Perspectives and concerns regarding antimicrobial agent shortages among infectious disease specialists☆,☆☆,★,★★

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and on behalf of The Infectious Diseases Society of America's Emerging Infections Network

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ABSTRACT

Antimicrobial shortages have made treating certain infections more difficult. A web-based survey asking about experience with antimicrobial drug shortages was distributed in 2011 to 1328 infectious diseases physician members of the Emerging Infectious Diseases Network of the Infectious Diseases Society of America. A majority (78%) of 627 respondents reported needing to modify antimicrobial choices because of drug shortages within the past 2 years. Antimicrobials most often reported as not available or available but in short supply were trimethoprim–sulfamethoxazole injection (by 65% of respondents), amikacin (by 58%), aztreonam (by 31%), and foscarnet (by 22%). Most respondents (55%) reporting a shortage indicated that the shortage adversely affected patient outcomes and that they were forced to use alternative and second line agents which were either less effective, more toxic, or more costly. Most (70%) indicated that they learned about the shortage from contact with the pharmacy after trying to prescribe a drug in short supply. More effective means of informing physicians about drug shortages is critical to lessen the impact on patient care.

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1. Introduction

The shortage of prescription medications has the potential to cause significant morbidity and mortality (Jensen and Rappaport, 2010; Steinbrook, 2009). Shortages of antimicrobial agents are of particular concern and have been characterized as a public health emergency (Griffith et al., 2012a) due to the need to start these agents promptly and also because rising antimicrobial resistance rates limit therapeutic options for an increasing number of pathogens (Pulcini et al., 2012). Furthermore, for lack of financial and other incentives, there is a shortage of new antimicrobial agents in the pharmaceutical industry pipeline (Freire-Moran et al., 2011; Spellberg et al., 2011).

Shortages of antimicrobials are reported by the Food and Drug Administration (FDA) (US FDA, 2012) and professional organizations such as the American Society of Health System Pharmacists (ASHP) (ASHP, 2012). Although the direct impact of shortages is not easy to measure, the effects on individual patients and public health are considered significant (Hampton, 2007; Harbarth et al., 2003; Pluss-Suard et al., 2012; Steinbrook, 2009). Recent surveys of pharmacists have documented shortages of medications including antimicrobial agents in the USA (ASHP, 2011), Canada (Canadian Pharmacists Association, 2010), and Europe (The ESCMID Study Group for Antibiotic Policies ESGAP, 2007). Recently, an analysis and review of recent anti-infective drug shortages from the web site of the AHSP addressed a list of shortages, reasons, and time periods (Griffith et al., 2012a). A survey directed exclusively at infectious diseases (ID) physicians was performed a decade ago (Sparling, 2001; Strausbaugh et al., 2001). To capture recent experiences and perspectives of practicing ID physicians on antimicrobial agent shortages, we report the results of a 2011 web-based survey that was sent to all registered members of the Infectious Diseases Society of America.

2. Materials and methods

A 9-question survey web link was sent by email in May 2011 to all 1328 physician members of the Infectious Diseases Society of America's Emerging Infections Network (IDSA EIN) from the USA

and Puerto Rico. Two reminders were sent to nonresponders in the month-long open period. The EIN is a sentinel network of ID physicians who regularly engage in clinical activity and who volunteer to participate. The network has been funded by the Centers for Disease Control and Prevention (CDC) since 1995 and has been known to be in the forefront of important clinical ID issues (Infectious Diseases Society of America, 2011).

The physicians were asked for their experiences regarding the need for modifying management of an infectious disease due to a shortage, availability of antimicrobial agents in their practices within the past 2 years, whether they had encountered any adverse events as a result of shortages, and how they learned of the shortage. Descriptive statistics were used to analyze survey responses.

3. Results

A total of 627 (47%) of the 1328 active members of the EIN responded. The respondents were from all US Bureau of Census divisions and Puerto Rico. Nearly equal proportions of respondents declared their primary place of practice to be either hospital or clinic, private or group practice, university or medical school, and the US Department of Veterans Affairs facilities (VA) or the military.

Seventy-eight percent of the respondents indicated a need to modify their antimicrobial choice for treating or preventing an infectious disease because of a drug shortage within the past 2 years. Physicians in the East North Central US Bureau of Census division reported the highest rate (83%) of shortages and in the New England region, the lowest (62%, $P = 0.27$). Reported shortages also varied by the type of hospital: ID physicians working in non-university teaching hospitals (82%) and community hospitals (80%) reported shortages significantly more often than those working in the VA or the military (70%, $P = 0.046$). Reported shortages did not vary by hospital size.

Of the medications that were either not available or available but in short supply in the past 2 years, the top 5 were all injectables: trimethoprim/sulfamethoxazole (TMP/SMX), amikacin, aztreonam, foscarnet sodium, and intravenous immune globulin (IVIG) (Table 1). Prominent oral medications reported in shortage included oseltamivir oral suspension and acyclovir tablets. Live zoster vaccine, yellow fever vaccine, and inactivated influenza vaccine were also reported to be in short supply.

