833

Characteristics and utilization patterns of colistin compared with newer agents in Gram-negative infections

Stephen Marcella, MD[1], Casey Doremus, MS[1], Roger Echols[2]

[1]Shionogi Inc., Florham Park, NJ, USA; [2] Infectious Disease Drug Development Consulting, LLC, Easton, CT, USA

Contact information:
Stephen Marcella
Address: 300 Campus Drive Florham Park, NJ 07932
TEL: 9733073543
E-mail address: stephen.marcella@Shionogi.com

ID Week, October 2020

INTRODUCTION

Polymyxins, including colistin, older and more neuro- and renal-toxic antibiotics, have resurfaced in light of Gram-negative resistance[1]. New antibiotics, including ceftazidime-avibactam, ceftolozane-tazobactam, and meropenem-vaborbactam (new agents), have recently been approved but it is unclear to what extent they are being used vs. colistin. We compared the overall use of colistin and new agents from 2014–2018 in patient days on therapy (PDOT). In a subset of data from 2016–2018 with microbiologically confirmed Gram-negative (MCGN) infections, their use is associated with patient and pathogen characteristics and by carbapenem resistance (CR) separately for Enterobacterales (fermenters) and non-fermenters.

OBJECTIVES

- Describe the patterns of use of colistin and new antibiotics for Gram-negative infections by patient characteristics, hospital course, and CR/CS status by site of infection.
- Estimate the trend of utilization in the US by PDOT for these agents from 2016 and commercial availability through 2018.

METHODS

Data source and setting: The Premier HealthCare Database collects de-identified patient-level clinical data from over 700 US hospitals annually, with a subset of 317 providing microbiological details, including specimen site, pathogen and antibiotic susceptibility.

Study design: Retrospective cohort

Population, inclusion/exclusion criteria and definitions: A subset of data from 2016-2018 with microbiologically confirmed Gram-negative (GNI) for inpatients age ≥ 18 receiving ≥ 3 days of therapy with colistin, new agents, or carbapenems. A new infection was defined as either the first carbapenem-resistant (CR) infection or the first carbapenem-sensitive (CS) infection if no CR infection occurred. We excluded patients with cystic fibrosis to minimize any use of aerosolized colistin. Patients could be treated with more than one antibiotic per infection. New agents that were considered include ceftazidime/avibactam (Ceftz/avi), ceftozolane/tazobactam (ceftolz/tazo) as well as carbapenems (carbap).

Descriptive variables: Data on baseline characteristics and hospital course as well as infection type by site and CR or CS status.

Outcomes: Inpatient mortality, length of stay (LOS), and patient cost

Statistical analysis*:* Categorical variables were described by percentages, means, and/or medians with interquartiles (IQR). Trend of utilization was measured in PDOT and was projected to the US population by the use of a weight that is provided by Premier based on hospital characteristics from the sample.

REFERENCES

1. Lim LM, Ly N, Anderson D, et al. Resurgence of colistin: a review of resistance, toxicity, pharmacodynamics, and dosing. Pharmacotherapy 2010; 30(12): 1279–91.doi: 10.1592/phco.30.12.1279

2. Polk RE, Fox C, Mahoney A, Letcavage J, MacDougall C. Measurement of adult antibacterial drug use in 130 US hospitals: comparison of defined daily dose and days of therapy. Clin Inf Dis 2007;44(5):664-70.

RESULTS

Table 1. Patient Characteristics by drug type

		Colistin N =3,3320		New Agents N= 5,781		Carbapenems N= 423,302	
		N	%	N	%	N	%
Gender	Female	1,390	42%	2,432	42%	223,158	53%
Race	White	2,063	62%	3,891	67%	317,942	75%
	Other	485	14%	771	13%	51,694	12%
Age	Mean (SE)		59.8 (0.29)		61.0 (0.21)		64.9 (0.03)
	Median (IQR)		62 (49,72)		63 (51,73)		67 (55,77)
Admit Source	Home	2,246	68%	3,964	69%	324,710	77%
	Nursing	293	9%	407	7%	17,871	4%
	Other	781	23%	1,410	24%	80,721	20%
Prior LOS 6 mo.	Mean (SE)		18.9 (0.59)		15.4 (0.29)		6.94 (0.02)
	Median (IQR)		6 (0,23)		7 (0,23)		0 (0,9)
CCI	Mean (SE)		3.3 (0.04)		3.4 (0.03)		3.2 (0.0)
	Median (IQR)		3 (1,5)		3 (2,5)		3 (1,5)

