Original Article

Antimicrobial Stewardship Programs: Comparison of a Program with Infectious Diseases Pharmacist Support to a Program with a Geographic Pharmacist Staffing Model

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ABSTRACT

Background: Stewardship of antimicrobial agents is an essential function of hospital pharmacies. The ideal pharmacist staffing model for antimicrobial stewardship programs is not known.

Objective: To inform staffing decisions for antimicrobial stewardship teams, we aimed to compare an antimicrobial stewardship program with a dedicated Infectious Diseases (ID) pharmacist (Dedicated ID Pharmacist Hospital) to a program relying on ward pharmacists for stewardship activities (Geographic Model Hospital).

Methods: We reviewed a randomly selected sample of 290 cases of inpatient parenteral antibiotic use. The electronic medical record was reviewed for compliance with indicators of appropriate antimicrobial stewardship.

Results: At the hospital staffed by a dedicated ID pharmacist, 96.8% of patients received initial antimicrobial therapy that adhered to local treatment guidelines compared to 87% of patients at the hospital that assigned antimicrobial stewardship duties to ward pharmacists ($P < .002$). Therapy was modified within 24 hours of availability of laboratory data in 86.7% of cases at the Dedicated ID Pharmacist Hospital versus 72.6% of cases at the Geographic Model Hospital ($P < .03$). When a patient's illness was determined not to be caused by a bacterial infection, antibiotics were discontinued in 78.0% of cases at the Dedicated ID Pharmacist Hospital and in 33.3% of cases at the Geographic Model Hospital ($P < .0002$).

Conclusion: An antimicrobial stewardship program with a dedicated ID pharmacist was associated with greater adherence to recommended antimicrobial therapy practices when compared to a stewardship program that relied on ward pharmacists.

Key Words—antibacterial agents, anti-infective agents, antimicrobial stewardship, pharmacists

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Antibacterial therapy is one of the major advances of modern medicine, providing cures for diseases that were previously fatal and making possible surgical procedures that would have excessive infectious complications in the absence of antimicrobial prophylaxis.¹ These advances are threatened by the rising tide of antimicrobial resistance. Increasing resistance to available agents has been promoted by overuse of antibiotics in hospitals and other settings. Despite the critical need for new antimicrobial agents to fill the gaps created by resistance, development of new agents by pharmaceutical firms has been falling for 3 decades.¹ It is imperative that all available measures be taken to enable us to use our limited antibiotic resources wisely. Careful stewardship of available antimicrobial agents is a critical component of the response to the resistance crisis.

The Infectious Diseases Society of America guidelines on antimicrobial stewardship recommend that the core multidisciplinary stewardship team include an infectious diseases (ID) physician and a clinical pharmacist with ID training.² Optimal team membership would also include a clinical microbiologist, information systems expert, hospital epidemiologist, and infection control practitioner. The Centers for Disease Control and Prevention has recommended that the appointment of a single pharmacist leader responsible for working to improve antibiotic use is a core element of hospital antibiotic stewardship programs.³ Many studies of teams with membership of this type have demonstrated successful reductions in antimicrobial use, hospital stay, and costs.⁴⁻⁶ Despite the benefits of antimicrobial stewardship, budgetary considerations have been a barrier to widespread implementation of robust programs.⁷ A shortage of clinical pharmacists⁸ may be a challenge to hospital leadership, as they endeavor to staff a stewardship team with a dedicated pharmacist. A geographic staffing model, with general clinical pharmacists taking responsibility for antimicrobial stewardship activities in their assigned inpatient area, may be attractive to pharmacy managers who are struggling to staff their services.

