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Concise Communication

Selective reporting of fluoroquinolone susceptibility as a stewardship measure is of marginal benefit

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Abstract

A retrospective time series analysis was conducted to compare inpatient fluoroquinolone use when susceptibilities were masked and after susceptibilities were unmasked. Although inappropriate culture-directed prescriptions increased, overall fluoroquinolone usage decreased. Culture-directed therapy was a small part of fluoroquinolone usage; hence, efforts should target empiric use to reduce overall consumption.

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Fluoroquinolones (FQs) are commonly prescribed for urinary tract and respiratory infections. Overprescription of FQs may cause collateral damage, such as increased rates of FQ resistance in gram-negative bacilli and *Clostridiodes difficile* infections.[1] Fluoroquinolone use has been associated with tendon rupture, QTc prolongation, aortic aneurysm rupture, and aortic dissection. Selective reporting of antibiotic susceptibility may reduce inappropriate and unnecessary antibiotic prescriptions when only first-line agents are reported, especially for samples in which colonization is possible (eg, urine or sputum). Reporting of antibiotic susceptibility may better guide prescribers to choose the most appropriate antibiotic; this strategy has been shown to effectively improve susceptibility rates in some settings.[2,3] Implementation of this strategy may have challenges, such as the lack of human resources and healthcare system support.[4] Selective reporting may have little impact on empiric antibiotic use.

The National University Hospital (NUH) in Singapore is a 1,200-bed tertiary-care hospital. As part of a robust antimicrobial stewardship program (ASP), selectively reporting of FQ susceptibility started in 2011, and results were released when requested by a clinician. The disclosure of FQ susceptibility results was sometimes delayed, particularly after office hours and on weekends, even when FQ use may have been appropriate. This practice was reviewed, and in April 2016, the practice of selective reporting was halted due to manpower constraints. In this study, we analyzed the impact of this change on prescribing patterns and resistance rates.

Methods

Study design

We conducted a time series analysis to compare FQ use between 2 time periods: (1) when selective reporting was in place (ie, FQ masked), and (2) after selective reporting was halted (ie, FQ unmasked) starting in April 2016. We conducted a chart review from 2015 to 2017 of patients receiving intravenous and oral FQ prescriptions for culture-directed therapy in all inpatient adult wards to determine appropriateness of therapy. Patients <18 years old and patients enrolled in clinical trials during the study period were excluded. Aggregate data on inpatient FQ use, ciprofloxacin resistance (the predominant FQ prescribed in this setting), and inpatient *C. difficile* rates were collected between 2014 and 2018 for comparison during masked and unmasked periods.

Inpatient FQ utilization data, measured in defined daily doses (DDD) per 100 inpatient days, were collected from electronic pharmacy dispensing records and were tabulated monthly from April 2014 to December 2018.

Appropriate versus inappropriate fluoroquinolone use in culture-directed therapy

We conducted chart reviews of inpatients regarding culture-directed FQ treatment. Culture-directed therapy was defined as antibiotics administered (newly prescribed or continued) on days 3–7 after a positive microbiological culture. Fluoroquinolone use was deemed appropriate if alternative agents had poor site penetration, were unsuitable (eg, allergy, intolerance, or unacceptable risk of adverse events, particularly renal impairment), or if carbapenems were the only alternative agents. Oral FQ use was considered appropriate if it had been prescribed within 48 hours of discharge and was the only suitable oral agent. Fluoroquinolone use was deemed inappropriate if other suitable antimicrobial agents were available based on site of infection and patient factors. Fluoroquinolone prescriptions for culture-directed therapy were

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Table 1. Patient Demographics, Antimicrobial Indications and Appropriateness, in Patients on Culture-Directed Fluoroquinolone (FQ) Therapy

