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ORIGINAL RESEARCH

Antimicrobial Stewardship in Hospitalized Patients with Respiratory Infections: Ten-Year Experience from the Robley Rex Louisville VA Medical Center

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Abstract

Rationale: Antibiotic stewardship has been defined as coordinated interventions designed to improve and measure the appropriate use of antibiotic agents. Respiratory infections are the most common infectious reason for hospitalization in the United States. Therefore, one could extrapolate that respiratory infections are then also the most common reason for hospital antibiotic use and possess the highest potential for hospital antibiotic misuse. The primary objective of this article was to evaluate the role of antimicrobial stewardship on improving antibiotic use for respiratory infections in hospitalized patients on intravenous (IV) antibiotics at the Robley Rex Louisville VAMC over a 10-year period.
Methods: This was a retrospective review of the Robley Rex Louisville VAMC ASP Switch Therapy and Antimicrobial Review database. The study included all Robley Rex Louisville VAMC patients admitted to the hospital and placed on IV antibiotics between January 1st 2007 and December 31st 2016.
Results: Recommendations from an antimicrobial stewardship team (AST) improve hospital IV antibiotic use in respiratory infections to a level above 90%.
Conclusion: AST recommendations regarding antibiotic use for respiratory infections improve compliance with hospital guidelines. There is an ongoing role for antimicrobial stewardship programs overtime.

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Introduction

Antibiotic stewardship has been defined as coordinated interventions designed to improve and measure the appropriate use of antibiotic agents. This is accomplished by promoting the selection of the optimal antibiotic drug regimen including dosing, duration of therapy, and route of administration [1]. Successful implementation of antimicrobial stewardship programs has been associated with several benefits. These include improved patient outcomes, reduced adverse events including Clostridium difficile infection (CDI), decreased antibiotic resistance, and resource optimization such as decreased length of stay and cost of care. As a result of this, The Joint Commission, a United States not-for-profit organization dedicated to improving quality and effectiveness in healthcare, now requires an antimicrobial stewardship program (ASP) for hospital accreditation and certification. Additionally, in 2016, The Infectious Disease Society of America (IDSA) released national guidelines on implementing an ASP [2].

Respiratory infections are the most common infectious reason for hospitalization in the United States [3]. Therefore, one could extrapolate that respiratory infections are then also the most common reason for hospital antibiotic use and possess the highest potential for hospital antibiotic misuse. To address this concern, as well as antibiotic misuse as a whole, a program to improve antibiotic use was created at the Robley Rex Louisville VA Medical Center (VAMC) in 1990 [4]. The antimicrobial stewardship team (AST) was formed as part of the ASP, and members included infectious diseases pharmacists, infectious disease physicians, and a microbiologist. Hospital guidelines for the management of different infections were created by the AST and monthly reports were generated detailing hospital antibiotic use. In general, hospital guidelines reflect the implementation of national guidelines at the local level. Antibiotic use was determined to be either complaint or non-compliant with hospital guidelines. If antibiotic use was found to be compliant with hospital guidelines, no antibiotic recommendations were made. If antibiotic use was determined to be non-complaint with hospital guidelines, recommendations were made by the AST in the medical record. In the instances where recommendations were made, we then tracked if the recommendations were accepted or not accepted. To generate these reports a program

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was developed in Microsoft Access and entitled Switch Therapy and Antimicrobial Review [5].

The primary objective of this article was to evaluate the role of antimicrobial stewardship on improving antibiotic use for respiratory infections in hospitalized patients on intravenous (IV) antibiotics at the Robley Rex Louisville VAMC over a 10-year period. The secondary objectives included describing the most common 1) types of infections, 2) pathogens associated with respiratory infections, and 3) IV antibiotics used for respiratory infections with respective compliance with hospital guidelines before and after recommendations over the same 10-year period.

