American Journal of Infection Control 44 (2016) 1381-4

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Practice Forum

Introducing an antibiotic stewardship program in a humanitarian surgical hospital

Naina Bhalla MD [a], Nagham Hussein MD [b], Maha Atari BSc [b], Rasheed M. Fakhri MD [b], Chiara Lepora MD [a], Nadia Walsh RN [a], Sara E. Cosgrove MD [c], Richard A. Murphy MD, MPH [d,*]

[a] *Médecins Sans Frontières, Paris, France*
[b] *Doctors Without Borders, Amman, Jordan*
[c] *Johns Hopkins University School of Medicine, Baltimore, MD*
[d] *Division of Infectious Diseases, Los Angeles Biomedical Research Institute at Harbor–UCLA Medical Center, Torrance, CA*

Key Words:
Antimicrobial stewardship
antibiotic resistance
war surgery
trauma surgery
chronic osteomyelitis
reconstructive surgery
bacterial infections
low- and middle-income countries
developing countries
resource-limited settings

Antibiotic stewardship program (ASP) implementation in humanitarian settings is a new endeavor. Doctors Without Borders/Médecins Sans Frontières introduced an ASP within a hospital in Amman, Jordan, where patients from Iraq, Syria, and Yemen with chronic, often multidrug-resistant, infections related to war are managed. Antibiotics were reviewed, and real-time recommendations were made to optimize choice, dose, duration, and route by a small team. Over the first year of implementation, acceptance of the ASP's recommendations improved. When compared with the year prior to implementation, antibiotic cost in 2014 declined considerably from approximately $252,077 (average, $21,006/month) to <$159,948 ($13,329/month), and a reduction in use of broad-spectrum agents was observed. An ASP in a humanitarian surgical hospital proved acceptable and effective, reducing antibiotic expenditures and use of broad-spectrum agents.

Antibiotic resistance is growing in low- and middle-income countries (LMICs), and antibiotic overuse is considered the major driver. Antibiotic stewardship programs (ASPs) aim to promote more optimal antibiotic use in hospitalized patients with some providing real-time support for better prescribing.[1] ASPs have been shown, in high-income settings, to reduce emergence of antibiotic resistance in hospitals, lower costs, and improve care quality, but few ASPs have been established in LMICs.[2-4]

In 2006, Médecins Sans Frontières (MSF) opened a surgical program in Amman, Jordan, for Iraqi victims of war, with a focus on surgical management of injury that could not be definitively managed in Iraq. Prior to arrival for definitive care, the median time since initial injury was 19 months, and the median number of prior surgical procedures was 4 (interquartile range, 2-6). The surgical program grew to include patients from Syria and Yemen.[5] Existing orthopedic infection was found to be common in patients at program entry, and the prevalence of multidrug-resistant pathogens was high.[6,7]

To optimize management of chronic trauma-related infections, a medical-surgical strategy was established, a collaboration with a local microbiology laboratory was developed, and broad-spectrum antibiotics, including glycopeptides (vancomycin), extended-spectrum aminoglycosides (amikacin), and carbapenems (imipenem), active against multidrug-resistant strains, were introduced for the first time in an MSF hospital. However, in the absence of support for optimized prescribing practices, broad-spectrum antibiotic use increased, opportunities for parenteral to oral antibiotic transitions were missed, unnecessarily postsurgical antibiotic prophylaxis was sometimes given, and as a result overall program costs escalated.

LOCAL SETTING

The MSF surgical program typically admits 50 patients per month, with most patients originating from Syria, Iraq, and Yemen.

* Address correspondence to Richard A. Murphy, MD, Division of Infectious Diseases, Harbor-UCLA Medical Center, 1000 W Carson St, Box 466, Torrance, CA 90509.
E-mail address: rmurphy@labiomed.org (R.A. Murphy).

Conflicts of Interest: None to report.

Additional Information: The protocols of the Médecins Sans Frontières (MSF) Amman surgical project were approved within the framework of a formal agreement between MSF, the Jordanian Red Crescent, and the Jordanian Ministry of Health. The present study involved the analysis of data collected for monitoring and evaluation and therefore satisfied the criteria for reports using routinely collected programmatic data, set by the MSF independent Ethics Review Board in Geneva, Switzerland.

