

INTRODUCTION

Prospective audit and feedback (PAF) in the critical care setting has consistently been shown to optimize antibiotic utilization leading to significant reductions in antibiotic use and expenditures.¹⁻² However, results of PAF studies conducted on surgical and medical wards have demonstrated conflicting results.³⁻⁵

OBJECTIVES

- Primary Objective:**
- To describe the impact of PAF on broad-spectrum antibiotic use measured in days of therapy (DOT) per 1,000 patient-days.
- Secondary Objectives:**
- To describe the impact of PAF on narrow-spectrum antibiotic use measured in days of therapy (DOT) per 1,000 patient-days, total antibiotic expenditure, hospital length of stay, readmission within 30 days of hospital discharge, mortality, and nosocomial *Clostridium difficile* infections.
 - To describe the uptake of the PAF recommendations and the type of recommendations made by the Antimicrobial Stewardship (ASP) team.

METHODS

Study Design and Setting:

- Prospective, single-center study on a 36-bed general internal medicine ward (4D) at the Scarborough Hospital (TSH) Birchmount site, an acute care community hospital in Toronto, Canada
- PAF was introduced on 4D on July 1, 2014. The pre-intervention period was defined as July 1 2013 to June 30 2014. Year 1 of the intervention period spanned from July 1 2014 to June 30 2015 while year 2 of the intervention period spanned from July 1 2015 to June 30 2016.

Intervention:

- During the pre-intervention period, antibiotic selection was at the discretion of the most responsible physicians (MRPs).
- During the post-intervention period, the ASP stewardship pharmacist reviewed any inpatient on 4D who was receiving an antibiotic on the day of PAF rounds (every Tuesday and Thursday). Patients were identified using ABx Alert™, an antibiotic stewardship software database integrated with the hospital's electronic medical records system. All identified opportunities for optimization of antibiotic therapy were reviewed with an infectious diseases (ID) physician and the MRPs for discussion and feedback. The MRPs maintained prescribing autonomy. Acceptance or rejection of stewardship recommendations and the type of intervention were recorded in the ABx Alert™ database.

Data Sources:

- Antibiotic utilization data and drug acquisition costs were obtained from the ABx Alert™ database. Nosocomial *C. difficile* infection data was provided by the TSH Infection Prevention and Control department. Patient days, hospital length of stay, and mortality data were provided by the TSH Performance and Decision Support department. Statistical analyses were performed using SAS (Version 9.4, Cary, North Carolina)

RESULTS

Table 1: Outcome of ASP Recommendations

Intervention Outcomes	Year 1 of PAF	Year 2 of PAF
Accepted	683 (94%)	671 (92%)
Partially Accepted	12 (2%)	23 (3%)
Rejected	28 (4%)	39 (5%)
Total	723	733

Discontinuation of antibiotic, optimization of antibiotic duration and de-escalation of antibiotics were the most common interventions that accounted for approximately 60% of all interventions for both year 1 and year 2 of PAF. Other interventions included IV to PO, change of therapy, dose optimization, start antibiotic therapy, broaden antibiotic therapy and recommendations related to diagnostic testing and imaging.

Table 2: Antibiotic Utilization

Class or Agent	Pre-intervention (DOTs/1,000 Patient Days)	Year 1 of PAF (DOTs/1,000 Patient Days)	p-value ^a	Year 2 of PAF (DOTs/1,000 Patient Days)	p-value ^a
Broad-spectrum Antibiotics	209.1	129.7	0.007	108.5	0.001
Fluoroquinolones ^b	112.9	47.7	0.001	43.9	0.0005
Piperacillin-Tazobactam	43.1	32.0	0.62	21.3	0.03
Vancomycin	23.3	14.2	0.09	10.1	0.03
Carbapenems ^c	17.0	18.6	0.73	11.5	0.09
Aminoglycosides ^d	5.9	0.4	0.02	2.4	0.31
Ceftazidime	2.4	8.9	0.01	6.2	0.08
Amoxicillin-Clavulanic Acid	4.5	7.9	0.38	13.2	0.03
Narrow-spectrum Antibiotics	438.6	369.9	0.08	376.0	0.08
First Generation Cephalosporins ^e	75.6	78.8	0.62	66.5	0.38
Second Generation Cephalosporins ^f	30.9	39.0	0.27	31.3	0.91
Ceftriaxone	144.3	104.9	0.03	136.4	0.57
Azithromycin	74.1	55.3	0.13	54.8	0.03
Metronidazole	65.9	57.1	0.13	50.7	0.09
Penicillins ^g	47.8	34.9	0.08	36.4	0.20

