71176: Resistance (R) Trends in Gram Negative Bacilli (GNB) to Fluoroquinolones (FQ), [Ciprofloxacin (CIP), Levofloxacin (LEV), Moxifloxacin (MOX)], Trimethoprim-sulfamethoxazole (TMP/SMX) and Nitrofurantoin (NFT) over a 7-year period: Pre- and Post- Implementation of FQ Restriction at a Tertiary Care Veterans Affairs Medical Center (VAMC).

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ABSTRACT

Background: Unrestricted use of FQ has been associated with emergence of drug resistance in GNB. Active surveillance measures are essential components of antibiotic stewardship practice. **Aim:** To evaluate antibiotic utilization, assess the impact of FQ restriction on resistance to FQ, TMP/SMX, and NFT, and identify quality improvement measures to prevent emergence of resistance in GNB. **Methods:** A retrospective records review and comparison of antimicrobial susceptibility data for GNB isolated at the Detroit VAMC over a 7-year period, pre- and post- FQ restriction, implemented in 2013. Susceptibility testing was performed by reference broth micro-dilution methods in a central laboratory. Antibiotic usage data were obtained from pharmacy computer records from 2011-17. Antibiotic use in inpatients was expressed as days of therapy/1000 patient-days (DOT/PD) and as number of prescriptions filled for outpatients. Data were analyzed using Pearson correlation coefficient score. **Results:** In 2016-17, the most common GNB isolated in our institution were E. coli (n=303), Klebsiella pneumoniae (n=100) and P. aeruginosa (n=70). Inpatient: During 2011-12, DOT/1000 PD for CIP, LEV and MOX were 34, 10 and 5 respectively, that dropped to 14, 5 and 3 during 2014-17, post- FQ restriction initiated in 2013. Outpatient: During 2013-17, outpatient CIP and MOX prescriptions decreased from 1936 to 781 and from 478 to 86 respectively; however, prescriptions for LEV, TMP/SMX and NFT increased from 33 to 128, 680 to 1074 and 95 to 322 respectively. Overall: Resistance to CIP, LEV and MOX had increased by 8% in *E. coli* (14 to 22%) and by 7% in *P. aeruginosa* (10 to 17%) during 2015-17; FQ-R in *K. pneumoniae* and NFT-R in *E. coli* stayed low at 7% and 2% respectively. Also, isolates of TMP/SMX-resistant *E. coli* and NFT-resistant *K. pneumoniae* increased from 20- to 27% and 40-51% respectively. **Conclusion:** Despite a decrease in FQ prescription due to restrictions implemented over a 4-year period, overall use of FQ among outpatients remained higher than expected (781 scripts in 2017). As a result, a high incidence of FQ-R was observed in GNB, especially *E. coli* and *P. aeruginosa*; also, a concomitant increase in TMP/SMX and NFT resistance was noted, attributed to a compensatory increased use of these agents during the study period ($p<0.05$).

INTRODUCTION

Global surveillance studies have shown that unrestricted use of FQ has been associated with emergence of multi-drug resistance in GNB. Resistance studies have demonstrated that Enterobacteriaceae producing extended-spectrum β-lactamases (ESBLs) were FQ- resistant too, thereby limiting the use of FQ in the treatment of community as well as healthcare-acquired urinary tract and intra-abdominal infections. Emergence of infections caused by ESBL producing GNB and increased incidence of *Clostridium difficile* colitis have been directly correlated with increased use of FQ. The continued increase in FQ- R affects patient management and necessitates changes in current guidelines for empiric therapy of community and hospital acquired infections. Active surveillance measures are essential to curtail emergence of FQ-R and are essential components of antibiotic stewardship practice.

Days of Therapy (DOT) - Defined by any amount of a specific antimicrobial agent administered in a calendar day to a particular patient as documented in the electronic bar coding medication record (BCMA); all antimicrobial days for a specific agent administered across a population are summed in aggregate.

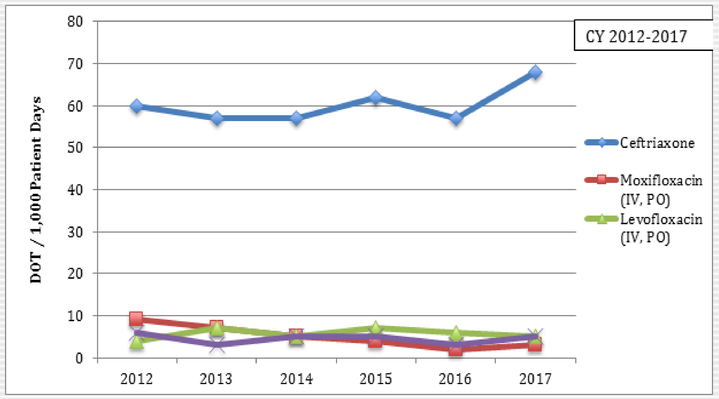
Patient Days - Defined as the aggregate number of inpatients (excluding Domiciliary) housed in the facility anytime throughout a day during a calendar year.