The impact on patient outcomes of focused experience in a content area appears to be self-evident and has been demonstrated for many areas of expertise. Outcomes of thyroid, gastrointestinal, and cardiothoracic surgery are improved when the team specializes in operations on those organ systems.⁹⁻¹¹ Survival is improved when patients infected with human immunodeficiency virus are cared for by HIV

specialists.^{12,13} ID consultation has been associated with improved outcomes in *Staphylococcus aureus* bacteremia.¹⁴ It would be reasonable to expect that an antimicrobial stewardship team staffed by an ID pharmacist would be more effective than a team lacking that expertise. However, clinical evidence to support this supposition has not been reported. To provide data on the impact of a pharmacist dedicated to antimicrobial stewardship on the quality of the program, we compared outcomes in 2 similar hospitals with stewardship teams with and without a dedicated ID pharmacist.

METHODS

Setting

Both hospitals are Department of Veterans Affairs tertiary care medical centers and provide a full range of services including neurosurgery, cardiothoracic surgery, and medical and surgical intensive care. The hospital with a dedicated ID pharmacist (ID Pharmacist Hospital) has 312 licensed acute care beds and an average daily census of 230; the hospital with a geographic pharmacist staffing model (Geographic Pharmacist Hospital) has 137 licensed acute care beds, with an average daily acute care census of 103, and 60 long-term care beds. The ID Pharmacist Hospital also provides long-term ventilator care in its medical intensive care unit and has a transitional care unit for patients requiring subacute care. Both hospitals provide inpatient rehabilitation services for medical and surgical conditions. Both hospitals serve as training sites for medical students, postgraduate medical trainees, and pharmacy doctorate students. ID consultation is available at all times at both hospitals; there are fellowship training programs with full-time attending staff coverage at both hospitals. ID physician staff participate in antimicrobial stewardship efforts at both hospitals. The ID Pharmacist Hospital has a dedicated full-time ID pharmacist who reviews all broad-spectrum parenteral antibiotic usage and rounds daily with the ID team. The Geographic Model Hospital uses a geographic model in which the 4 individual ward pharmacists are responsible for antimicrobial stewardship in their assigned area. Each ward pharmacist rounds daily with their assigned internal medicine, intensive care, or surgery team and provides advice to the team when antimicrobial usage differs from guidelines. Each pharmacist has a doctor of pharmacy degree, board certification in pharmacotherapy, and experience in inpatient pharmacy. One of the 4 clinical pharmacists at the Geographic Model

Hospital is trained in ID and is assigned to 2 of the internal medicine ward teams. His duties are identical to the other ward pharmacists.

Case Selection

Pharmacy records were reviewed to identify all acute care inpatients treated for longer than 24 hours with a targeted agent (third- or fourth-generation cephalosporin, extended spectrum penicillin, carbapenem, fluoroquinolone, or vancomycin). Patients who were receiving hemodialysis, who were treated for multiple infections, or who were transferred from an outside hospital after initiation of antimicrobial therapy were excluded prior to randomization. The randomizer function in Microsoft Excel was used to randomly select patients. At the Dedicated ID Pharmacist Hospital, 263 records were screened; at the Geographic Model Hospital, 163 records were screened.

Endpoints

The primary endpoint was a composite of compliance with all of the following: (a) therapy modification within 24 hours of laboratory data, (b) discontinuation of therapy when determined not bacterial, and (c) intravenous to oral (IV to PO) conversion completed when appropriate.

Data Abstraction

We reviewed a randomly selected sample of 290 cases of inpatient parenteral antibiotic use (190 cases at the ID Pharmacist Hospital from October 2011 to October 2012, and 100 cases at the Geographic Model Hospital from July 2010 to June 2011). The electronic medical record was reviewed for compliance with indicators of appropriate antimicrobial stewardship.¹⁵ Documentation for antibiotic use, collection of culture material, empirical antimicrobial selection, and de-escalation or streamlining therapy when indicated, based on objective evidence, were evaluated. If a physician note stated the indication for antibacterial therapy within 24 hours of start of therapy, the case was considered compliant for the stewardship element “indication of antibiotic therapy documented.” If a sample for culture was collected prior to first-dose antibiotic administration, the case was considered compliant for the culture element. Empirical therapy was considered appropriate if the agent selected was one of the agents recommended by the local treatment guidelines for the indication stated. Guidelines at each site are based

