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Impact of an Antibiotic Restriction Program on Antibiotic Utilization in the Treatment of Community Acquired Pneumonia in a Veterans Affairs Medical Center

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Abstract

Purpose—The impact of an Antibiotic Restriction Program (ARP) on the patterns of antibiotic use in the treatment of community-acquired pneumonia (CAP) was examined. We also evaluated the association between the ARP and the length of hospital stay in regard to CAP treatment and cost savings associated with the implementation of the ARP.

Methods—A retrospective cohort study of patients admitted with CAP was conducted at two six-month periods, one prior to the ARP and one after the ARP. The health system's Computerized Patient Record System (CPRS) was used to obtain demographics, length of hospital stays, readmission rates, blood culture results, co–morbidities, antibiotic use, and durations of therapy. A total of 130 patients met the inclusion criteria for the final analyses. Average drug costs, employee salaries, and the cost of laboratory procedures were used to assess cost savings associated with the ARP.

Results—From a total of 132 antibiotics that were ordered to treat CAP in the pre-ARP period, 28 were restricted (21.2%). However, the number of restricted antibiotics ordered was significantly reduced to 12 out of 114 (10.2%) antibiotics ordered in the post-ARP period (P = 0.024). In post-ARP implementation, mean length of hospital stay was also significantly reduced from 7.6 to 5.8 days (P = 0.017), and although not statistically significant, 30-day readmission rates declined from 16.9% to 6.2% (P = 0.097). The ARP was also associated with $943 savings per patient treated for CAP.

Conclusions—In addition to a decrease in the antibiotic utilization and the mean length of hospital stay, the ARP may have yielded cost savings and reduced the readmission rates for those patients admitted and treated for CAP.

Keywords

Antibiotic restriction program; infection; antibiotics; hospital

Introduction

Antimicrobial agents are among the most frequently and inappropriately prescribed medications worldwide [1]. Broad evidence indicates that approximately 64% of all hospitalized patients receive antibiotic drugs during their hospital stay [2]. It has been

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Conflict of interest None.

reported that more than half of antibiotics may be inappropriately prescribed [3]. With the high volume of broad spectrum antibiotics prescribed, there may be severe consequences if simple management of prescribing habits are not initiated. Unnecessary use of antibiotics can contribute to the development of antimicrobial resistance leading to possible development of suprainfections [4,5], increased time and effort to care for these infections, and consequent increased health care costs [3,6]. Despite published guidelines, efforts to curtail unnecessary use of antimicrobial agents, surveys of individual hospitals have implicated frequent inadequacy in implementing these guidelines [6]. Medical centers have increasingly initiated programs to restrict the use of antibiotics [7]. However, the degree to which these programs can decrease healthcare costs and the development of resistance is uncertain [8,9].

In September 2005 the Michael E. DeBakey Veterans Affairs Medical Center (MEDVAMC) in Houston, Texas implemented an Antibiotic Restriction Program (ARP) to curtail the incidence of *Clostridium difficile*-associated disease (CDAD) [10-12] and to reduce the spread of multidrug resistance pathogens. A secondary objective was to reduce the costs associated with the excessive use of antibiotics throughout the medical center.

In order to evaluate the impact of the ARP on the antibiotic use, we specifically chose to study a subgroup of patients with community-acquired pneumonia (CAP), an inflammatory infection of the alveoli, distal airways, and interstitium of the lungs that requires antibiotic therapy and that has well-established risk factors, symptoms, and treatment options.

An estimated 2 to 5 million cases of CAP are diagnosed in the United States alone every year leading to more than one million inpatient hospitalizations and more than 50,000 deaths [13].

Inappropriate use of antibiotics to treat CAP has been associated with higher morbidity and mortality rates [13,14,15].

In this study, we compared the antibiotic utilization in the treatment of CAP before and after the initiation of the ARP and evaluated the association between the ARP and the length of hospital stay in regard to CAP treatment. We also examined potential cost savings associated with the implementation of the ARP.

Methods

IRB approval

This study was approved by the Institutional Review Boards (IRB) at both Baylor College of Medicine and the Research and Development (R&D) Committee at the MEDVAMC in Houston, Texas.

Site of study

The MEDVAMC is a teaching hospital with 375 hospital beds, a 40-bed Spinal Cord Injury Center, and a 120-bed transitional care unit. This state-of-the-art facility serves as the primary health care provider for almost 120,000 veterans in southeast Texas and logged more than 800,000 outpatient visits in the fiscal year 2007.

