REPORT OF THE BOARD OF TRUSTEES
B of T Report 20-A-12
Subject: Enhancing Antibiotic Stewardship to Improve Patient Outcomes in the Inpatient Setting (Resolution 226-A-11)
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Referred to:
Reference Committee E (Frederick R. Ridge, Jr., MD, Chair)

At the 2011 Annual Meeting, the House of Delegates (HOD) referred Resolution 226-A-11 introduced by the Infectious Diseases Society of America (IDSA). The resolution asked our American Medical Association (AMA): (1) to urge the Centers for Medicare & Medicaid Services (CMS) to require antimicrobial stewardship and infection prevention programs, which are overseen by qualified physicians, as Medicare and Medicaid Conditions of Participation for health care facilities; (2) to urge CMS to allot a portion of the payment withhold used to fund the Hospital Value-Based Purchasing Program to reimburse health care facilities for implementation and maintenance of antimicrobial stewardship and infection prevention programs; (3) to urge CMS to allow flexibility in the establishment of such programs so that adherence to national requirements does not limit the ability of providers to design programs based on local variables, such as facility size, and to address local antimicrobial stewardship and infection prevention challenges; and (4) regardless of Medicare and Medicaid Conditions of Participation, to state that it is the fiduciary duty of each health care facility's governing body to promote and support robust antimicrobial stewardship and infection prevention programs as critical components of assuring safe patient care.

INTRODUCTION

Antibiotic resistance has continued to increase even as pharmaceutical companies are reducing their research and development efforts to create new antibiotic agents that have novel mechanisms of action. The impact of antibiotic resistance on patient mortality, length of hospitalization, and cost to the healthcare system is substantial, and it is now well documented that inappropriate use of antibiotics is a primary driver of resistance in bacteria. In the IDSA/Society for Healthcare Epidemiology of America (SHEA) guidelines for antibiotic stewardship programs, it is reported that up to 50% of inpatient antimicrobial use is inappropriate.1 Inappropriate use includes: (1) the prescribing of antibiotics when they are not indicated; (2) continuation of antibiotic therapy when no longer necessary; (3) incorrect dosing; (4) use of broad spectrum agents to treat very susceptible pathogens; and (5) use of the wrong antibiotic to treat an infection. Antibiotic exposure is also the single most important risk factor for the development of Clostridium difficile associated disease (CDAD), and the emergence of the NAP-1/BI or "epidemic" strain of C. difficile has intensified the risks associated with antibiotic exposure.2

This report is not a systematic review of the literature on antibiotic stewardship, which is the responsible use of antibiotics by healthcare professionals, particularly with respect to selection of the most appropriate agent, its dosage, its duration of use, and its route of administration. Instead, it provides an introduction to the concept of antibiotic stewardship within a healthcare facility and

describes recommended elements for such an antibiotic stewardship program. The report also discusses process-related and outcome-related measurements that can be used to evaluate antibiotic stewardship programs. Recommendations supporting increased use of antibiotic stewardship programs are proposed. Significantly, these recommendations suggest that before unfunded mandates imposing new regulatory burdens are used to improve utilization of antibiotic stewardship programs, systematic adoption of voluntary approaches should be explored.

The continuing problem of antibiotic resistance

Antibiotic resistance remains a growing healthcare problem that kills tens of thousands of people in the United States and across the world each year, significantly increasing the length of hospital stays and increasing costs to the healthcare system.[3] Beyond the implications of antibiotic exposure for CDAD, a meta-analysis indicates a significant increase in mortality associated with methicillin resistant Staphylococcus aureus (MRSA) bacteremia compared to methicillin-susceptible S. aureus (MSSA) bacteremia.[4] Additionally, studies indicate that methicillin resistance in Staphylococcus aureus has been associated with significant increases in length of hospitalization and hospital costs.[5] This is true not just for MRSA but also for vancomycin resistant enterococci, penicillin- and cephalosporin-resistant Strepotococcus pneumoniae, and also with various resistant gram-negative organisms such as Enterobacter spp. and Klebsiella.[6] In 1995, the Congressional Office of Technology Assessment calculated that resistance in just six types of bacteria increased hospital treatment costs by $1.3 billion.[7] Resistance continues to develop despite significant efforts by not only the AMA, but also by many leading national healthcare organizations and by federal agencies, to institute appropriate antibiotic use guidelines. A significant percentage of inappropriate use of antibiotics occurs in animal agriculture,[8] and the AMA has remained very active in efforts to rein in inappropriate use of antibiotics in animal agriculture, consistent with existing AMA HOD Policy H-440.895, Antimicrobial Use and Resistance (AMA Policy Database). The negative outcomes of resistance are particularly harsh on vulnerable populations, such as the pediatric and the older adult population, those who are immunocompromised, and those with chronic health conditions. Young children and infants are at increased risk of developing extraintestinal focal disease and disseminated disease from enteric pathogens, and when the bacteria are multi-drug resistant, there is increased risk of adverse outcomes, including fatality.[9]