on the Department of Veterans Affairs (VA) National Formulary and guidance from the national VA Pharmacy Benefits Management group.¹⁶ If the indication was not stated, it was inferred from the admission diagnosis or from the type of cultures obtained when calculating the proportion of cases for which an appropriate agent was selected for the indication. If cultures returned negative, and an alternative diagnosis was identified, the diagnosis of bacterial infection was considered to be excluded. Streamlining was defined as indicated if conversion from IV to PO therapy was possible, if culture and susceptibility results demonstrated a pathogen for which a narrower agent was available, or if the working diagnosis of bacterial infection was excluded. Streamlining was considered compliant if therapy was adjusted accordingly.

Statistical Analysis

Data were analyzed using Prism (GraphPad, San Diego, California). Fisher’s exact test was used for dichotomous variables and Student *t* test was used for continuous variables. All tests were 2-tailed. A *P* value of less than .05 was considered statistically significant. Power calculations were not performed for this descriptive study.

Ethics Review

The study was approved by the Colorado Multiple Institutional Review Board and the Institutional Review Board of the VA Greater Los Angeles Healthcare System.

RESULTS

The patient population receiving parenteral antimicrobial therapy was predominantly male at both hospitals. The population at the ID Pharmacist Hospital was younger and more ethnically and racially heterogeneous than the Geographic Model Hospital (Table 1). Reasons for exclusion from the study are presented in Table 2. Indications for antimicrobial therapy are presented in Table 3. Antimicrobial resistance was more prevalent at the ID Pharmacist Hospital, as shown in Table 4.

Cultures were obtained appropriately in 64.2% of cases at the ID Pharmacist Hospital and in 82% of cases at the Geographic Model Hospital (*P* = .002). At the ID Pharmacist Hospital, 96.8% of patients received initial antimicrobial therapy that adhered to local treatment guidelines compared to 87% of patients at the Geographic Model Hospital (Table 5)

Antimicrobial Stewardship Pharmacist Staffing

Table 1. Demographics of patient populations at the two hospitals

	ID Pharmacist Hospital (N = 190)	Geographic Model Hospital (N = 100)	P*
Male, <i>n</i> (%)	184 (96.8%)	95 (95%)	.52
White, <i>n</i> (%)	96 (50.5%)	84 (84%)	<.0001
Black, <i>n</i> (%)	55 (29.5%)	11 (11%)	.0003
Other (Hispanic, Pacific Islander, American Indian), <i>n</i> (%)	24 (13.5%)	5 (5%)	.041
Mean age $\pm$ SD, years	67.44 $\pm$ 12.11	60.98 $\pm$ 13.55	<.0001

Note: The ID Pharmacist Hospital has an antimicrobial stewardship program staffed by a full-time infectious diseases pharmacist. At the Geographic Model Hospital, ward pharmacists provide support for antimicrobial stewardship. Differences in categorical variables were assessed using chi-square analysis; continuous variables were assessed using Student *t* test.

*P < .05 was considered significant.

Table 2. Reasons for exclusion of cases

Exclusion criterion	ID Pharmacist Hospital	Geographic Model Hospital
Surgical prophylaxis	26	5
Transferred from outside facility while receiving antibiotic therapy	20	40
Multiple infections	17	14
Hemodialysis	10	4

Note: The ID Pharmacist Hospital has an antimicrobial stewardship program staffed by a full-time infectious diseases pharmacist. At the Geographic Model Hospital, ward pharmacists provide support for antimicrobial stewardship.