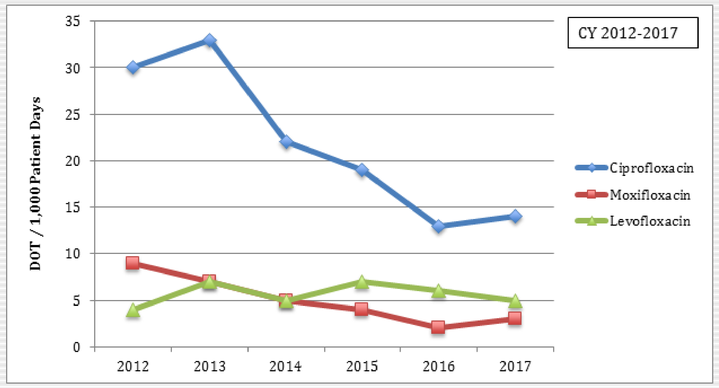
Note: Days of therapy is calculated per every 1,000 patient days to obtain the desired metric.
Days of therapy per 1,000 patient days is the primary antimicrobial use metric recommended by the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN). It is used by hospitals around the country to monitor antimicrobial usage.

METHODS

A retrospective record review of antimicrobial susceptibility data for GNB isolated at the Detroit VAMC over a 7-year period, was performed.
Susceptibility testing was performed by reference broth micro-dilution methods in a central laboratory. Antimicrobial susceptibility data pre- and post- FQ restriction (implemented in 2013) was compared. Antibiotic usage data were obtained from pharmacy computer records from 2011-17. Antibiotic use in inpatients was expressed as days of therapy/1000 patient-days (DOT/PD) and as number of prescriptions filled for outpatients. Data were analyzed using Pearson correlation coefficient score.

Acute Care Units - Fluoroquinolone (IV, PO) Usage





Number of Outpatient Antibiotic Scripts 2012-17

	2012	2013	2014	2015	2016	2017
Ciprofloxacin	1396	1396	955	523	521	567
Levofloxacin	33	62	65	100	122	128
Moxifloxacin	416	478	246	102	81	86
Total FQ	1845	1936	1266	725	724	781
Trim/sulfa	682	845	1294	1277	1116	1074
Nitrofurantoin	95	69	107	178	277	322

RESULTS

- In 2016-17, the most common GNB isolated in our institution were *E. coli* (n=303), *Klebsiella pneumoniae* (n=100) and *P. aeruginosa* (n=70).
- **Inpatient:** During 2011-12, DOT/1000 PD for CIP, LEV and MOX were 34, 10 and 5 respectively, that dropped to 14, 5 and 3 during 2014-17, post- FQ restriction initiated in 2013.
- **Outpatient:** During 2013-17, outpatient CIP and MOX prescriptions decreased from 1936 to 781 and from 478 to 86 respectively; however, prescriptions for LEV, TMP/SMX and NFT increased from 33 to 128, 680 to 1074 and 95 to 322 respectively.
- **Overall:** Resistance to CIP, LEV and MOX had increased by 8% in *E. coli* (14 to 22%) and by 7% in *P. aeruginosa* (10 to 17%) during 2015-17.
- FQ-R in *K. pneumoniae* and NFT-R in E coli stayed low at 7% and 2% respectively.
- Also, isolates of TMP/SMX-resistant *E. coli* and NFT-resistant *K. pneumoniae* increased from 20- to 27% and 40-51% respectively.

CONCLUSIONS

- **Despite significant reduction of FQ use in inpatients, (from 34 to 14 DOT/1000 PD), use of FQ among outpatients continued to be high (781 scripts in 2017).**
- **A high rate of FQ-R was noted especially in *E. coli* and *P. aeruginosa* isolates**
- **A concomitant increase in TMP/SMX and NFT resistance was noted, attributed to a compensatory increase in use of these agents during the study period ($p<0.05$).**
- **Reversal of FQ- resistance trends post restriction may take several years.**
- **Antimicrobial stewardship activities need to be enhanced in both ambulatory and inpatient settings in order to achieve optimal results.**

References:

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