Characteristic	FQ Sensitivity Masked	FQ Sensitivity Unmasked		*P* Value
	2015 (May–June)	2016 (May–June)	2017 (May–June)	
Total no.	95	153	190	
Mean age, y (SD)	71 (15)	64 (16)	64 (16)	
Men, no. (%)	42 (44.2)	83 (54.2)	103 (54.2)	
Inappropriate FQ prescribed, no. (%)	47 (49.5)	88 (57.5)	125 (65.8)	
Inappropriate FQ prescribed, prescriptions/100 inpatient days	0.069	0.173		<.001
Indications for FQ, no. (%)				
Urinary tract infection	42 (44.2)	56 (36.6)	65 (34.2)	
Bacteremia	22 (23.2)	28 (18.3)	36 (18.9)	
Respiratory tract infection	14 (14.7)	23 (15.0)	24 (12.6)	
Intra-abdominal infection	7 (7.4)	16 (10.5)	12 (6.3)	
Skin and soft tissue infection including diabetic foot infection	9 (9.4)	20 (13.1)	36 (18.9)	
Prostatitis	1 (1.1)	1 (0.7)	1 (0.5)	
Bone and joint infection		7 (4.6)	11 (5.8)	
Other[a]		2 (1.3)	5 (2.7)	

[a]Epididymitis, tubular-ovarian abscess, line sepsis, head and neck infections, and febrile neutropenia.

audited for appropriateness for a 2-month period each year (May and June) in 2015, 2016, and 2017.

Fluoroquinolone resistance

Ciprofloxacin susceptibility rates for inpatient clinical isolates of *Escherichia coli, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa* were reviewed from laboratory records between January 2014 and December 2018. Duplicate isolates within a calendar year were excluded. Susceptibility testing was routinely performed using the Vitek 2 system (bioMérieux, Marcy l'Etoile, France). Due to changes in ciprofloxacin breakpoints during this period, interpretation of minimum inhibitory concentration was standardized using European Committee on Antimicrobial Susceptibility Testing (EUCAST) 2019 break points.

Clostridium difficile *rates*

New inpatient *C. difficile* cases between January 2014 and December 2018 were obtained from surveillance data, per 10,000 patient days.

Outcomes

The outcomes of this study were comparisons of inpatient consumption of FQs in DDD per 100 inpatient days, inappropriate FQ prescriptions for culture-directed therapy, rates of ciprofloxacin susceptibility, and rates of inpatient *C. difficile* between the 2 periods: FQ susceptibilities "masked" versus "unmasked."

Statistical analysis

Rates of FQ consumption, appropriate usage, and *C. difficile* rates between "masked" and "unmasked" periods were assessed using independent 2-sample *t* tests. Results were reported as incidence rate ratios (RR) and 95% confidence intervals (CI). Percentages for organism susceptibility were compared using the Fisher exact test. All statistical tests were 2-sided, and $P < .05$ was considered statistically significant. Analyses were conducted using STATA version 12 software (StataCorp, Cary, NC).

Results

In total, 438 patient charts were reviewed; patient demographics and diagnoses are reported in Table 1. The total number of culture-directed FQ prescriptions increased from 95 in 2015 to 153 in 2016 and 190 in 2017; the proportion of inappropriate prescriptions also increased. Overall, inappropriate FQ prescriptions for culture-directed treatment increased from 0.069 to 0.173 prescriptions per 100 inpatient days after FQ unmasking, with a relative risk (RR) of 2.50 (95% confidence interval [CI], 1.84–3.39; $P < .001$). Fluoroquinolone prescriptions for culture-directed treatment comprised only 20% of total FQ prescriptions over the study period.

Although usage of other commonly prescribed inpatient antibiotics remained fairly constant over the study period, inpatient consumption of FQs decreased from 10.90 to 9.93 DDD per 100 inpatient days after FQ unmasking (Fig. 1). The RR of 0.91 (95% CI, 0.90– 0.92; $P < .001$) showed statistical significance.

Ciprofloxacin susceptibility of *E. coli* decreased from 56.8% to 55.8% (95% CI, 0.881–1.044; $P = .335$), *K. pneumoniae* decreased from 66.1% to 63.0% (95% CI, 0.783– 0.973; $P = .013$) and *P. aeruginosa* increased from 83.9% to 85.4% (95% CI, 0.941–1.328; $P = .197$). Changes in *E. coli* and *P. aeruginosa* susceptibility were not statistically significant; however, the change in susceptibility of *K. pneumoniae* had a RR of 0.873, which was statistically significant.

