



Managing ESBL-producing Enterobacteriaceae-related urinary tract infection in primary care: a tool kit for general practitioners

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Abstract

In Southern France, approximately 4% of *E. coli* isolates from community-acquired urinary tract infections are extended spectrum beta-lactamase producers, while carriage rates for enterobacteriaceae (ESBL-E) range from 3 to 6%. General practitioners (GP) are unfamiliar with the management of patients harboring ESBL-E. Providing them with a specific tool kit should assist in their therapeutic approach and optimize antimicrobial prescription an ESBL-E tool kit was developed by a multidisciplinary team: infectious diseases (ID) specialists, microbiologists, pharmacologists, and nursing home staff. This tool kit includes treatment protocols, GP and patient information leaflets, a list of infection control measures, and contact details of ID physicians for specialized advice. A community-based (including nursing homes) prospective study was conducted in 2012 in Southeastern France to test the tool kit in the context of ESBL-E-related urinary tract infections (UTI). ESBL-E-related UTI were identified in 88 patients, 66 GPs were contacted by the microbiology laboratory, 56 stated they were offered the tool kit, 48 said they had received it, and 41 stated they had read its contents. Use of the tool kit was significantly correlated with appropriate antibiotic prescription, which concerned 36/39 tool kit users versus 13/20 non-users ($p=0.0125$) and 40 GPs expressed an average satisfaction rate of 4.2 on a scale of 0 to 5. Availability of a specific tool for managing patients harboring ESBL-E, now completed with a website, can assist community-based GPs and improve antimicrobial prescription.

Introduction

Expansion of extended spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-E) has resulted in increasing morbidity and mortality rates as a result of selective pressure exerted through widespread antibiotic use [1–3] Although ESBL-E-infected patients presenting with UTI may be successfully treated, carriage can persist in their digestive tract long after clinical resolution creating a reservoir that may lead to recurrent infection and transmission to contacts.

Only recently, in 2014, has the French-language Society for infectious diseases (SPILF) published recommendations for the management of ESBL-E infection. However, these are essentially theoretical and not easily accessible for general practitioners (GPs) in their day-to-day context. A recent survey of management of UTI due to antibiotic-susceptible *E. coli* by GPs in Southeastern France in 2015 showed only

half of them were familiar with the recommendations. Indeed, 47% of prescriptions were inadequate: no indication for antimicrobial treatment, inappropriate antimicrobial agent, and inadequate treatment duration. [V Blanc et al. Antibiotic therapy of community-acquired urinary tract infection due to multi-susceptible *Escherichia coli*: also a challenge for infectious disease referrers? Poster presentation EV0696 ECCMID 2015; https://www.escmid.org/escmid_publications/escmid_elibrary/?q=amrane&id=2173&L=0&x=0&y=0&tx_solr%5Bfilter%5D%5B0%5D=main_filter_eccmid%253Atrue&tx_solr%5Bfilter%5D%5B1%5D=pub_date%253A201601010000-201612312359

GPs are thus confronted with an unfamiliar situation for which they lack training, but are expected to provide patients with clear, intelligible, and yet complex information while avoiding generating unnecessary anxiety, in the context of limited knowledge regarding the prognosis of ESBL-E carriage.

French public health authorities advise informing all healthcare workers, applying suitable infection control measures and antimicrobial treatment protocols, and organizing access to expert advice (<http://www.hcsp.fr/Explore.cgi/>

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[Telecharger?NomFichier=hcpr20100202_enterobactBLSE_en.pdf](#)).

As a regional initiative, a tool kit intended to assist community-based GPs in the management of ESBL-E infections was developed. It was initially tested in the hospital setting [See corresponding article in the same issue of the journal]. The present study aims to assess to what extent the ESBL tool kit is conveyed to GPs and its related procedures duly followed. GPs' opinion on the tool kit in terms of its usefulness was investigated and its potential impact on antimicrobial prescription explored.

Methods

Our regional multi-institutional organization Réso-Infectio-PACA-Est consists in a network of infectious disease physicians, microbiology laboratories, public and private hospitals and clinics, and public health institutions in Southeastern France (<http://www.reso-infectio.fr/rubrique-0>). To facilitate management of ESBL-E infection and asymptomatic carriage in primary care, members of this network invited community-based microbiology laboratories, GPs, and residential care facility staff to take part in developing and implementing a tool kit for community-based general practitioners.

