Impact of Prospective Audit and Feedback on Fluoroquinolone Use: A Large Academic Medical Center Experience

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BACKGROUND

- Fluoroquinolones (FQ) are commonly used antimicrobials, with high propensity for collateral damage. Due to recent warnings, the FDA recommends reserving FQ for bacterial infections with no alternative.

Fluoroquinolone Class-wide Warnings	
C. difficile-associated diarrhea	**Risk of multi-drug resistance (MDR)**
Tendon rupture / Tendinopathies	Peripheral neuropathy / CNS effects
Hypoglycemic coma	Aortic aneurysm and rupture

- Fluoroquinolone stewardship has been demonstrated to reduce:
  - Overall yearly incidence of *C. difficile* infections (CDI)
  - Incidence of extended-spectrum β-lactamase (ESBL)-producing infection
  - Incidence of infection with methicillin-resistant *S. aureus* (MRSA)
- **Objective:** Assess the impact of a prospective audit and feedback intervention on inpatient FQ use at our institution

METHODS

Study Design

- Retrospective, two-phase, single-center study performed at a 1,500-bed level 1 tertiary academic medical center
  - Phase I: Pre-intervention period (Jul 2018 - Jan 2019)
  - Phase II: Pharmacist-led fluoroquinolone initiative (Jul 2019 - Jan 2020)

Inclusion Criteria	Exclusion Criteria
• Adults, aged ≥ 18 years	• Pregnancy
• Ciprofloxacin or Levofloxacin ≥3d	• Corrections facility
• Pneumonia or urinary tract infection	• Prostatitis

Outcome Measures

- Primary outcome: Fluoroquinolone days of therapy (DOT)
- Secondary outcomes: Length of stay (LOS), CDI and ESBL infection rates by 3 months post-exposure, Incidence of QTc prolongation, Proportion of interventions accepted

Statistics

- Descriptive statistics, Chi-squared, Student's t and Mann-Whitney U tests were used to analyze the outcomes presented
- A sample size of 324 with 1:1 enrollment was required to be 95% powered to detect at least a 30% reduction in FQ use at alpha = 0.05

RESULTS

Baseline Demographics					
	Phase I	**Phase II**		**Phase I**	**Phase II**
Sample Size, n	**182**	**151**	**Sample Size, n**	**182**	**151**
Median age (IQR)	62 (20)	61 (22)	CAP	67 (37)	40 (26)
Male, n (%)	94 (52)	97 (64)	HAP/VAP	35 (19)	54 (36)
β-lactam allergy reported, n (%)	39 (21)	40 (26)	Uncomplicated cystitis	34 (19)	31 (20)
Recent IV antibiotic use, n (%)	70 (38)	57 (38)	Complicated UTI	46 (25)	26 (18)
Recent PPI use, n (%)	76 (42)	40 (26)			

Table 1: Baseline characteristics and infectious indication of 333 admitted patients in the prospective audit and feedback cohort (Phase II) vs. control cohort (Phase I). CAP: Community-acquired pneumonia, HAP: Hospital-acquired pneumonia, VAP: Ventilator-associated pneumonia, UTI: Urinary tract infection. PPI: Proton Pump Inhibitor. Recent IV antibiotic use: broad spectrum antimicrobials used within 90 days. UTI: Complicated UTI was defined as structural urinary tract abnormalities (ie. fistula) or instrumentation (ie. foley, stent), obstruction, nephrolithiasis, or immunocompromised

Outcome Data			
	Phase I	**Phase II**	**P-value**
Overall DOT, median (IQR)	7 (2)	5 (4)	< 0.001
DOT per 1000 pt-days	54.35	34.61	< 0.001
LOS, median (IQR)	8 (12)	9 (19)	0.20
CDAD infection, n (%)	2 (1)	2 (1)	1.00
ESBL infection, n (%)	1 (0.6)	0	0.13
Prolonged QTc, n (%)	3 (2)	3 (2)	0.72

Table 2: Study Outcomes. A reduction of 2 DOT observed between Phase I vs. Phase II. Additionally, a 36% reduction in DOT per 1000-patient days was observed (P < 0.001). No difference observed for LOS or for outcomes related to adverse effects. QTc prolongation defined as QTc interval of >500msec or >60msec prior to quinolone therapy

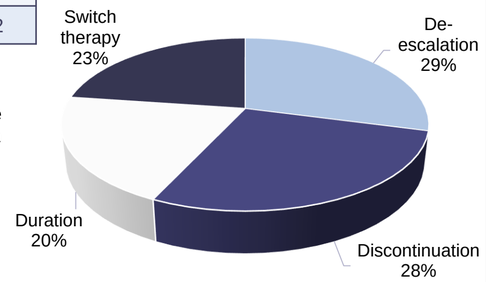

Figure 1: Pharmacist led-interventions. 97 total interventions were performed of which 80% were accepted. De-escalation involved a switch to a narrower-spectrum antimicrobial. Discontinuation was defined as cessation of antimicrobial therapy. Interventions on duration optimized length of therapy. Switch therapy optimized empiric coverage with an agent of similar spectrum based on our institutional antibiogram.

DISCUSSION

- 25% of patients reported to have β-lactam allergy, most unconfirmed, and half tolerated previous β-lactam treatment. Allergy screening or de-sensitization may aid in identification of additional options to reduce FQ use
- Prospective audit and feedback reduced inpatient fluoroquinolone use by 36% without increasing length of stay, indicating a positive impact of this intervention to reduce unnecessary antimicrobial use
- 80% of interventions were accepted by the treating provider, indicating feasibility of this practice.
- No difference in adverse effects were noted between groups in this study, however, this study is underpowered to detect a difference.
- Limitations of this investigation include the single-center retrospective design, short follow up for finding secondary infections, and lack of accounting for outpatient prescribing of fluoroquinolones.

CONCLUSION

- Prospective audit and feedback interventions can effectively reduce inappropriate fluoroquinolone consumption.
- Larger studies will be needed to observe if stewardship interventions reduce incidence of fluoroquinolone-related adverse effects.

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