Pneumonia is the major infection-related cause of death in older persons, and urinary tract infection is the most common bacterial infection seen in geriatric patients.[10] The emergence of highly resistant pathogens among geriatric patients for which no effective antibiotics will be available will result in significant morbidity and mortality in this vulnerable population.[10] In those infected with HIV, bacterial pneumonia infections are particularly common, and when caused by penicillin resistant bacteria, the mortality rate for AIDS patients is approximately 7.8 times higher compared to infections caused by bacteria that are fully or even partially sensitive to penicillin.[11] The loss of effective antibiotics as a result of resistance will have far-reaching implications for the treatment of bacterial infections in these vulnerable populations.

It is important to recognize that 53% of antibiotic use occurs in the outpatient setting.[12] Additionally, data from a recent meta-analysis by Costelloe, et al. indicate that antibiotics prescribed to an individual in primary care were consistently found to be associated with the development of resistance to those antibiotics in urinary and respiratory bacteria in that individual.[13] Thus, while not a topic of this report, appropriate management of antibiotic use within the primary care outpatient setting is also important.

Finally, major pharmaceutical companies are losing interest in the antibiotics market because these drugs simply are not as profitable as drugs that treat chronic conditions and lifestyle issues. Additionally, drug research and development is expensive and risky. In 2002, out of 89 new drugs, no new antibiotics were approved. Thus, IDSA has issued a monograph titled “Bad Bugs, No Drugs” highlighting in detail the issues that are causing the pharmaceutical pipeline for new antibiotics to dry up. [14] This monograph was then followed by a call to action titled the “10 x ‘20” initiative to spur development of new antibiotics.[15] The AMA has endorsed these two IDSA initiatives to incentivize research and development within major pharmaceutical companies.

What is an antibiotic stewardship program?

Antibiotic stewardship is the multi-faceted approach to optimize antibiotic prescribing. In particular, an antibiotic stewardship program should encompass components such as policy, guidelines, surveillance, education, epidemiology of current resistance, and process measurement. Such a multidisciplinary approach requires the participation of all members within the healthcare facility including infection control staff, pharmacists, physicians, administrators, laboratory technicians, a member of the IT department, nurses, and other allied health professionals. A successful antibiotic stewardship program monitors and directs antimicrobial use, providing a standard, evidence-based approach to judicious antibiotic use in a healthcare facility.[1, 16]

More specifically, the goals of an antibiotic stewardship program are to:

• Optimize dose, antimicrobial selection and duration of treatment;
• Prevent and/or reduce the emergence of antibiotic resistance;
• Reduce adverse drug events (including CDAD);
• Reduce length of patient stay;
• Reduce healthcare costs; and
• Reduce patient morbidity and mortality.

Thus antibiotic stewardship programs include not only limiting inappropriate use, they also optimize antibiotic selection, dosing, route of administration, and length of treatment in order to limit unintended consequences (resistance, cost, adverse reactions) while improving patient outcomes and patient safety.[1, 16] According to the IDSA/SHEA guidelines for developing an institutional program to enhance antibiotic stewardship, there are 11 recommendations that should be considered to create a comprehensive antibiotic stewardship program. Depending on the needs and resources of the institution, as well as the epidemiology of local resistance, elements can be chosen from these recommendations.[1] These 11 recommendations are summarized in the appendix of this report. Of increasing interest, and not mentioned in the IDSA/SHEA recommendations, is the use of new rapid molecular diagnostic testing that would allow earlier identification of the causative pathogen, leading to improved decision making with regards to antibiotic therapy.[17]