Materials and Methods

This was a retrospective review of the Robley Rex Louisville VAMC ASP Switch Therapy and Antimicrobial Review database. The study included all Robley Rex Louisville VAMC patients admitted to the hospital and placed on IV antibiotics between January 1st 2007 and December 31st 2016. This study was approved by the Robley Rex Louisville VAMC and informed consent was waived (IRB ID: 00049 Prom#: 0061). Data on each patient was collected by the antimicrobial stewardship pharmacist after they were alerted that the patient was receiving IV antibiotic treatment. The data collection included the following 15 variables; patient age, gender, admit date, discharge date, onset date and where infection was acquired, diagnosis, antibiotic name as well as antibiotic start and stop date, antibiotic indication and dose, culture results, and annotation indicating if antibiotic therapy was pathogen-directed or empiric and whether or not a patient was a candidate for oral switch therapy. This information was then used to evaluate antibiotic use.

The AST pharmacist gave real time feedback on intravenous antimicrobial orders and evaluated the compliance with local hospital antimicrobial guidelines. Areas of compliance that were reviewed consisted of the following; evaluation of the initial empiric regimen for appropriateness of spectrum of coverage, appropriateness of dose based on diagnosis, and potential for use of a less toxic antimicrobial agent. Continued review occurred throughout the patient's hospitalization following the initial evaluation and was based on clinical response and culture results with an evaluation of length of therapy and possibility for de-escalation of the empiric regimen. Prospective audit and feedback occurred with recommendations from the AST documented in the patient electronic record and in some cases through additional phone call or face to face discussion with the prescriber.

Study Definitions

Respiratory infections in this study were classified at the time of diagnosis in the database as either community-acquired pneumonia (CAP), healthcare-associated pneumonia (HCAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), acute exacerbation of chronic obstructive pulmonary disease (AECOPD), empyema, or lung abscess. The type of respiratory infection was defined by the primary physician's diagnosis as documented in the patient's record.

Infectious cases were defined as an infection requiring IV antibiotics upon or during a hospital admission. Each inpatient infection requiring IV antibiotics represented a case.

Antibiotic courses were defined by each individual IV antibiotic regimen a patient received during a particular infectious case. A single infectious case may have received numerous antibiotic courses.

The following 4 criteria were used to define when a patient should be considered a candidate for oral switch therapy: [1] cough and shortness of breath improving, [2] afebrile (temperature, <37.8°C) for at least 8 hours, [3] white blood cell count normalizing, and [4] adequate oral intake and gastrointestinal tract absorption. A patient who was able to take food by mouth without evidence of diarrhea or malnutrition was considered to have adequate oral intake and gastrointestinal tract absorption.

Antibiotic compliance was assessed daily during admission regarding appropriateness of empiric or pathogen directed therapy, dosing, and duration.

Statistical Analysis

Descriptive statistics were performed. Data was reported as frequencies (n) and percentages (%). The percent compliance before and after AST recommendation was calculated by dividing the total number of compliant evaluations and the total number of compliant opportunities. Line graphs were produced to display changes in compliance over time. Statistical analysis was performed with R version 3.3.2 [6].

Results

Antibiotic compliance with hospital guidelines before and after the AST recommendations are demonstrated by year for the most prominent respiratory infections including CAP, HCAP, HAP, as well as all respiratory infections combined in **Figures 1-4**.

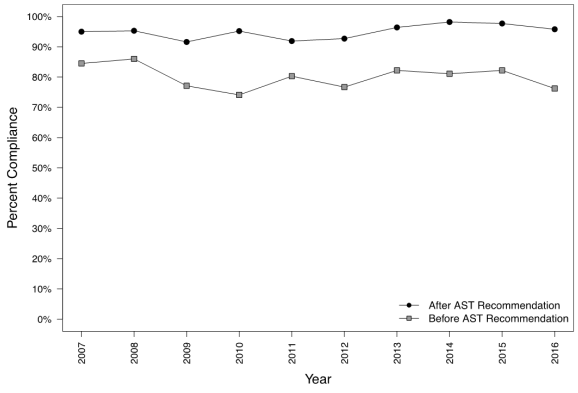

Fig. 1. Antibiotic compliance with hospital guidelines for community-acquired pneumonia before and after antimicrobial stewardship team (AST) recommendations.