Table 3. Indications for antimicrobial therapy

Indication	ID Pharmacist Hospital	Geographic Model Hospital	P*
Skin and soft tissue infection	26.3% (50/190)	33% (33/100)	.27
Respiratory tract infection	24.2% (46/190)	25% (25/100)	.89
Urinary tract infection	18.4% (35/190)	6% (6/100)	.004
Sepsis/Neutropenic fever	13.7% (26/190)	11% (11/100)	.58
Intraabdominal infection	8.4% (16/190)	21% (21/100)	.01
Bacteremia	6.8% (13/190)	2% (2/100)	.10
Central nervous system infection	2.1% (4/190)	0% (0/100)	.30
Osteomyelitis	0% (0/190)	2% (2/100)	.12

Note: The ID Pharmacist Hospital has an antimicrobial stewardship program staffed by a full-time infectious diseases pharmacist. At the Geographic Model Hospital, ward pharmacists provide support for antimicrobial stewardship. Differences in categorical variables were assessed using chi-square analysis.

*P < .05 was considered significant.

Table 4. Proportion of selected organisms that are sensitive to representative antibacterial agents at two hospitals: antimicrobial stewardship teams with and without a dedicated infectious disease (ID) pharmacist

	ID Pharmacist Hospital	Geographic Model Hospital	P*
<i>Escherichia coli</i>	(N = 199)	(N = 350)	
Cefepime	88%	99%	<.0001
Fluoroquinolones	65%	79%	.0005
Imipenem-cilastin	100%	100%	NA
<i>Klebsiella pneumoniae</i>	(N = 123)	(N = 132)	
Cefepime	80%	99%	<.0001
Fluoroquinolones	80%	97%	<.0001
Imipenem-cilastin	97%	99%	.2
<i>Pseudomonas aeruginosa</i>	(N = 254)	(N = 91)	
Cefepime	64%	80%	<.01
Fluoroquinolones	53%	76%	<.0001
Imipenem-cilastin	71%	84%	.02

Note: The ID Pharmacist Hospital has an antimicrobial stewardship program staffed by a full- time infectious diseases pharmacist. At the Geographic Model Hospital, ward pharmacists provide support for antimicrobial stewardship. Differences in categorical variables were assessed using chi-square analysis.

*P < .05 was considered significant.

Table 5. Proportion compliant with treatment guidelines at the start of antimicrobial therapy: antimicrobial stewardship teams with and without a dedicated ID pharmacist

	Antibiotic courses compliant with indicator ^a (%)		P
	ID Pharmacist Hospital (N = 190)	Geographic Model Hospital (N = 100)	
Indication of antibiotic therapy documented	189/190 (99.5%)	95/100 (95%)	.020
Collection of appropriate cultures	113/176 (64.2%)	82/100 (82%)	.002
Appropriate empirical therapy	184/190 (96.8%)	87/100 (87%)	.002

Note: The ID Pharmacist Hospital has an antimicrobial stewardship program staffed by a full- time infectious diseases pharmacist. At the Geographic Model Hospital, ward pharmacists provide support for antimicrobial stewardship. Differences in categorical variables were assessed using chi-square analysis. P < .05 was considered significant.

^aDenominator denotes number of antibiotic courses where specified action was indicated.

(P = .002). Therapy was modified within 24 hours of availability of laboratory data in 86.7% of cases at the ID Pharmacist Hospital versus 72.6% of cases at the Geographic Model Hospital (Table 6) (P = .029). When a patient's illness was determined not to be caused by a bacterial infection, antibiotics were discontinued at the ID Pharmacist Hospital in 77.1% of cases and at the Geographic Model Hospital in 33.3% of cases (P = .0002). When all 3 streamlining

activities were combined, and cases were grouped according to presence or absence of an ID consult, streamlining remained significantly more common at the ID Pharmacist Hospital (Table 6).