0196-6553/
http://dx.doi.org/10.1016/j.ajic.2016.03.036

On average, monthly there are 140 surgeries, 120 inpatient admissions, and 800 outpatient consultations; there are approximately 220 patients in Amman under management at any given time. On project admission, all patients with suspected chronic osteomyelitis (amounting to >50% of admitted patients) based on prevalent sinus tract discharge from bone or chronic nonunion undergo surgical exploration and debridement, at which time intraoperative cultures are routinely obtained. Among patients with infection at admission, the most common pathogens were cephalosporin-resistant *Enterobacteriaceae* or methicillin-resistant *Staphylococcus aureus*.[4] An infection control program in the hospital includes an infection control focal point, an infection control committee, and a committed hospital management. Monitoring for nosocomial infections is active with a focus on surgical site infection. Cohort isolation is enforced for patients with multidrug-resistance pathogens.

APPROACH

On October 1, 2013, MSF implemented an ASP within the framework recommended by the Centers for Disease Control and Prevention with the core elements of leadership, commitment, accountability, drug expertise, action, tracking, reporting, and education.[8] The main activity of the ASP team was to review new hospital antibiotic prescriptions and make real-time recommendations to optimize antibiotic choice, dose, duration, and route based on MSF treatment protocols and patient-level microbiology results. An experienced, existing project physician was promoted to be the antibiotic focal point (AFP) and led the program in collaboration with a pharmacist, both under the supervision of the hospital manager. The aim of the AFP within the Amman project was to assure good bug-drug match, to narrow the spectrum of parenteral antibiotics, to transition to oral antibiotics when appropriate, to consider comorbidities and drug-drug interactions in decisions, and to stop antibiotics when intraoperative cultures were sterile.

Although given protected time for reviewing prescriptions, liaising with surgical staff to assure implementation of recommendations, and creating monthly reports, the AFP remained engaged in clinical care as part of the overall hospital team. The pharmacist was as an active part of the ASP whose focus was appropriate drug dosing, review of potential drug-drug interactions, and—in collaboration with nursing—assuring optimized antibiotic administration, particularly for special patient groups. The pharmacist implemented tools for the nursing staff, including the development of tables outlining the appropriate administration of common antibiotics, and provided regular in-service trainings. The pharmacist also contributed knowledge of cost, current antibiotic inventory, and could suggest the substitution of an equivalent drug when shortages demanded it.

Weekly multidisciplinary antibiotic rounds provided the forum where the members of the ASP team could interact with each other and with hospital stakeholders, including the infection control nurse, surgeons, and nursing staff. The agenda included current hospital antibiotic use, review of current patients receiving parenteral antibiotics with a focus on oral antibiotic transition, patient issues affecting antibiotic management (eg, adverse drug events), and aligning antibiotic strategy with planned surgical interventions. The AFP recorded—for each stewardship interaction—the antibiotic recommendation, uptake recommendation, reason for rejection (if necessary), and if there was a need for adjudication by an outside specialist. For contentious or complex cases, an infectious diseases specialist was available (R.A.M.) for telemedicine consultation, allowing some management controversies to be resolved by a specialist outside of the hospital. The infectious diseases specialist also provided regular remote mentoring to the AFP. The activities of the ASP were recorded in a monthly report that was shared within the organization.

RELEVANT CHANGES

During the initial year of implementation, an average of 22 surgical patients initiated antibiotic treatment monthly. The volume of patients starting antibiotics as inpatients remained relatively consistent throughout the first year of the ASP (Table 1). In the period from February-March, 52 patients initiated antibiotics; in April-June 72 patients initiated antibiotics; in July-September 52 patients initiated antibiotics; and in October-December 57 patients initiated antibiotics. Overall, all 233 patients requiring inpatient antibiotics in 2014 were reviewed during antibiotic rounds (Box 1).

In the first year of implementation, a modification was recommended in the original antibiotic prescription in 106 of 233 patients (45%). Recommendations were accepted by surgical staff in 94 of 106 patients (88%), with the rate of acceptance increasing with each quarter: in February-March, 18 of 23 changes (78%) were accepted; in April-June, 18 of 22 changes (82%) were accepted; in July-September, 25 of 27 changes (93%) were accepted; and in October-December, 33 of 34 changes (97%) were accepted. Over the

Box 1 Lessons learned

- A simple antibiotic stewardship model that places one antibiotic focal point physician and one pharmacist at the center of hospital prescribing was feasible and effective, reducing hospital antibiotic expenditures.
- A nonspecialist physician can lead antibiotic stewardship in contexts where specialists in infectious diseases are not readily available.
- Implementation of inpatient antibiotic stewardship led to recognition of related needs, specifically to other clinical care quality improvements, including follow-up of patients receiving outpatient antibiotic enhanced therapy.

