC (mcg/mL)	Mean MIC (mcg/mL)	Highest MIC (mcg/mL)
Eravacycline	13	8.6	1	2	2
Meropenem/vaborbactam	9	9.1	0.25	50	256
Ceftolozane/tazobactam	4	8.3	12	211	256
Ceftazidime/ avibactam	3	16.7	2	8	16
Cefidericol	2	17	5*	--	--

\*Based on CLSI 2019 disk diffusion breakpoints for *P. aeruginosa* ( $\leq 4$  = Susceptible, 8 = Intermediate,  $\geq 16$  = Resistant)

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**2276. Clinical Epidemiology of the Carbapenem-Resistant *Enterobacteriaceae* (CRE) Epidemic in Colombia: A Multicenter Prospective Study**

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**Background.** The CRE epidemic in Colombia is amplified by horizontal transmission of mobile genetic elements encoding KPC among *Enterobacteriaceae* and clonal expansion of *K. pneumoniae* clonal group (CG) 258, making the country hyperendemic for CRE. However, the clinical impact of CRE infections has not been comprehensively assessed.

**Methods.** In the framework of a prospective study assessing the clinical epidemiology of CRE (CRACKLE II), we report the results of the first 246 patients enrolled in 5 Colombian hospitals (from July 2017 to November 2018). Clinical variables, outcomes at 90 days post-hospitalization and susceptibility patterns were collected. Resistance to carbapenems was defined per CDC guidelines. Infection was defined with standardized criteria. All isolates which did not meet these criteria were considered colonization.

**Results.** The majority of patients were men (66%); median age was 62 years [IQR 37-73]; 67% were admitted from home and 33% were hospital transfers. The mean Charlson Comorbidity Index and Pitt Bacteremia scores were 2 (SD = 2) and 3 (SD = 3), respectively. Most patients (60%; n = 148) were considered to be infected. The most frequent source of culture was urine (36%), followed by blood (30%) and wound secretions (13%). A respiratory source was found in the minority (6%) of patients. Species of CRE are summarized in Table 1 with the majority being *K. pneumoniae*. The best *in vitro* activity against CRE was found for fosfomicin (80% susceptible (47/59)), tigecycline (75% (67/89)), colistin (70% (35/50)) and amikacin (67% (148/220)). From 234 patients with available information at 90 days of follow-up, 13% were readmitted after discharge. Mortality at 30 and 90 days after a positive culture was 31% and 35%, respectively.

**Conclusion.** *K. pneumoniae* are the main drivers of the CRE epidemic in Colombia isolated mainly from non-respiratory sources. Non-susceptibility to last resource antibiotics (tigecycline, colistin and fosfomicin) is substantial among the Colombian isolates leaving few therapeutic options, a finding that correlates with high mortality. Our findings indicate that introduction of novel therapeutics in Colombia is urgently needed with a rampant epidemic of CRE causing high burden of disease.

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

**2277. Comparison of 30-day Crude Mortality Rates in Patients with Bloodstream Infections (BSIs) Caused by Colistin Susceptible-(ColS-CRKp) vs. Colistin and Carbapenem-Resistant *Klebsiella pneumoniae*(ColR-CRKp)**

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**Background.** Colistin is a last resort antibiotic against infections with CRKp. Its increased use has led to resistance to this antibiotic.

**Methods.** This was a single-center, retrospective, cohort study including all CRKp BSIs treated between January 1, 2014 and July 31, 2018. Antibiotic therapy was appropriate if initiated within 5 days from the onset of BSI including at least an active drug with an adequate dosage. Exclusion criteria were missing key data, death < 24 h after inclusion, subsequent episodes in the same patients, pregnancy, polymicrobial BSI, < 18 years of age, no ID consultation, no carbapenemase gene detection by multiplex PCR for bla<sub>KPC</sub>, bla<sub>NDM</sub>, bla<sub>VIM</sub>, bla<sub>IMP</sub>, and bla<sub>OXA48</sub>. EUCAST breakpoints were used for antibiotic susceptibilities. Colistin MIC was determined by using broth microdilution. FDA criteria were applied for tigecycline susceptibility.

**Results.** Among 174 CRKp BSIs, 129 met all inclusion criteria. Susceptibility to antibiotics was as follows: colistin (51.9%), tigecycline (67.4%), gentamicin (38.0%), amikacin (43.0%), meropenem (32.6%), ciprofloxacin (18.6%), TMP-SMX (24.0%), ceftazidime (7.8%), cefepime (7.8%).

66.1% and 19.4% of the patients received inappropriate therapy in ColR-CRKp and ColS-CRKp groups, respectively ( $P \leq 0.001$ ). We incorporated interaction between colistin susceptibility and inappropriate therapy into multivariate logistic regression analysis (MLRA) that was constructed for identification of independent risk factors for 30-day mortality. The variables having  $P \leq 0.1$  in crude analysis were included in MLRA. After checking correlation between variables by Pearson correlation analysis and multicollinearity analysis, the final model was built. The results are shown in Table 2.

**Conclusion.** Colistin resistance and inappropriate therapy were not associated with decreased mortality individually, however their interaction significantly increased 30-day mortality rate (OR: 4.04; 95% CI: 1.62-10.02;  $P = 0.003$ ). 85.5% of ColR-CRKp isolates produced an OXA-48 enzyme which can be inhibited by ceftazidime-avibactam, but not available in our setting, treatment with this agent may have altered the mortality rates. Thus, high rate colistin resistance among CRKp isolates remains as a significant cause of mortality in our setting.