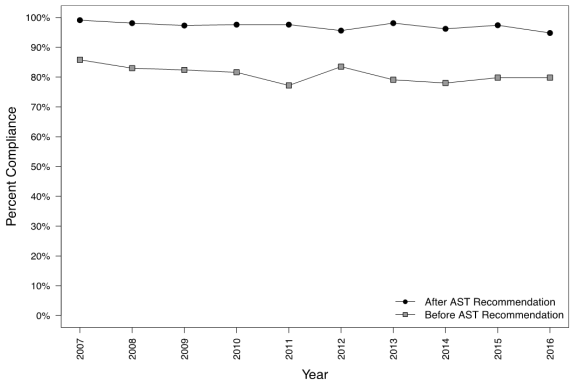

Fig. 2. Antibiotic compliance with hospital guidelines for healthcare-associated pneumonia before and after antimicrobial stewardship team (AST) recommendations.

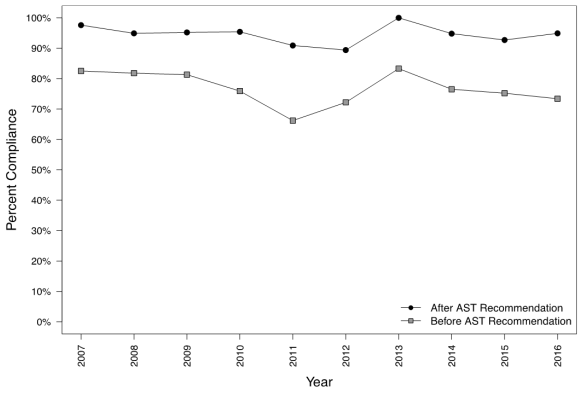

Fig. 3. Antibiotic compliance with hospital guidelines for hospital-acquired pneumonia before and after antimicrobial stewardship team (AST) recommendations.

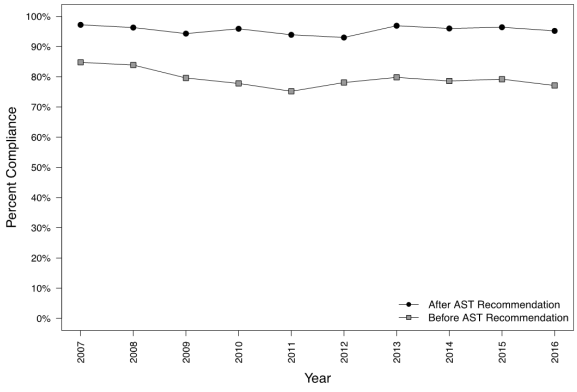

Fig. 4. Antibiotic compliance with hospital guidelines for all respiratory infections before and after antimicrobial stewardship team (AST) recommendations.

A total of 18,932 IV antibiotic courses were reviewed by the AST at the Robley Rex Louisville VAMC during the 10-year time period. This was representative of 5,928 infectous cases. Respiratory infections accounted for 6,882IV antibiotic courses used in 2,133 infectious. The total of IV antibiotic courses and infectious cases reviewed by the AST for respiratory infections are listed by infection type in **Table 1**.

Table 1. Respiratory Infections and Antibiotic Courses

Diagnosis	Infections (n=2,133)	Antibiotic Courses (n=6,882)
CAP	778 (36)	2143 (31)
HCAP	580 (27)	2092 (30)
HAP	465 (22)	1771 (26)
AECOPD	186 (9)	280 (4)
Empyema	69 (3)	374 (5)
VAP	50 (2)	208 (3)
Lung Abscess	5 (0)	14 (0)

CAP: community-acquired pneumonia; **HCAP:** healthcare-associated pneumonia; **HAP:** hospital-acquired pneumonia; **AECOPD:** acute exacerbation of chronic obstructive pulmonary disease; **VAP:** ventilator-associated pneumonia

The complete list of IV antibiotic courses and infectious cases reviewed by the AST for all other types of infections are listed by infection type in **Table 2**.