Table 1
Process indicators for implementation of antibiotic stewardship in a humanitarian surgical project, Amman, Jordan

Time period	Initiating antibiotic, n	Changes suggested, n (%)	Changes accepted, n (%)	Reason for rejection	Referred to infectious diseases specialist, n (%)
February-March 2013	52	23 (44)	18 (78)	Presence of internal hardware; patient allergies/previous reported intolerance to suggested antibiotic; reason cannot be explained or classified	7 (13)
April-June 2013	72	22 (31)	18 (82)	High clinical suspicion/elevated CRP; patient nearing end of planned therapy (2); reason cannot be explained or classified (2)	10 (14)
July-September 2013	52	27 (52)	25 (93)	High clinical suspicion/elevated CRP (2)	11 (21)
October-December 2013	57	34 (60)	33 (97)	Patient allergies/previous reported intolerance to suggested antibiotic	8 (14)

CRP, C-reactive protein.

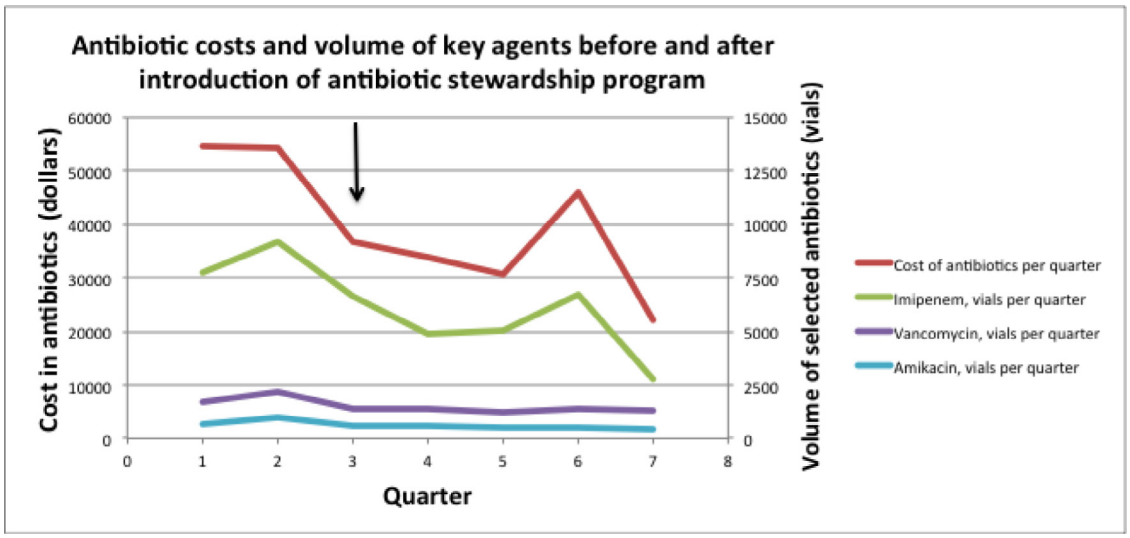

Fig 1. Monthly total antibiotic costs (U.S. dollars) after stewardship program implementation and use of selected antibiotics. Vertical arrow indicates timing of introduction of the antibiotic stewardship program.

entire period, 36 of 233 patients (15%) were referred for telemedicine consult with the infectious diseases specialist.

Despite a similar program volume (2013: N = 563; mean admissions, 106 per month; 2014: N = 533; mean admissions, 104 per month), when compared with the year prior to ASP implementation, project antibiotic use in 2014 declined considerably. Despite a similar program volume, when compared with the year prior to implementation, project antibiotic cost in 2014 declined from approximately $252,077 (average, $21,006/month) to <$159,948 ($13,329/month). Most of the costs savings were achieved with a reduction in the inappropriate use of imipenem and the substitution of another—more narrow-spectrum—parenteral or oral agent. There were no significant differences in basic patient characteristics and case mixture between the 2 periods.

A major goal of the ASP was to reduce unnecessary use of costly parenteral antibiotics, including carbapenems, glycopeptides, and broad-spectrum aminoglycosides, when an alternative antibiotic was appropriate. In the period after introduction of the ASP, use of imipenem declined from a mean of 2,206 vials per month to 1,620 vials per month, use of vancomycin declined from a mean of 545 vials per month to 438 vials per month, and use amikacin declined from a mean of 242 vials per month to 164 vials per month (Fig 1).

With respect to the cost of the ASP itself, the ASP used existing human resources. Although the monthly compensation of the physician leader was increased by approximately 15%, the ASP did not require the addition of full-time positions. Mortality data for the Amman surgical project were reviewed to explore if the introduction of antibiotic stewardship was associated with a change in inpatient mortality. In the year prior to ASP implementation (October 1, 2012-September 30, 2013), inpatient mortality was observed in 2 of 1,268 total admitted patients (0.2%), and in the year after, mortality occurred in 0 of 1,121 patients (0%).

