CONCISE COMMUNICATION

Computer-Assisted Antimicrobial Recommendations for Optimal Therapy: Analysis of Prescribing Errors in an Antimicrobial Stewardship Trial

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Clinician education and prospective audit and feedback interventions, deployed separately and concurrently, did not reduce antimicrobial use errors or rates compared to a control group of general medicine inpatients at our public hospital. Additional research is needed to define the optimal scope and intensity of hospital antimicrobial stewardship interventions.

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The relative impact of different antimicrobial stewardship interventions on acute-care hospital rates of antimicrobial use and errors is largely unknown.[1] After improving antimicrobial use at a long-term and acute-care hospital through clinician education and institutional infection management guideline implementation,[2] we sought to determine the effectiveness of this approach by deploying a clinician education intervention concurrently with computer-assisted prospective audit and feedback by infectious disease (ID) pharmacists and with no intervention on the 3 inpatient internal medicine firms of our urban teaching hospital.

METHODS

All adult patients admitted over a 24-week period beginning in February 2005 to inpatient medicine services in our publicly funded Chicago teaching hospital were assigned sequentially to 3 inpatient medicine firms, each staffed for 4-week rotations by 4 physician teams. These patients were cared for across 9 general medical-surgical wards with shared facilities and services. Interventions were assigned to firms by coin flips. Interventions were developed as quality improvement initiatives under the auspices of the hospital's Anti-Infective Committee, and the study was approved by the hospital's institutional review board.

An investigator (D.N.S.) presented teaching sessions to physicians in the clinician education firm twice during each 4-week rotation. Case vignettes using the Audience Response System[3] were used to explore the diagnosis and treatment of common infection syndromes, reinforcing recommendations from our hospital-wide infection management guidelines (see below) and emphasizing changing susceptibility patterns and syndromes associated with antimicrobial overuse.

A second firm was assigned to prospective audit and feedback by an ID pharmacist. Infectious disease pharmacists (R.C.G., G.S.I.) reviewed the charts of each inpatient antimicrobial recipient (excluding discharged patients or those whose antimicrobials had been discontinued) on each nonholiday weekday, using a computer program that reported patient demographic characteristics, test results, and antimicrobial therapy. Institutional guidelines provided a reference standard. Clinical pharmacist case review was not otherwise routinely available at our hospital.

The control firm was not subjected to active interventions but had access to hospital-wide antimicrobial stewardship programs, including institutional infection management guidelines implemented in 2004 to support the diagnosis and treatment of common infection syndromes, and restrictions for 7 antimicrobials necessitating ID pharmacist or physician approval before dispensing. The primary outcomes were the proportion of initial antimicrobial regimens with error, antimicrobial courses, and antimicrobial treatment days in which 1 or more antimicrobial use errors could be identified during retrospective review of a random sample of antimicrobial recipients hospitalized on the inpatient medicine firms during the study period. Methods for conducting case reviews were published previously.[4] Secondary outcomes included the mean number of days of therapy with any error and the overall antimicrobial utilization (expressed as days of therapy (DOT) per 1,000 patient days).[2] Weekly aggregate antimicrobial use rates for each firm during the study period were programmed from hospital pharmacy and administrative data stored in a data warehouse.[5]

A χ^2 analysis or ANOVA test was used for comparisons of proportions or means when appropriate. For the secondary outcome, error days were modeled as counted data with an overdispersion variable (negative binomial regression) offset for total days of antimicrobial therapy (exposure). Analyses were performed using STATA SE 12 software (StataCorp, College Station, TX).

RESULTS

During the intervention period, 2,682 antimicrobial courses were administered among 5,804 admissions. Patients admitted to the control firm had shorter median lengths of stay than those in the other firms (4, 5, and 5 days, respectively; $P < .001$; Table 1). Among antimicrobial recipients randomly selected for antimicrobial error review, nearly 80% of antimicrobial courses were initiated in the emergency department (ED) (Table 1).

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TABLE 1. Inpatient Medicine Firms and Reviewed Antimicrobial Cases

	Control Firm	Education Firm	Pharmacists' Firm	Total	*P* Value
Admissions, no.[a]	1,942	1,920	1,942	5,804	…
Patient days, no.	7,993	9,587	9,040	26,620	…
Length of stay, median d (range)	4 (1–59)	5 (1–88)	5 (1–56)	…	<.001
Antimicrobial courses	877	904	901	2,682	…
Cases randomly selected for error adjudication					
Cases reviewed, no. (%)	144 (28.9)	178 (35.7)	176 (35.3)	498 (100)	.07
Age, mean y (SD)	52.8 (15.3)	53.4 (16.1)	54.2 (15.7)	53.5 (15.7)	.70
Females, no. (%)	64 (44)	91 (51)	93 (53)	248 (49.8)	.30
ED antimicrobial course starts, no. (%)	112 (77.8)	148 (83.2)	135 (76.7)	395 (79.3)	.30
Antimicrobial indications[b]					
Lower respiratory, no. (%)	45 (31)	73 (41)	77 (43.8)	195 (39.1)	.06
Upper respiratory, no. (%)	3 (2.1)	2 (1.1)	2 (1.1)	7 (1.4)	.70
Urinary tract, no. (%)	26 (18.1)	34 (19.1)	30 (17.1)	90 (18.1)	.90
Skin/Soft tissue, no. (%)	27 (18.8)	34 (19.1)	30 (17.1)	91 (18.3)	.80
Intra-abdominal, no. (%)	24 (16.7)	25 (14.0)	25 (14.2)	74 (14.9)	.80
Febrile neutropenia	4 (2.8)	5 (2.8)	6 (3.4)	15 (3.0)	.90
Clostridium difficile	9 (6.2)	11 (6.2)	7 (3.9)	27 (5.42)	.50
Other	35 (24.3)	60 (33.7)	61 (34.7)	156 (31.3)	.09

NOTE. SD, standard deviation; ED, emergency department.
[a]All patients admitted to that firm during the intervention period (February to July, 2005).
[b]Each case can have more than one indication so the sum percentages may exceed 100%.