Measuring antibiotic stewardship programs

It is important to recognize that there are two ways that the success of antibiotic stewardship programs can be measured: by process measures, which are easier to accomplish; or by outcome measures, which are far more difficult.[17] As is often the case, once a process is established at an institution and process measurement is in place, the incentive to actually measure the impact on health outcomes is diminished. Additionally, measuring outcomes such as reduction in the incidence of specific types of infections, reduction in the emergence of antibiotic resistance, or other similar patient-focused health outcomes, is very time consuming and often confounded by other environmental factors. Thus, data remain limited on these outcome measurements.

Process outcomes on the other hand, are fairly easy to measure, and much data exist on the steps necessary to implement a successful antibiotic stewardship program. Three different outcome measures are summarized below, all of which are associated with improving the quality of patient care and patient outcomes.

Impact of antibiotic stewardship programs on antibiotic resistance

Data remain limited on the impact of antibiotic stewardship programs on reducing the emergence of resistance. There have been several studies that have shown reduction in resistance in gram negative bacteria following the implementation of antibiotic stewardship programs. Buising, et al. describe a program featuring the implementation of a computerized antimicrobial approval system or ordering restricted antibiotics, limiting duration of dispensing, and facilitating communication with pharmacy, infection control staff, and prescribers. This program improved susceptibility of Pseudomonas to many antibiotics studied.[18] Rahal et al. noted that a 80.1% reduction in hospital wide cephalosporin use correlated with a 44% reduction in the incidence of ceftazidime-resistant Klebsiella infection and colonization throughout the medical center.[19] Bantar and coworkers, using a four-intervention, multidisciplinary approach, demonstrated significant reduction in resistance to different agents in Proteus, Enterobacter cloacae, and Pseudomonas.[20] Finally, Pakyz and colleagues demonstrated in a consortium of 22 university teaching hospitals that carbapenem resistant P. aeruginosa incidence was lower in hospitals that restricted carbapenem use than those that did not.[21] There are also limited data with respect to gram positive organisms. The Buising study described above showed improved susceptibility of S. aureus to methicillin when an antibiotic stewardship program was implemented.[18] Cook, et al. showed that active monitoring of oral and IV ciprofloxacin use led to a 31% reduction in ciprofloxacin use and was significantly correlated with an almost 6% reduction in prevalence of MRSA.[22] The Bantar study detailed above demonstrated a significant reduction in the prevalence of MRSA following implementation of the stewardship program.[20]

Impact of antibiotic stewardship programs on cost

The implementation of antibiotic stewardship programs that successfully reduce antibiotic misuse corresponds with decreased cost to the institution by an average of $200,000 to $900,000, without a negative impact on the quality of clinical care.[1,16] For example, Maswoswe and coworkers demonstrated that, in a 580-bed, county teaching hospital, restricting antibiotic use resulted in a savings of more than $300,235 over a nine-month period.[23] Agwu et al. utilizing a web-based program to provide automated clinical decision support and facilitate approval and real-time communication with prescribers related to antibiotics, showed a reduction of $370,069 in projected, annual cost associated with antimicrobial use, and an 11.6% reduction in doses of restricted antibiotics over one year.[24] These direct savings likely pale when compared to potential decreases in overall healthcare costs that can be achieved with effective implementation of an antibiotic stewardship program. While indirect cost savings are more difficult to document, extrapolation is possible. Since reduced antibiotic resistance, adverse outcomes, and secondary unintended infections are linked with increased patient mortality and morbidity, longer hospital stays, and increased healthcare costs,[6, 25- 26] proper antibiotic stewardship should optimize patient care and consequently lower these costs.