Description

Prior to the ARP implementation, restricted antibiotics were dispensed without prior approval from a member of the Infectious Diseases (ID) Team, which was appointed after the implementation of the ARP to oversee the appropriate prescription of these antibiotics. The ID Team included a multidisciplinary team of infectious diseases staff physicians and

clinical/staff pharmacists. However, after the implementation of the ARP, the ID Team's approval was necessary prior to dispensing and initiating a course of restricted antibiotic, which included: piperacillin/tazobactam, cefepime, ertapenem, imipenem, moxifloxacin, ciprofloxacin, clindamycin, linezolid, vancomycin, daptomycin, dalfopristin/quinupristin, liposomal amphotericin B, caspofungin, voriconazole, and itraconazole. Those patients that did not receive approval for the restricted antibiotics received formulary (unrestricted) antibiotics that included ampicllin, penicillin, aztreonam metronidazole, gentamicin, amikacin, nafcillin, cefazolin, and first line agents: ceftriaxone and ampicllin/sulbactam. Orders for restricted antibiotics were not honored by the intravenous (IV) room pharmacists without a verbal telephone approval by the ID attending physician or the ID Clinical Pharmacist. Prescribing physicians were required to contact the ID attending physician via a dedicated pager to obtain approval Monday through Friday, 8:00 am to 5:00 pm. The approval process included recommendations for dosage and duration of therapy. After 5:00 pm on weekdays and on weekends, restricted antibiotics were dispensed without approval until 8:00 AM on the next working day when the ID Clinical Pharmacy Specialist reviewed all after-hour and weekend orders for appropriateness. The Clinical Pharmacist could then approve or disapprove the continuation of antibiotic use after further discussions with the ID physician on the consulting service. If the drug was disapproved, the pharmacist called the prescribing physician to discuss the reasons for disapproval (e.g. possibility of use of formulary antibiotics, erroneous microbiology laboratory diagnosis, or no further indication for infection) and to make recommendations for alternative therapy. The prescribing physician then had the option of responding by requesting a formal consultation by the ID service.

Assessment of impact

The impact of the ARP was analyzed in this retrospective cohort study by comparing antibiotic utilization in a six months period prior to the implementation of the program and a six months period after the initiation of the program. The pre-intervention period was defined from October 2004 to March 2005. The ARP was initiated on September 2005, and the post intervention period was defined from October 2005 to March 2006. It was important that the two time frames contain identical months to avoid possible selection bias due to the likelihood of increased pneumonia infections during the winter months.

Average drug costs, employee salaries, and the cost of laboratory procedures were all combined and used to calculate the average bed-care cost per day per patient throughout the various medicine wards at the MEDVAMC. Most patients with CAP are admitted to a general medicine floor, with an average bed-care cost of about $539 per day.

Patient inclusion

Data for this single center, observational, retrospective, cohort study were obtained by the review of electronic patient medical records from patients who were admitted to the MEDVAMC with the diagnosis of CAP, defined as infectious pneumonia in patients who had not been hospitalized in the preceding two weeks and who had been admitted (< 48 hours) previously [13,16]. Patients were identified using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9 codes) [18] for pneumonia. We included patients in the study if they had fever, productive cough, chest pain, localized rales, wheezes on examination of the chest, and pulmonary infiltrate or consolidation on chest x–ray, assessed by the radiology report. Fever was defined as having a body temperature of ≥102°F (38.9°C) [17]. Patients already receiving antimicrobial treatment upon admission, those with prior antibiotic exposure for the past 30 days prior to admission and those with suspected hospital acquired (health care associated or aspiration pneumonia) were excluded. Furthermore, patients on antibiotic therapy with any interruption in the prescribed duration

and those with >1 prescription for the same antibiotic during the course of the study were included. None of the patients included in this study was ventilated. We did not include patients that were hospitalized in the intensive care units. For consistency of the reviews, only one ID clinical pharmacist performed the chart reviews. The health system's Computerized Patient Record System (CPRS) was used to obtain demographics as well as data on the length of hospital stays, readmission rates, blood culture results, co-morbidities, allergy status, antibiotic use (including dosage and frequency), and durations of therapy. Only those patients fulfilling the above inclusion criteria were included in the study (Figure1). Outcomes defined in this cohort study included change in the antibiotic utilization, change in the mean length of hospital stay, change in 30-day readmission rate (with an ICD-9 code for infection), and change in the health care cost post implementation of the ARP.

Statistical analyses

Statistical analyses were performed using Stata software version 8.2 for Windows (Stata, College Station, TX). Chi–square or Fisher's exact tests were performed to compare the frequencies of restricted antibiotics ordered and to compare baseline characteristics and frequencies of co-morbidities, bacteremia, and readmission rates between pre- and post-ARP. Student's *t*–tests were performed to compare the average age, mean number of co-morbidities, mean number of white blood cells (WBC), and mean length of hospital stay between the two groups. A level of significance was set at type I error of 5%.