DISCUSSION/CONCLUSIONS

A simple ASP in a humanitarian surgical project proved to be feasible, well-accepted, and effective in markedly reducing antibiotic expenditures and reducing use of broad-spectrum antibiotics. Over time, adoption of the recommendations of a nonspecialist physician—who was recognized locally as an expert—by surgical staff improved from 78% to 97%, suggesting increasing acceptability of the ASP. The approach, premised on real-time active review of antibiotic prescriptions and using existing physician and pharmacist human resources, may be a useful model for initiating an ASP in hospitals in LMICs with high levels of antibiotic utilization.

Several additional changes were associated with ASP introduction. We observed a shift in the previous practice of antibiotic initiation or modification by the surgical staff without clear justification and observed a significant decrease in the use of empirical antibiotics before culture reporting. An initial reluctance expressed by project surgeons to share responsibility for antibiotic management with the stewardship team improved markedly over the first year as evidenced by the improvement in the recommendation acceptance rate. This may have stemmed from the approach of the stewardship team toward transparent, collaborative decision-making and the introduction of a new clinic for follow-up of patients receiving long-term antimicrobials where treatment failure and toxicity concerns were addressed. This improvement in decision transparency and additional outpatient oversight of surgical patients receiving oral antibiotics may also have strengthened the confidence of the surgeons in the ASP. The ASP led to the recognition of related needs in the project, including the need to train more junior physicians on appropriate antibiotic use and to make greater use of pharmacy expertise toward improving patient care in the hospital.

This study has limitations. The rollout of the ASP was not part of a research study, but it was a pragmatic response to the need to improve the use of antibiotics within a humanitarian surgical hospital; some process and outcome data are not available. Further, it is not possible to fully associate the reduction in antibiotics costs over the period of interest to the impact of the ASP alone because there were concomitant improvements in antibiotic prices, including for imipenem-cilastatin. However, the overall volume of broad-spectrum antibiotic use also declined, which would not be expected from price shifts alone. Prospective studies will better define the impact of an ASP in LMIC hospitals.

The management of chronic, frequently multidrug-resistant chronic osteomyelitis with surgery and long-term antibiotic therapy is expensive. The Amman reconstructive surgery project is among the most costly in the MSF portfolio. As a result, the implementation of an ASP was seen as a way to improve the quality of care and to optimize MSF resources in contexts where the cost of medical

care is relatively higher than in traditional MSF settings. In very varied humanitarian environments, ASPs are being piloted in MSF hospitals in African contexts with flexibility to account for differences in human resources available, variations in how antibiotics are overused or misused, and availability of microbiology laboratory support.

Acknowledgments

We thank all those who supported the initiation and the stewardship team in MSF hospital in Amman, Jordan, for their support, particularly the nursing and surgical staff.

References

1. Tamma PD, Cosgrove SE. Antimicrobial stewardship. Infect Dis Clin North Am 2011;25:245-60.
2. Davey P, Brown E, Charani E, Fenelon L, Gould IM, Holmes A, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev 2013;(4):CD003543.
3. Del Arco A, Tortajada B, de la Torre J, Olalla J, Prada JL, Fernández F, et al. The impact of an antimicrobial stewardship programme on the use of antimicrobials and the evolution of drug resistance. Eur J Clin Microbiol Infect Dis 2015;34:247-51.
4. Boyles TH, Whitelaw A, Bamford C, Moodley M, Bonorchis K, Morris V, et al. Antibiotic stewardship ward rounds and a dedicated prescription chart reduce antibiotic consumption and pharmacy costs without affecting inpatient mortality or re-admission rates. PLoS ONE 2013;8:e79747.
5. Fakri RM, Al Ani AM, Rose AM, Alras MS, Daumas L, Baron E, et al. Reconstruction of nonunion tibial fractures in war-wounded Iraqi civilians, 2006-2008: better late than never. J Orthop Trauma 2012;26:e76-82.
6. Murphy RA, Ronat JB, Fakhri RM, Herard P, Blackwell N, Abgrall S, et al. Multidrug-resistant chronic osteomyelitis complicating war injury in Iraqi civilians. J Trauma 2011;71:252-4.
7. Teicher CL, Ronat JB, Fakhri RM, Basel M, Labar AS, Herard P, et al. Antimicrobial drug-resistant bacteria isolated from Syrian war-injured patients, August 2011-March 2013. Emerg Infect Dis 2014;20:1949-51.
8. Pollack LA, Srinivasan A. Core elements of hospital antibiotic stewardship programs from the Centers for Disease Control and Prevention. Clin Infect Dis 2014;59(Suppl):S97-100.