Indeed, a large study in a tertiary care academic center estimated more than $4.25 million in total healthcare savings over one year when an antibiotic stewardship program using both preauthorization and prospective audit and feedback was implemented.[17]

In a University of Maryland study, implementation of one antibiotic stewardship program saved a total of $17 million over 8 years at one institution, and when the program was discontinued, antibiotic costs increased over $1 million in the first year (an increase of 23 percent) and continued to increase the following year. [27] Finally, a study of cost-effectiveness of antibiotic stewardship on the reduction of morbidity and mortality associated with nosocomial bacteremia demonstrated a cost of $2,367 per quality-adjusted life year (QALY) gained for the stewardship interventions. This compares favorably with many currently funded healthcare interventions and services.[28]

Impact of antibiotic stewardship programs on appropriate antibiotic use

Antimicrobial stewardship programs have been shown to increase the likelihood that hospitalized patients receive the right antibiotic, at the right dose, at the right time, and for the right duration.[1, 16]

As a result, there is reduced mortality, reduced risks of CDAD, reduced length of hospital stays, and reduced overall antimicrobial resistance within the facility, which will also contribute to reduced costs for the institution. One arena where appropriate and targeted use of antibiotics has been successful is in CDAD. For example, Valiquette and coworkers demonstrated in a secondary/tertiary-care hospital that the implementation of an antimicrobial stewardship program to optimize antibiotic usage resulted in a 60% decrease in the incidence of CDAD.[29]

Additionally, studies indicate that optimization of antibiotic use also optimizes patient safety. Thus, a study by Singh et al. showed that an antibiotic stewardship program reduced overtreatment with antibiotics of patients with pulmonary infiltrates in the ICU.[30] This resulted in significant reductions in antibiotic resistance and superinfections in the patients. Fishman and colleagues have reported that an antibiotic stewardship program implemented at the Hospital of the University of Pennsylvania resulted in a significant increase in appropriate therapy that correlated with a significant increase in
cure rates and a significant decrease in treatment failures.[31] Finally, a meta-analysis of 14 studies of the application of antimicrobial stewardship principles to the management of community-acquired pneumonia showed improvement in physician awareness of guidelines, improved appropriate antibiotic use and a reduction in unnecessary prescribing. This improved utilization led to decreased 30-day mortality and in-hospital mortality rates, reduced length of hospital stay, reduced treatment failure rates and reduced healthcare costs.[32]

Policy Statement from the IDSA, SHEA, and the Pediatric Infectious Diseases Society (PIDS)

In April 2012, the IDSA, SHEA, and PIDS released a joint policy statement with regards to antibiotic stewardship programs.[33] The five recommendations from this policy statement are presented here.

1. Antimicrobial stewardship programs should be required through regulatory mechanisms;
2. Antimicrobial stewardship should be monitored in ambulatory healthcare settings;
3. Education about antimicrobial resistance and antimicrobial stewardship must be accomplished;
4. Antimicrobial use data should be collected and readily available for both inpatient and outpatient settings; and
5. Research on antimicrobial stewardship is needed.

CONCLUSION

Well designed and properly implemented antibiotic stewardship programs will reduce inappropriate use of antibiotics, can optimize outcomes for patients, and may preserve the effectiveness of currently available antibiotics. Additionally, an effective program will generally reduce overall healthcare costs for the facility.

More data are still needed to confirm the impact of antibiotic stewardship programs on different patient-centered outcomes in order to provide impetus for continued implementation of effective antibiotic stewardship programs. As a result of the multifaceted approaches of an antibiotic stewardship program, individual medical facilities will need to adapt more standardized recommendations to fit with the needs of their institution.

RECOMMENDATIONS

The Board of Trustees recommends that the following be adopted in lieu of Resolution 226-A-11 and the remainder of this report be filed:

1. That our American Medical Association (AMA) support antimicrobial stewardship programs, which should be overseen by qualified physicians, as an effective way to ensure appropriate antibiotic use, to optimize patient outcomes, and to reduce overall healthcare costs for a healthcare facility. (New HOD Policy)
2. That our AMA support the development of antibiotic stewardship programs that allow flexibility so that adherence to national requirements does not limit the ability of providers to design programs based on local variables, such as healthcare facility size, and to address local antimicrobial stewardship and infection prevention challenges. (New HOD Policy)
3. That our AMA urge each healthcare facility's governing body to promote and support robust antimicrobial stewardship and infection prevention programs as critical components of assuring safe patient care. (Directive to Take Action)
4. That our AMA support continued research into the impact of antibiotic stewardship programs on process outcomes, and encourage increased research on the impact of such programs on patient-centered outcomes. (New HOD Policy)

Fiscal Note: Less than $500.

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