The tool kit includes four items: an information sheet to raise physicians' awareness of ESBL-related issues with a telephone number to access expert advice from a dedicated infectious diseases specialist, a list of infection control measures intended for the patient, a checklist for physicians to ensure the necessary measures have been implemented, and a list of antimicrobial treatment protocols. In accordance with French recommendations, all microbiologists are expected to systematically warn physicians each time an ESBL-producing *E. coli* is identified, with details of antibiotic susceptibility testing specifically mentioning isolation of an ESBL-E. Local community-based microbiology laboratories were invited to offer the tool kit to the prescribing GP when reporting such an isolate from a urine culture. UTIs, i.e., cystitis, complicated cystitis, pyelonephritis, and prostatitis, were those defined according to the national French recommendations. Five laboratories accepted to participate; the present study focuses on the first two who took part in this pilot project. These laboratories offer technical facilities to analyze samples provided by various peripheral labs and thus cover a large part of the study area. Provision of this kit began in September 2011.

This prospective observational study was conducted from May to December 2012 and focused on non-hospitalized patients, including those in nursing homes, who were diagnosed with a community-acquired ESBL-producing *E. coli* isolated on a urine culture, regardless of clinical context.

The ESBL tool kit was intended to be sent by email or fax to the GP after the phone call alert, along with the microbiology laboratory result.

Each patient was included only once. Data collection by the microbiology labs included patients' age and gender, date of sample collection, resistance profile of the isolate, and name of the prescribing GP.

GPs were interviewed by telephone approximately 1 month after sample collection. They were asked to specify the clinical diagnosis for which they had requested microbiological investigation, whether they had been notified by the laboratory of a diagnosis of ESBL-producing *E. coli* infection in their patient, whether they had been offered the tool kit; had accepted it; received it; used it; found it helpful; and had any comments, and which antimicrobial agent they had prescribed, including dose and duration, once the antibiotic susceptibility test was available. This last parameter was compared to the suggested treatment protocols. Overall satisfaction with the tool kit was recorded on a scale of 0 to 5.

ESBL isolates were identified by double-disk synergy test on agar plates.

Statistical analysis

Data were analyzed using Epi Info™ software. Appropriateness of antimicrobial prescription according to use of the tool kit was tested using Yates' corrected chi-square test. A *p* value < 0.05 was considered statistically significant.

Results

Population characteristics and *E. coli* resistance profile

Among the 88 patients with ESBL-producing *E. coli*, 69 (78.4%) were female, aged 8 to 96 years with a median of 79 years, while the age range for male patients was 1 to 92 years with a median of 69 years.

High resistance rates were observed for quinolones and cotrimoxazole, and 48% of isolates were resistant to both agents.

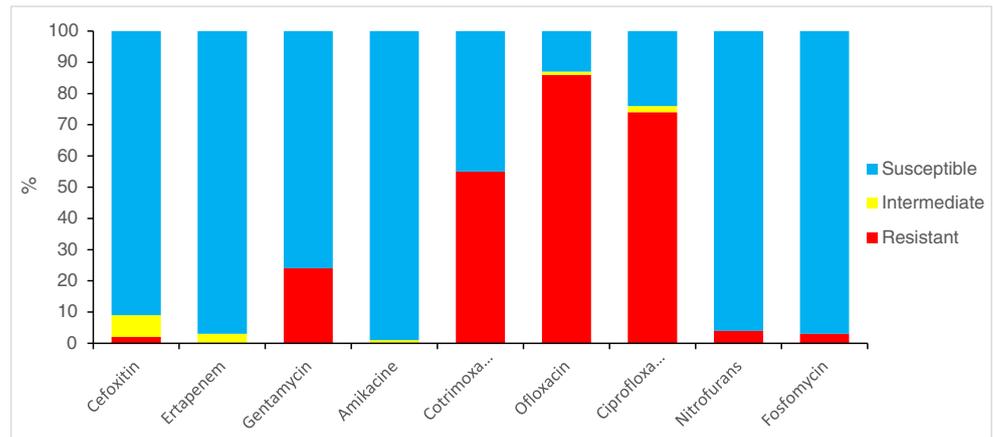
GP questionnaires

From May 1st to December 31st 2012, 3754 urine cultures were positive for *E. coli*, among which 135 were ESBL producers, i.e., 3.6%.

Figure 1 shows a flowchart of the GPs involved in the study.

According to the 69 responders, UTIs leading to a diagnosis of ESBL-related *E. coli* infection included acute cystitis (20), complicated cystitis (14), acute pyelonephritis (19),

Fig. 1 Antimicrobial resistance profile of ESBL-producing *E coli* isolates



acute prostatitis (8), chronic prostatitis (3), colonization (3), and pyelonephritis with bacteremia (1), while no diagnosis was provided for one patient who was admitted to hospital very shortly after sample collection.