^a Wilcoxon signed-rank test
^b Fluoroquinolones = ciprofloxacin, levofloxacin, moxifloxacin
^c Carbapenems = ertapenem, imipenem, meropenem
^d Aminoglycosides = gentamicin, tobramycin
^e First Generation Cephalosporins = cefazolin, cephalexin
^f Second Generation Cephalosporins = cefuroxime, cefprozil
^g Penicillins = ampicillin, amoxicillin, cloxacillin, penicillin

Table 3: Secondary Outcomes (Antibiotic Expenditures, Clinical Outcomes, Nosocomial *C. difficile* Rates)

	Pre-intervention	Year 1 of PAF	p-value	Year 2 of PAF	p-value
Antibiotic Expenditures					
Total Antibiotic Expenditures per Patient-Day, \$ CAD	2.80	2.34	0.03 ^a	1.83	0.007 ^a
Total Antibiotic Expenditures, \$ CAD	30,806	28,515	0.62 ^a	22,726	0.02 ^a
Clinical Outcomes					
Mean Length of Stay, d	8.43	7.90	0.27 ^b	8.59	0.55 ^b
Mortality, %	6.30	5.96	0.71 ^b	6.67	0.86 ^b
Mean Readmission Within 30 Days	10.33	11.75	0.24 ^b	10.92	0.44 ^b
Microbiologic Outcomes					
Nosocomial <i>Clostridium difficile</i> infections (No. of cases/10,000 patient-days)	0	3.28	0.04 ^c	1.61	0.34 ^c

^a Wilcoxon signed-rank test ^b Wilcoxon rank-sum test ^c Student's t test with Satterthwaite's correction

DISCUSSION AND CONCLUSION

During the two year intervention period, the ASP team made a total of 1,456 recommendations related antibiotic therapy with an overall acceptance rate of 93%. The timeliness of ASP recommendations was facilitated by the use of ABx Alert™ software to identify opportunities for antibiotic optimization. Uptake of ASP recommendations by the most responsible physicians is crucial to the impact of PAF on the ward because they retained full prescribing autonomy during the intervention period.

The efficacy of PAF on the medicine ward was confirmed by the substantial and sustained reduction in broad-spectrum antibiotic usage. Compared to the pre-intervention period, broad-spectrum antibiotic use decreased by 38% (from 209 to 130 DOTs per 1,000 patient-days) in year 1 of PAF and 48% (from 209 to 109 DOTs per 1,000 patient-days) in year 2 of PAF. The reduction was driven by a dramatic decrease in fluoroquinolone, piperacillin-tazobactam and vancomycin use. Antibiotic expenditures decreased by 16% in year 1 of PAF and 35% in year 2 of PAF compared with the pre-intervention period. Mean length of stay, mean readmission rates within 30 days of hospital discharge and crude mortality rates did not significantly change during the PAF period compared to the pre-intervention period. While the nosocomial *C. difficile* rate appeared to increase during the post-intervention period, it should be noted that the rate of 0 cases per 10,000 patient-days during 12 month pre-intervention period is atypical for the ward. A review of historic data found 2.24 *C. difficile* cases per 10,000 patient-days from July 2011 to June 2012, and 4.40 cases per 10,000 patient-days from July 2012 to June 2013, that are comparable to year 1 and year 2 PAF *C. difficile* rates.

Choosing between strategies to optimize antibiotic use with limited resources is a common challenge faced by many hospitals. The results of this study has found that systematic reassessment of antibiotics, even when conducted on a twice weekly basis, with case-by-case feedback to the prescribing physicians, appears to be a safe and effective means to improve antibiotic use on a general internal medicine ward.

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