Inpatient *C. difficile* infections decreased from 7.64 to 5.35 per 10,000 patient days during the study period. The RR of 0.70 (95% CI, 0.62–0.79; $P < .001$) showed statistical significance.

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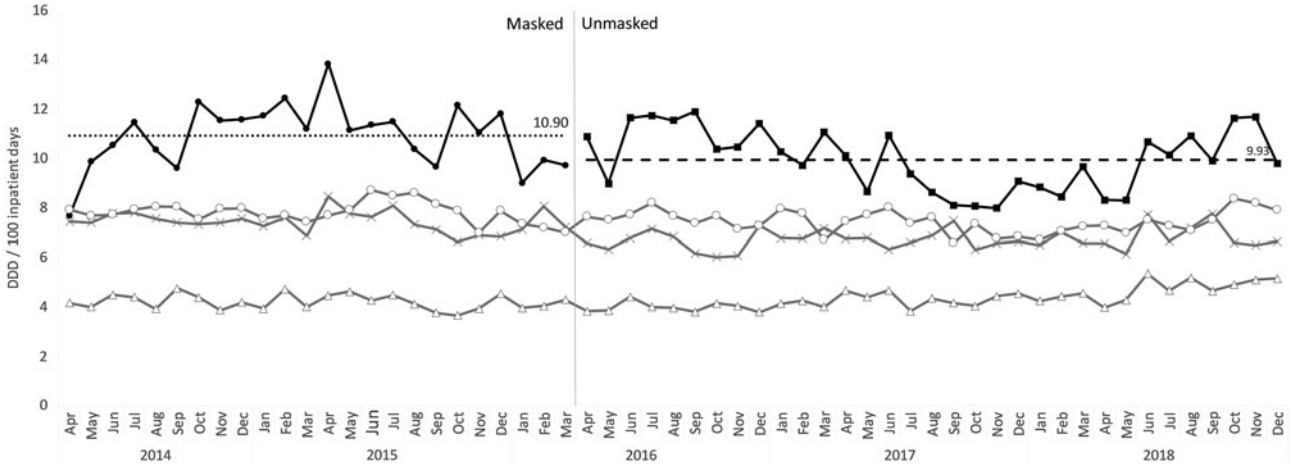

Fig. 1. Inpatient fluoroquinolone (FQ) usage (defined daily doses per 100 inpatient days), compared to other commonly prescribed inpatient antimicrobials; before and after unmasking of FQ susceptibilities.

FQ usage (masked)
FQ usage (unmasked)
Average FQ usage (masked)
Average FQ usage (unmasked)
Pipercillin-tazobactam usage
Amoxicillin-clavulnate usage
Ceftriaxone usage

Discussion

Although the unmasking of FQ susceptibility seemed to drive a rise in inappropriate culture-directed prescribing, the number of culture-directed prescriptions did not drive up overall FQ usage and overall inpatient FQ use actually decreased over the study period. Possibly, the updated black box warning issued by the US Food and Drug Administration[5] in July 2016 played a role in tempering the overall usage of FQs.

Selective reporting of antibiotic susceptibility results is one of the recommended strategies in the Infectious Diseases Society of America's guidelines for implementing an ASP.[6] In our study, the masking of FQ susceptibilities may have limited their use in culture-directed therapy, but a dramatic rise in other unintended consequences was not observed when this practice was halted. No discernible changes in ciprofloxacin resistance among *E. coli* or *P. aeruginosa* isolates was detected, overall FQ usage remained largely unchanged, and *C. difficile* rates were not adversely affected. Ciprofloxacin resistance among *K. pneumoniae* increased slightly, but similar trends have been noted elsewhere.[7,8]

Because culture-directed use was a minor component of usage (20% of inpatient FQ prescriptions) in our setting, the benefits of masking FQ sensitivities were obscured by the large number of FQs prescribed for empiric therapy. The most significant gains from an ASP perspective are likely related to the control of empiric use by other strategies, such as audits with feedback,[9] improved uptake of empiric guidelines, education of prescribers, and/or prior authorization.[10]

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2020.74

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