Table 2. Patient Hospital events and outcomes by drug type

		Colistin 3,320		New Agents 5,781		Carbapenems 423,302	
		N	%	N	%	N	%
ICU stay	Yes	2,117	64%	3,131	54%	173,089	41%
Mech vent	Yes	1,992	60%	2,435	42%	97,848	23%
Admit to 1st dose (days)	Med (IQR)		6 (2,14)		5 (2,12)		2 (1,4)
Culture in ICU	Yes	304	47%	491	38%	13,386	29%
Length of stay (days)	Med (IQR)		17 (10,32)		15 (9,29)		8 (5,15)
Patient cost$	Mean (SE)		$93,815 ($2,670)		$84,013 ($1,791)		$36688 ($99)
	Med		$44,759		$40,377		$18,532
	(IQR)		($22,768, $96,207)		($21,294, $91,339)		($10,028, $39,001)
Hospital mortality	Yes	594	18%	712	12%	33,854	8%
Inf. associated LOS	Median (IQR)		12 (7,21)		12 (7,20)		7 (4,12)

Fig. 1. Sensitivity by antibiotic group and site: Enterobacterales

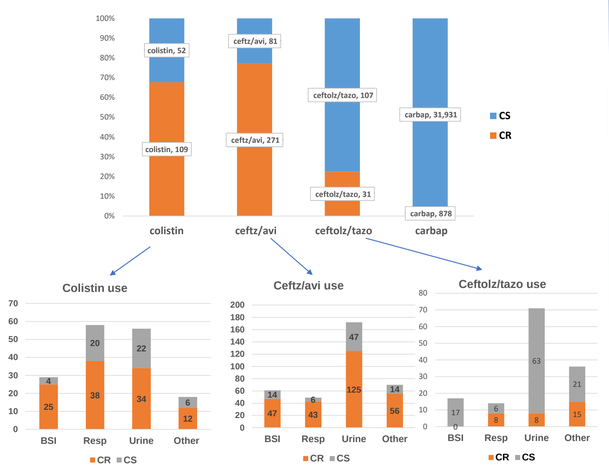


Fig. 2. Sensitivity by antibiotic group and site: non-fermenters

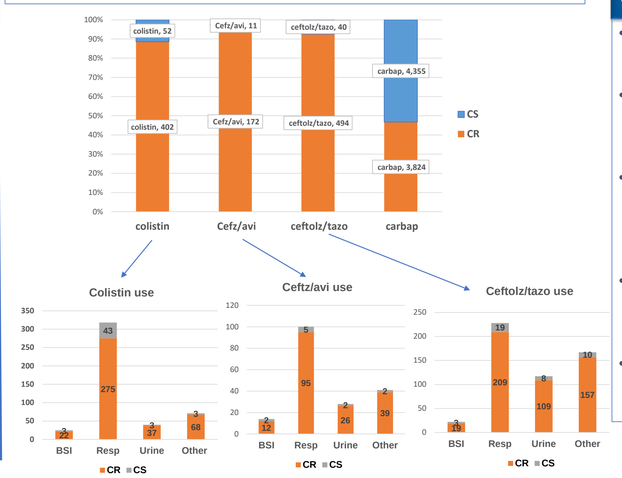
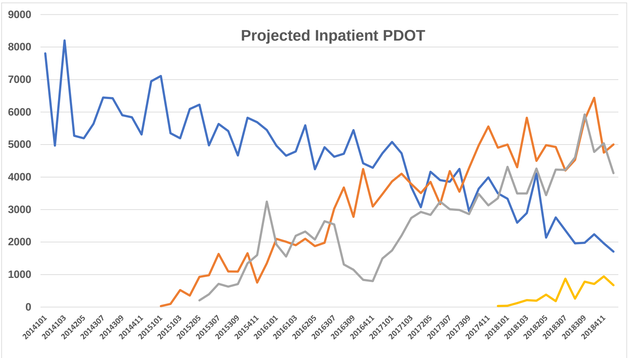


Fig. 3. Trends in utilization of colistin and newer agents from 2014 -2018 in PDOT



CONCLUSIONS

- Colistin treated patients were generally similar in baseline demographic characteristics compared to patients on newer agents. Both groups were sicker than patients on carbapenems (increased LOS in prior 6 months).
- Patients on colistin were more likely to have infection later in the hospital course, require mechanical ventilation, and to have greater length of stay, total costs and inpatient mortality than either those on new agents or carbapenems.
- Colistin was used more commonly in infections with non-fermenters while this varied between new agents. Proportionately, for Enterobacterales, colistin and ceftz/avi were used predominantly in CR infections but ceftolz/tazo was used more commonly for CS infections as were carbapenems, especially in UTIs.
- In non-fermenter infections, colistin and two new agents, ceftz/avi and ceftolz/tazo, were used similarly, mostly for CR infections and especially in respiratory infections. Overall, for all sites, carbapenems were used almost as much for CR as for CS pathogens.
- From 2014 through 2018, the overall use of colistin has been decreasing in the US while the use of new agents has been increasing from the point of commercial availability.