Most GPs ($n = 66$) were alerted by telephone and received the tool kit by fax or email. Among the 41 GPs who stated they had read its contents, 40 considered this had assisted them in managing their patient. When asked whether they would use it again, six were unsure and two said they would not. Overall mean stated satisfaction with the tool kit on a scale of 0 to 5 was 4.2, with a median value of 4. One GP gave a score of 0, saying he had received the tool kit too late.

Impact on antimicrobial treatment

Among the 69 episodes of ESBL-producing *E coli*-related UTI, 59 prescriptions were recorded. Nine patients were admitted to hospital either before or following receipt of the antibiotic susceptibility pattern, and one was a locum GP who was unable to trace the prescription.

Of the 59 available antimicrobial prescriptions, 10 were considered inappropriate: ineffective compound (3), sub-optimal dosage (2), and insufficient duration (3). Details of prescribed agents are shown in Table 1.

Use of the tool kit was significantly correlated with appropriate antibiotic prescription, which concerned 36/39 tool kit

users versus 13/20 non-users ($p = 0.0125$; Yates’ corrected chi-square test).

Discussion

This intervention, which aimed to assist GPs in the management of ESBL-E related UTI, was met with a positive response and resulted in improved antimicrobial prescription.

This study has several limitations:

Of the 80 GPs who prescribed a urine culture, only 69 were available for interviewing and 21 stated they had not received the ESBL tool kit. The microbiologist may have directly communicated the result by telephone or knew that the patient had been admitted to hospital or had some technical issue. Of those GPs who received the tool kit, seven stated they had not read it, among whom two had received it too late. The others did not provide any explanation.

GPs in France have a heavy workload and receive numerous guidelines which they cannot always easily put into practice [4]; an additional document such as the tool kit may have been considered an extra burden, especially by those not particularly concerned by antibiotic resistance nor aware of antibiotic stewardship. A survey conducted in 2015 in France revealed that GPs were likely to oppose any measure restricting their freedom of prescription, as the present study may have been

Table 1 Distribution of antimicrobial prescriptions according to diagnosis

| | Fosfomycin | Nitrofurantoin | Co-trimoxazole | Amoxicillin-clavulanate | Ciprofloxacin | Ofloxacin | ? |
|----------------------|------------|----------------|----------------|-------------------------|---------------|-----------|----|
| Simple cystitis | 16 | 4 | | | | | |
| Complicated cystitis | | 13 | 1 | | | | |
| Acute pyelonephritis | | | 4 | 3 | 2 | 4 | 6* |
| Acute prostatitis | | | 8 | | | | |
| Chronic prostatitis | | | 3 | | | | |

*Hospitalized patients

perceived. [5]. In an attempt to reach physicians who do not adhere to antimicrobial stewardship guidelines, a restricted antibiotic susceptibility test report by the laboratory was assessed on a randomized controlled case vignette study which resulted in improved prescription [6].

Telephone interviews are prone to bias: responders may be inclined to provide assessments that please the interviewer, which may have interfered with an objective evaluation. However, the outcome in terms of appropriate antimicrobial prescription was positive among responders for those physicians who had used the tool kit, compared to those who had not. Two laboratories were able to implement the procedure during the study period.

The prevalence rate of 3.6% of ESBL-producing *E. coli* isolates from urine samples was in line with that reported among community-acquired isolates in France from ambulatory patients or in nursing homes for the elderly [7].

While many efforts to control nosocomial spread of multi-drug-resistant organisms have been developed, to our knowledge, no multidisciplinary initiative aiming to establish a community-hospital integrative model as a practical solution for managing ESBL-E infection in primary care is available to this date [8]. A study conducted in Sweden among GPs revealed that only those who expressed concerns about resistance closely followed prescribing guidelines [9]. Our local organization, linking microbiologists and primary care physicians, with the availability of expert advice from an ID specialist, conforms to the recommendations put forward in the National Early Warning Response System, although these currently only concern hospital-acquired infections (http://www.sante.gouv.fr/IMG/pdf/plan_antibiotiques_2011-2016_DEFINITIF.pdf). The presence of ESBL-E in the community warrants extending the focus towards front-line, primary care physicians. Our study suggests pursuing such efforts by improving the accessibility of our tool kit to GPs, while insisting on providing patients with the necessary information for implementing control measures. A website and a smart-phone application have now been developed, to facilitate access by microbiologists, physicians, and patients (<http://kit-blse.com/?lang=en>). Microbiology laboratories in the area now provided with the website link when reporting results.

Further studies including a larger sample of physicians should allow confirmation of the efficacy of the tool kit in improving antimicrobial prescription and informing patients of the necessary infection control measures to be implemented in their home.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

Ethical approval For this type of study, ethical approval was not required.

Informed consent Informed consent was not required for this study.

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