Of the 490 respondents who reported a shortage, 253 (52%) expressed an opinion that the resulting change in treatment due to the shortage had adversely affected patient care or outcomes. Of the 253 respondents who reported adverse effects, the most common concerns were use of more toxic antimicrobials (62%), more expensive agents (41%), broader-spectrum antimicrobials (38%), long-term morbidity from inadequate treatment of infection (28%), and longer hospitalizations (26%). Use of suboptimal, less-effective, or more toxic therapy was the most commonly mentioned additional adverse outcome in an open-text field (7%). Specific examples included use of oral TMP/SMX or pentamidine for *Pneumocystis jiroveci* pneumonia instead of intravenous TMP/SMX, and increased use of colistin for multidrug-resistant Gram-negative bacilli in place of amikacin. Physicians also reported 5 deaths attributed directly to antimicrobial agent shortages. No further information regarding these deaths was provided by the respondents.

A majority (70%) of the respondents indicated that they had learned of the shortage from their pharmacy only after prescribing the drug in short supply. Other common modes of learning about the shortage were from a colleague (59%) and from the FDA or ASHP websites (24%). A majority (70%) indicated that they had never visited the FDA shortages website. Fifty-four percent indicated that they were not notified once the shortage was resolved. Suggestions to improve overall communication about drug shortages focused on messages from federal agencies, professional associations such as the IDSA, from pharmaceutical companies, and from the respondents'

own institutions and pharmacies. The preferred mode of communication was electronic.

The 137 respondents who did not report experiencing an antimicrobial drug shortage within the past 2 years were from all 9 US Bureau of Census regions and represented all levels of infectious diseases experience from fellows-in-training to those in practice for more than 25 years. Respondents whose primary employment was with state or local government were somewhat more likely to report not experiencing a shortage (by 55%, $P = 0.32$) as compared to military physicians (50%), federal government employees (33%), university or medical school faculty (25%), hospital/clinic-based physicians (19%), and those in private or group practice (15%). This may reflect less time in providing direct patient care in those settings.

4. Discussion

We found that 78% of ID physician respondents had experienced an antimicrobial drug shortage within the past 2 years. The agents most often reported as not available or available but in short supply were trimethoprim–sulfamethoxazole injection, amikacin, aztreonam, and foscarnet. Thus, our results indicate that antimicrobial agent shortages are commonly noted in the USA. Furthermore, almost half of respondents indicated that, in their opinion, the shortage adversely affected patient care most often by exposing patients to less effective, more toxic, or costly medications. Disturbingly, most respondents learned about the shortage from their pharmacy when trying to prescribe that agent for a patient. These reports often came several hours after the prescription had been written, leading to delays in treatment even when an alternative agent was procured.

In the decade since the last EIN survey of ID physicians on the topic of antimicrobial shortages, much has remained the same: shortages continue to occur with only the specific agents changing (Strausbaugh et al., 2001). In 1999 and 2000, the top 5 agents noted to be in short supply were a different group of injectables: penicillin G, meropenem, ticarcillin ± clavulanate, cephazolin, and gentamicin. Similar

Table 1
Antimicrobial agents, biologicals, and vaccines reported to be in short supply by infectious disease physicians, May 2011 (n = number of ID physicians reporting a shortage, % = percent of 627 respondents).

	Not available, n (%)	Available but short supply, n (%)
TMP/SMX injection	198 (32)	209 (33)
Amikacin injection	120 (19)	242 (39)
Foscarnet sodium injection	66 (11)	72 (11)
Aztreonam injection	54 (9)	143 (23)
Cefotetan injection	50 (8)	34 (5)
Zoster vaccine live	39 (6)	64 (10)
Posaconazole	25 (4)	61 (10)
Penicillin G (aqueous or benzathine)	24 (4)	86 (14)
Erythromycin lactobionate injection	25 (4)	24 (4)
Acyclovir tablets and capsules	22 (4)	54 (9)
Oseltamivir oral suspension	19 (3)	77 (12)
Yellow fever vaccine	13 (2)	65 (10)
Intravenous Immune Globulin IVIG (Human)	12 (2)	105 (17)
Inactivated influenza vaccine	10 (2)	60 (10)

Other shortages reported by at least 1 physician (typed into 'Other' field): *anti-bacterial agents*: amoxicillin/clavulanate, ampicillin-sulbactam, azithromycin, capreomycin, cefazolin, ceftazidime, chloramphenicol, ciprofloxacin oral, clarithromycin tabs, clindamycin injection, clofazimine, dapsone, doxycycline (IV or not specified), erythromycin ophthalmic ointment, gentamicin (including preservative free), isoniazid intravenous, kanamycin, meropenem, metronidazole injection, metronidazole oral, nafcillin injectable, piperacillin injection, piperacillin–tazobactam injection, pyrimethamine, quinupristin–dalfopristin, rifampin injection, streptomycin, ticarcillin/clavulanate; *anti-viral agents*: acyclovir injection, ganciclovir capsules; *Anti-parasitic agents, anti-fungal agents, immune globulins, vaccines, and others:* albendazole, amphotericin–liposomal, ethanol for central venous catheter locks, hemophilus influenza B vaccine, itraconazole, Japanese encephalitis virus vaccine, measles/rubella vaccine, rabies immune globulin, rabies vaccine, varicella zoster immune globulin.