Table 2. Other Infections and Antibiotic Courses

Diagnosis	Infections	Antibiotic Courses
Bone and Joint Infections	**517 (14)**	**2475 (21)**
Osteomyelitis	453 (88)	2285 (92)
Septic Joint	64 (12)	190 (8)
Central Nervous System Infections	**63 (2)**	**189 (2)**
Meningitis	50 (79)	151 (80)
Encephalitis	9 (14)	26 (14)
Syphilis	2 (3)	2 (1)
Brain Abscess	1 (2)	4 (2)
Ventriculoperitoneal Shunt Infection	1 (2)	6 (3)
Endovascular Infections	**293 (8)**	**1213 (10)**
Intravenous Catheter Infection	153 (52)	585 (48)
Endocarditis	108 (37)	428 (35)
Vascular graft	32 (11)	200 (16)
Intra-abdominal Infections	**508 (13)**	**1393 (12)**
Peritonitis	148 (29)	478 (34)
Cholecystitis	116 (23)	253 (18)
Intra-abdominal Abscess	97 (19)	375 (27)
C. difficile Colitis	89 (18)	138 (10)
Diverticulitis	38 (7)	93 (7)
Pancreatitis	20 (4)	56 (4)
Skin and Soft Tissue Infections	**706 (19)**	**2238 (19)**
Cellulitis	540 (76)	1587 (71)
Surgical Wound Infection	72 (10)	236 (11)
Diabetic Foot Infection	54 (8)	223 (10)
Perirectal Abscess	24 (3)	55 (2)
Necrotizing fasciitis	13 (2)	118 (5)
Myonecrosis	3 (0)	19 (1)
Urinary Tract Infections	**971 (26)**	**2209 (18)**
Pyelonephritis	713 (73)	1853 (84)
Cystitis	258 (27)	356 (16)
Other Infections	**737 (19)**	**2333 (19)**

The most common respiratory pathogens identified in our hospital are listed in **Table 3**.

Table 3. Most Frequent Organisms by Type of Pneumonia

CAP	n (%)	HAP	n (%)	HCAP	n (%)
S. pneumonia	73 (27)	*MRSA*†	85 (28)	*MRSA*†	77 (27)
H. influenzae	32 (12)	*Pseudomonas*	40 (13)	*Pseudomonas*	45 (16)
MSSA	31 (11)	*Klebsiella*	33 (11)	*MSSA*‡	33 (11)
MRSA	24 (9)	*Enterobacter*	21 (7)	*S. pneumoniae*	25 (9)
Pseudomonas	18 (7)	*E. coli*	18 (6)	*E. coli*	24 (8)
Streptococcus other	16 (6)	*MSSA*‡	18 (6)	*H. influenzae*	13 (4)
Klebsiella	13 (5)	*H. influenzae*	15 (5)	*Proteus*	12 (4)
E. coli	9 (3)	*S. pneumoniae*	10 (3)	*Klebsiella*	11 (4)
Moraxella	6 (2)	*Acinetobacter*	6 (2)	*Enterobacter*	8 (3)

†**MSSA:** methicillin-susceptible *Staphylococcus aureus*; ‡**MRSA:** methicillin-resistant *Staphylococcus aureus*

The most frequently used IV antibiotics for respiratory infections in our hospital as well as compliance with hospital guidelines before and after recommendations are listed in **Table 4**.

Table 4. Most frequently used antibiotics for respiratory infections with respective compliance with hospital guidelines.