TABLE 2. Antimicrobial Regimen Error Rates

	Control	Education		Pharmacist Intervention		Total
Overall Antimicrobial Errors	n/N (%)	n/N (%)	*P* Value[a]	n/N (%)	*P* Value[a]	n/N (%)
Initial regimen with error, no. (%)	96/144 (66.7)	129/178 (72.5)	.26	129/176 (73.3)	.20	354/498 (71.1)
Any error during therapy	112/144 (77.8)	152/178 (85.4)	.08	156/176 (88.6)	.01	420/498 (84.3)
DOT with error / Total DOT (%)	292/612 (47.7)	461/862 (53.5)	.03	484/886 (54.6)	.01	1,237/2,360 (52.4)
Mean DOT with error per course[b]	Days	Days	*P* Value[c]	Days	*P* Value[c]	Days
Any error	2.1	2.6	.31	2.8	.15	2.5
Too narrow-spectrum	0.5	0.8	.07	0.4	.37	0.6
Safety issue	0.1	0.1	.35	0.1	.46	0.1
Antimicrobials not needed	0.6	0.8	.96	0.8	.64	0.8
Too broad-spectrum or complex	0.8	0.9	.43	1.4	.22	1.0

NOTE. DOT, antimicrobial days of therapy.
[a]χ^2 analysis of proportions relative to control.
[b]The mean DOT per antimicrobial course, regimens could have >1 error type.
[c]Negative binomial regression, test of intervention error days vs control, offset for total days of therapy.

Attendance at each of the 12 teaching sessions presented to the clinician education firm exceeded 80% of resident physicians and 50% of attending physicians. Infectious disease pharmacists reviewed 567 of 901 antimicrobial courses (62.9%) given in their firm, generating 202 (35.6%) recommendations for improvement, of which 129 (63.9% of the recommendations conveyed; 14.9% of total antimicrobial courses) were accepted. Recommendations that would reduce overall antimicrobial use (ie, to discontinue therapy or simplify redundant regimens) were made 94 times and were accepted 43 times.

Moreover, 1 or more antimicrobial use errors were identified in 420 of the 498 case vignettes reviewed (84.3%), including errors in the initial antimicrobial regimen in 354 (71.1%), and errors were identified during 1,237 (52.4%) of the 2,389 days of therapy reviewed (Table 2). The proportions of antimicrobial courses, course initiations, and treatment days with 1 or more errors at any time and the mean number of days per antimicrobial course during which specific error types were identified were higher in the education firm and in the pharmacist intervention firm than in the control firm. However, these differences held variable statistical significance (Table 2).

Weekly antimicrobial use rates for each of the 3 firms during the 24-week intervention period were highly variable and frequently overlapped, with no suggestion of reduced antimicrobial use in either intervention firm compared with the control firm (data not shown).

DISCUSSION

When concurrently deployed over 24 weeks in operationally equivalent inpatient medicine firms, neither clinician education nor prospective audit and feedback was associated with

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reductions in antimicrobial use errors or rates compared with the control. The limited reliability of our computer-assisted case vignette for error adjudication[4] is a potential explanation for this finding. In addition, nearly 80% of cases in which antimicrobial regimens were initiated in the emergency department (ED) where the interventions used in this study were not implemented. However, the proportions of antimicrobial courses begun in the ED were similar among the 3 firms (Table 2), and study outcomes were similar between courses begun in the ED and in the hospital (data not shown).

Our clinician education intervention had been effective in a public, long-term, acute-care hospital staffed by a small cadre of dedicated attending physicians and no residents.[2] In comparison, the current intervention presented a broader range of topics to much larger groups of attending and resident physicians who regularly rotated to other duties. Also, our ID pharmacists' recommendations for improvement were accepted for only 129 of the 901 antimicrobial regimens administered during the study period (14.9%), with only 43 (4.8%) of these leading to discontinuation of 1 or all drugs. This factor limited that intervention's impact on antimicrobial errors and use.

The median length of stay was significantly shorter in the control firm than in either of the intervention firms (4, 5 and 5 days, respectively; $P < .001$; Table 1), and the prevalence of lower respiratory tract infection was lower in control firm cases randomly selected for error adjudication than for cases selected from the intervention firms. Because shorter lengths of stay have been associated with improved quality of care, reduced medical complexity, and greater physician experience among cardiac[6] and general medical inpatients,[7] unmeasured differences in patient or physician characteristics could plausibly have confounded our findings. If true, a different randomization of the 3 firms could have led to a type 1 error.

Both informational interventions intended to improve antimicrobial prescribing generally (eg, clinician education and infection management guidelines), and interventions providing patient-level decision support such as audit and feedback and drug restrictions are essential to hospital antimicrobial stewardship.[1,8] However, our findings reinforce our hypothesis that the optimal scope[10] and intensity of these interventions remain poorly defined and difficult to measure. Clarification of this dynamic through additional research is needed to guide better integrated and better resourced antimicrobial stewardship.[8,9]

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SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2017.74

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