Results

A total of 287 patients, 137 prior to ARP implementation and 150 post ARP implementation, were identified during the two established time frames using ICD - 9 codes for pneumonia. With the exclusion of patients with prior antibiotic therapy and those with nosocomial, aspiration, or health care associated pneumonia, 130 patients were included in the study. There were no statistically significant differences in the baseline characteristics between the two groups in this study (Table I). Table 2 displays the total number of antibiotics ordered during the two established time frames. Except with moxifloxacin, the use of restricted antibiotics declined post ARP implementation with the largest decline with clindamycin (from 8 to 2). The ARP was associated with a 57% reduction (n = 16) in the frequency of total restricted antibiotics administered to treat CAP. Prior to the ARP implementation, 28 of the 132 total antibiotics ordered were restricted agents (21%). Post-ARP implementation, however, the number of restricted antibiotics used was significantly reduced to 12 out of a total of 114 antibiotics (11%) ($P = 0.024$) considering that the total number antibiotics (restricted and non-restricted) to treat CAP was also reduced by 14%. A significant reduction in the mean length of stay for CAP treatment ($P = 0.017$) was also observed after the implementation of the ARP. Prior to the initiation of the program, the mean length of stay for patients being treated for CAP was 7.6 days compared to 5.8 days post implementation of the ARP. Although statistically insignificant ($P = 0.097$), readmission rates within 30 days of discharge with any ICD-9 code for infection were also reduced post-ARP implementation. For pre-ARP implementation, there were 11 patients (16.9%) with 30 day readmissions compared with 4 patients (6.2%) in the post-ARP implementation group. There were no significant statistical difference between the mean duration of antibiotic therapy pre-ARP (5.59 ± 3.2 days) vs. post-ARP (6.22 ± 3.0 days) (p-value=0.108; two-tailed Student's *t*-test).

With a reduction in length of stay from 7.6 to 5.8 days, the ARP program was associated with an average saving of about $943 per patient being treated for CAP. This number does not include the cost savings associated with a reduction in 30 day readmission rates.

Discussion

Infection control programs, although insufficient, may be important in controlling the spread of pathogens and limiting the development of antibiotic resistance [19,20]. Uncontrolled and widespread prescription of many antibiotics, particularly broad-spectrum agents, is believed to contribute to the development of antibiotic resistance [20]. Altering antibiotic prescription practices through guideline development, restricting antibiotic usage through ARPs, and narrowing the spectrum of antibiotics have all shown varying degrees of effectiveness [21]. However, some studies have indicated that antibiotic control programs may work where traditional infection control programs fail [22].

Some antibiotic control programs have slowed the emergence of antibiotic resistance [23-24], reduced the total number of antibiotics administered, and decreased health care cost [25-26], without compromising the patient quality of care. Other studies based on biomarkers have also shown promising results in reducing the number of antibiotic prescriptions [27]. In this study, we examined the impact of an ARP on the antibiotic use, length of hospital stay, and overall cost in patients with CAP and the complications from that disease without monitoring for antibiotic susceptibility patterns as a measured outcome at the MEDVAMC.

We observed significant reductions in the antibiotic utilization and the mean length of hospital stay when compared patients with CAP during a six-month period prior to the ARP implementation with patients with CAP in a six-month period following the ARP implementation. Although moxifloxacin is the only fluoroquinolone that was increased post APR, but not statistically significant (2-tailed p-value of 0.42), the total use of restricted antibiotics significantly declined post-ARP implementation with the largest decline with clindamycin. However, Infectious Diseases Society America (IDSA) and American Thoracic Society (ATS) guidelines recommend empiric monotherapy with a fluoroquinolone with enhanced activity against *S. pneumoniae* (gemifloxacin, levofloxacin, moxifloxacin) as the standard of care for community acquired pneumonia in patient with risk factors for drug resistant *S. pneumoniae* [6].

Furthermore, the total number of antibiotics (both restricted and unrestricted) used to treat CAP also declined 14% after the implementation of the ARP. The largest decrease in the utilization of clindamycin may have been due to the duplication of therapy in the selection of this antibiotic prior to the ARP program. With the increasing antibiotic resistance rates along with the development of supra-infections due to broad-spectrum antibiotic use, a significant reduction in antibiotic utilization may help to limit emergence of resistant pathogens [23,24].

Budget restrictions continue as healthcare costs increase. Pharmacy and medication costs are no exception. However, hospital costs are often reduced to a greater extent with a reduction in length of stay than by the expenditures of the antimicrobial agents themselves due to the high costs of bed-care cost for inpatients per day. Although it is difficult to determine to what extent the reduced mean length in hospital stay is attributed to the ARP itself, as infection control measures (such as hand washing and sanitization, utilization of protective clothing/masks/gloves, isolation of patients with MRSA, tuberculosis, or CDAD, etc.) may have influenced the outcomes of the study, the reduction in mean length of stay, not including 30 day readmissions, may have been associated with a yearly cost saving of $122,550 based on a $943 per patient savings over the six month study period after the implementation of the ARP. This number is solely in regard to the CAP treatment, and if extrapolated further to include other disease states, an even greater cost savings may have been observed.