Community Acquired Pneumonia			
Antibiotic Given	**n (%)**	**Compliance Before†**	**Compliance After†**
Ceftriaxone	428 (21)	91	98
Moxifloxacin	300 (15)	83	97
Azithromycin	272 (13)	89	99
Vancomycin	272 (13)	63	91
Levofloxacin	240 (21)	79	96
Piperacillin/Tazobactam	146 (7)	53	80
Clindamycin	57 (3)	75	91
Ampicillin/Sulbactam	53(3)	93	96
Cefepime	39 (2)	77	97
Ciprofloxacin	29 (1)	72	97
Hospital Acquired Pneumonia			
Antibiotic Given	**n (%)**	**Compliance Before†**	**Compliance After†**
Vancomycin	468 (26)	77	95
Piperacillin/Tazobactam	368 (21)	81	97
Levofloxacin	157 (9)	76	94
Ciprofloxacin	108 (6)	77	95
Cefepime	93 (5)	88	99
Meropenem	89 (5)	83	92
Imipenem/Cilastin	78 (4)	74	95
Linezolid	73 (4)	85	97
Moxifloxacin	41 (2)	63	95
Ceftriaxone	38 (2)	50	87
Healthcare Associated Pneumonia			
Antibiotic Given	**n (%)**	**Compliance Before†**	**Compliance After†**
Vancomycin	653 (31)	77	96
Piperacillin/Tazobactam	431 (21)	83	98
Levofloxacin	335 (16)	81	95
Cefepime	106 (5)	86	99
Meropenem	87 (4)	83	95
Moxifloxacin	80 (4)	81	99
Ceftriaxone	71 (3)	80	99
Ciprofloxacin	50 (2)	78	100
Azithromycin	45 (2)	89	96
Imipenem/Cilastin	38 (2)	61	97

†Percent compliance

Reasons for non-compliance by our evaluation included inappropriate empiric or pathogen directed antimicrobial therapy regarding agent, dose, duration, or toxicity.

Discussion

The results of this study demonstrate that recommendations from an AST regarding antibiotic use for respiratory infections improve compliance with hospital guidelines. This is consistent with other studies that have demonstrated improvement in antibiotic use after intervention from an ASP for other types of infection such as skin and soft tissue infections [7,8]. However, while our study demonstrated improved compliance with hospital guidelines after AST recommendations each year, the data did not demonstrate an overall improvement in antibiotic use before recommendations over time as one may expect with continuous audit and feedback. This is can be explained by the fact that our institution is a teaching hospital. Residents rotate through regulary providing an essentially continual influx of new learners.

Lack of improvement in antibiotic use over time prior to guideline based recommendations, highlights the importance of and role for an ongoing antimicrobial stewardship presence. This suggests that not only developing guidelines but forming and supporting an AST to assist with implementation of the guidelines on a local level is essential. Local implemenation of national guidelines is an area that has been shown to need improvement [9]. Our study suggests that an AST may help to bridge that gap.

Going forward, in the absence of uniform national guidelines, the creation of locally based hospital guidelines for a particular infection type via an ASP may further promote appropriate antibiotic use where it would otherwise be lacking. For example, at the Robley Rex Louisville VAMC we are developing local guidelines for hospitalized patients with COPD exacerbations, a common reason for hospitalization for which national guidelines are not yet established.

Lastly, our study reinforced that respiratory infections are a common reason for hospitalization and administration of IV antibiotics. In fact, our results demonstrated that overall, respiratory infections were the most common reason for hospitalization requiring IV antibiotics at the Robley Rex Louisville VAMC. As one might expect, the most common etiology for CAP was *Streptococcus pneumoniae*, and the most common pathogens causing healthcare-associated respiratory tract infections included MRSA and *Pseudomonas aeruginosa*. This exemplifies the reason for differing guideline recommendations regarding empiric therapy for respiratory infections depending on the type of infection and patient risk factors. Illustrating the effectiveness of antimicrobial stewarship, the most commonly used IV antibiotics for those infections in this study were appropriate.

This study had several limitations including that is was a retrospective review with no utcome data. Without outcome data it is impossible to say that improved antibiotic use was associated with improved patient outcomes. Also, because this study took place in a teaching hospital we cannot assume that the results are generalizable to all inpatient hospital settings.

In conclusion, there is an ongoing role for ASP's and antibiotic guidance over time as it does appear to improve antibiotic use. Following national trends, the most common reasons for hospitalization requiring IV antibiotics were respiratory-associated infections.

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