DISCUSSION

This study demonstrates a strong association between an antimicrobial stewardship program with a dedicated ID pharmacist and higher levels of

Table 6. Indicators associated with streamlining of antimicrobial therapy: antimicrobial stewardship teams with and without a dedicated ID pharmacist

	Appropriate streamlining of therapy (%) ^a		P [*]
	ID Pharmacist Hospital	Geographic Model Hospital	
Discontinuation of therapy when determined not bacterial	37/48 (77.1%)	11/33 (33.3%)	.0002
Therapy modification indicated based on laboratory data	143/190 (75.2%)	51/100 (51%)	<.0001
Therapy modification within 24 hours of laboratory data	124/143 (86.7%)	37/51 (72.6%)	.029
IV to PO conversion completed when appropriate	97/120 (80.8%)	41/67 (61.2%)	.0052
All of the above streamlining activities	165/182 (90.7%)	47/95 (49.5%)	<.0001
ID consult	41/43 (95.3%)	11/25 (44%)	<.0001
No ID consult	124/139 (89.2%)	36/70 (51.4%)	<.0001

Note: The ID Pharmacist Hospital has an antimicrobial stewardship program staffed by a full-time ID pharmacist. At the Geographic Model Hospital, ward pharmacists provide support for antimicrobial stewardship. Differences in categorical variables were assessed using chi-square analysis. IV = intravenous; PO = oral.

^aDenominator denotes number of antibiotic courses where specified streamlining was indicated.

^{*}P < .05 was considered significant.

adherence to recommended stewardship strategies, as compared to a similar program at a similar hospital using a geographic model of clinical pharmacists to provide antimicrobial stewardship. Adherence was improved across all prescribing measures, including selection of empirical therapy, therapy modification at 24 hours, discontinuation of therapy when an illness was determined not to be a bacterial infection, and conversion from parenteral to oral therapy when appropriate. Compliance with cultures was lower at the dedicated ID Pharmacist Hospital. Reasons for this difference are not clear and may be the focus of future efforts. Adjustment of antimicrobial therapy based on culture data was indicated more frequently at the ID Pharmacist Hospital, possibly because antimicrobial resistance was more prevalent there. The higher prevalence of resistance at the ID Pharmacist Hospital likely represents local resistance patterns and is not an effect of the ID pharmacist. The higher rate of adherence to stewardship guidelines at the hospital with a dedicated ID pharmacist was maintained in cases where ID consultation was obtained, indicating that an ID pharmacist provided value in addition to an ID physician consultation. To our knowledge, this study represents the only direct comparison of similar hospitals with antimicrobial stewardship programs that differ in the pharmacist staffing model.

Our study builds on previous work showing the value of multidisciplinary stewardship teams. Previous work has demonstrated the benefits of antimicrobial stewardship programs staffed with ID pharmacists compared to hospitals without a defined stewardship program.⁶ A multidisciplinary team composed of an ID specialist, clinical microbiologist, and pharmacists was studied in a trial that randomly assigned patients to intervention by the team versus usual care. Intervention resulted in significantly reduced lengths of hospital stay, laboratory and imaging costs, and overall costs.¹⁷ A randomized trial of pharmacist intervention in cefotaxime prescribing demonstrated that a hospital pharmacist was effective in communicating hospital antibiotic guidelines to physicians.¹⁸ In a nonrandomized study, the appropriateness of approvals for restricted antimicrobial agents was higher when performed by ID pharmacists compared to ID fellow physicians.¹⁹

The strength of our study is the review of individual cases for indicators of the antimicrobial stewardship program's efficacy. Our study has several limitations. Although the hospitals were similar, there were differences that could not be controlled. We were unable to compare APACHE scores or other measures of severity of illness. We were unable to obtain data on defined daily doses of antimicrobial agents used at each hospital. The Geographic Model

Hospital had one ID pharmacist on staff, providing general clinical pharmacist services to approximately 40% of internal medicine patients. Despite this factor, which would be expected to diminish differences between the programs, the hospital with the dedicated ID pharmacist had significantly better antimicrobial stewardship measures. If this study was repeated in a setting where the geographic model hospital did not include a ward pharmacist with ID training, the difference may be even greater.

In summary, this study provides evidence that an antimicrobial stewardship team staffed by a dedicated ID pharmacist is associated with better adherence to multiple antibiotic prescribing measures, including selection of empirical therapy, therapy modification at 24 hours, discontinuation of therapy when an illness was determined not to be a bacterial infection, and conversion from parenteral to oral therapy

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