Although in this study we examined the association between the implementation of the ARP and antibiotic utilization, duration of hospital stay, and possible cost savings, we did not assess any trends. Furthermore, the outcomes of the study may have been confounded due to several factors including the implementation of infection control measures, differences in the severity of the pneumonia, and an earlier switch to oral therapy. However, more stringent guidelines on dispensing restricted antibiotics may have lead to increased targeted therapy rather than empiric therapy after the implementation of the ARP, hence contributing to a possible shorter mean length of hospital stay.

Larger studies may be needed to further assess the associations between the outcomes in this study and the implementation of the ARP. In addition, studies investigating the possible changes in the multiresistant trends due to the implementation of the ARP may also be warranted.

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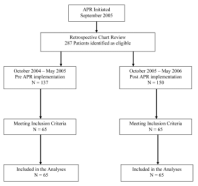

Figure 1.
Study Flow Chart

Table I

Baseline demographics and clinical status before and after the implementation of antibiotic restriction program (ARP)

Characteristic	Pre-intervention period (n=65)	Post-intervention Period (n=65)	*p*-value
Mean age, yrs (±SD)	69.7 (±14.21)	66.7 (±11.28)	0.180
Male sex (%)	62 (95.4)	64 (98.5)	0.619
Race no. (%)			
Caucasian	32 (49.2)	40 (61.5)	0.217
African American	26 (40.0)	21 (32.3)	0.465
Hispanic	6 (9.2)	4 (9.2)	0.744
Asian	1 (1.5)	0 (0)	1
Mean no. of co-morbidities (±SD)	1.52 (±0.13)	1.57 (±0.13)	0.803
COPD (%)	26 (40.0)	32 (49.2)	0.378
Diabetes mellitus (%)	23 (35.4)	19 (29.2)	0.574
Coronary artery disease (%)	11 (16.9)	21 (32.3)	0.066
Malignancy (%)	11 (16.9)	12 (18.5)	0.642
Alcoholism (%)	3 (4.6)	4 (6.15)	1
Liver disease (%)	7 (10.8)	6 (9.2)	1
Heart failure (%)	7 (10.8)	10 (15.4)	0.604
Renal disease (%)	7 (10.8)	3 (4.62)	0.324
Mortality (%)	4 (6.2)	2 (3.1)	0.680
Mean WBC (1000/mm^3) (±SD)	13.4 (±0.87)	19.5 (±4.99)	0.227
Bacteremia[1] **(%)**	35 (53.8)	31 (47.7)	0.599
***Citrobacter* ssp.**	1 (1.5)	0 (0)	1
Morganella morganii	1 (1.5)	0 (0)	1
Staphylococcus aureus	16 (24.6)	14 (21.5)	0.835
MRSA	2 (3.0)	1 (1.5)	1
Streptococcus pneumoniae	10 (15.4)	14 (21.5)	0.498
***Pseudomonas* ssp.**	3 (4.6)	0 (0)	0.244
Escherichia coli	1 (1.5)	0 (0)	1
Haemophilus influenzae	1 (1.5)	2 (3.1)	1
Chlamydia pneumoniae	0 (0)	1 (1.5)	1
Staphylococcus epidermidis	2 (3.1)	0 (0)	0.496
None (%)	30 (46.2)	34 (52.3)	0.599
Allergy status [2]	0	0	1

SD - Standard Deviation

[1] Bacteremia was defined as the presence ≥ 1 species grown from the participants' blood cultures

[2] Allergies to any of the restricted antibiotics

Table II

Antibiotic prescriptions, hospital stays, and readmissions before and after the implementation of ARP

Attribute	Pre-intervention period (n=65)	Post-intervention Period (n=65)	*p*-value
Mean length of stay, days (±SD)	7.55 (±0.6)	5.80 (±0.3)	0.017*
Readmission within 30 days (%)	11 (16.9)	4 (6.20)	0.097
Mean duration of antibiotic therapy, days (±SD)	5.59 (±3.2)	6.22 (±3.0)	0.108
No. of antibiotics used [a]	132	114	
No. of Restricted Antibiotics (%) [b]	28 (21.2)	12 (10.5)	0.024*
Moxifloxacin	2	4	
Cefepime	6	2	
Clindamycin	8	2	
Vancomycin	6	3	
Ertapenem	2	1	
Piperacillin/Tazobactam	3	0	
Linezolid	1	0	

[a] Total number of antibiotics ordered during the two periods

[b] Total number of restricted antibiotics and percentages ordered during the two periods

* Statistically significant with a type I error of 5%