Active surveillance of antibiotic resistance prevalence in urinary tract and skin infections in the outpatient setting

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Abstract

The aim of the study was to evaluate the need for active surveillance of antibiotic resistance in ambulatory infections. We measured the prevalence of antibiotic resistance in urinary tract infections (UTIs) (n = 1018) and skin infections (n = 213) diagnosed in outpatients between September 2008 and February 2009 in the Canton of Bern, Switzerland. Samples were stratified into 'solicited' (diagnostic work-up for study purpose only) and 'routine' (diagnostic work-up as part of standard care). Susceptibility patterns were compared for 463 *Escherichia coli* isolates from UTIs (231 solicited; 232 routine) and 87 *Staphylococcus aureus* isolates from skin infections (35 solicited; 52 routine). Overall, *E. coli* showed higher susceptibility to ampicillin, amoxicillin–clavulanic acid and norfloxacin in solicited than in routine samples. Among 15–45-year-old patients, susceptibility rates were comparable between solicited and routine samples for all antibiotics except for amoxicillin–clavulanic acid. However, among patients >45 years old, isolates from routine samples showed lower susceptibility to all β-lactams tested and quinolones than those from solicited samples. Extended-spectrum β-lactamase (ESBL)-producing *E. coli* isolates were rare (solicited, 0.4%; routine, 1.7%; p 0.4). Susceptibility patterns of *S. aureus* were comparable between solicited and routine samples. Therefore, in the outpatient setting, susceptibility rates for *E. coli* isolates differ by indication for urinary culture and age. Surveillance based on samples taken during standard care may underestimate susceptibility rates for uncomplicated infections, especially among the elderly. Reports of resistance data should include age stratification.

Keywords: Active, multiresistance, skin infection, surveillance, Switzerland, urinary tract infection
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Introduction

Antibiotic resistance is increasing worldwide in developed and developing countries [1]. Multidrug resistance in important human pathogens is no longer restricted to high-risk settings such as acute-care hospitals, but is now spreading in the population at large [2]. Community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) and extended spectrum β-lactamase (ESBL)-producing *Escherichia coli* are timely examples of multidrug-resistant organisms causing community-acquired infections [3]. Increasing resistance trends introduce uncertainty about the correct choice of empirical antibiotic treatment if information about the local resistance epidemiology is lacking. This applies to the outpatient setting, in which microbiological diagnosis in individual patients is not recommended in standard care for common non-invasive infections.

Enormous effort and progress have been made in the establishment of large-scale resistance surveillance systems around the globe [4]. There are now several databases available, many of which also provide resistance information for the community setting. For economic reasons, such surveillance programmes usually rely on passive collection of routine microbiological data, and some programmes are based mainly on data from invasive isolates. Therefore, the resistance information represents a selection of clinical situations, such as severe infections and infections associated with high-risk populations, and it may overestimate the resistance prevalence of mild community-acquired infections, such as those of the upper respiratory tract, the lower urinary tract, and the skin. These infections account for the majority of prescribed antibiotics, and standard care does not require microbiological work-up. Changes of empirical treatment habits to broader regimens based on erroneous interpretation of surveillance data will introduce an unnecessary selection pressure and promote further resistance spread. An illustrative example is provided by uncomplicated lower urinary tract infections. Concerns about the rapid increase in resistance to trimethoprim–sulphamethoxazole in *E. coli* has started a vicious circle of increased use of quinolones followed by raising quinolone resistance rates and the emergence of ESBL-producing clones [5,6].

In this study, we present the resistance rates observed in an active surveillance study conducted in ambulatory-care patients presenting with acute uncomplicated urinary tract infections (UTIs) or purulent skin infections. We compare the resistance results of samples that would not have been sent for analysis outside this study (solicited samples) with those of routine samples.

Patients and Methods

Study population and definitions

This study fulfilled the ethical requirements of the Canton of Bern. In August 2008, all general practitioners and dermatologists practising in the Canton of Bern, Switzerland, were asked by the Department of Public Health to participate in this prevalence study. Patients were recruited between 1 September 2008 and 28 February 2009. Consecutive patients >15 years of age were included in the study if they fulfilled the following criteria: (i) residing in the Canton of Bern; and (ii) first visit with a purulent wound infection or with a new episode of a UTI, defined as the presence of typical symptoms and a positive dipstick test result. Patients with wound infections were recruited only once. Patients with UTIs could be recruited twice, if the time interval between the current and the last episode was longer than 30 days. Physicians filled in a short questionnaire for each patient about the clinical diagnosis, living conditions (at home vs. long-term care), antibiotic consumption during the last 3 months, and history of colonization with a multiresistant microorganism. Physicians stated for each patient whether microbiological diagnosis would have been performed independently of this study. Physician residence was categorized into rural or non-rural, according to the definition of the Swiss Federal Office of Statistics (http://www.bfs.admin.ch). Microbiological diagnosis included a wound swab for skin infection and a mid-stream urine sample for UTI. All microbiological analyses were performed at the Institute for Infectious Diseases, University of Bern. Wound swabs were placed in Amies transport medium without charcoal (Venturi Transystem; Copan, Brescia, Italy). Urine samples were transported in containers prefilled with boric acid preservative (Becton Dickinson, Franklin Lakes, NJ, USA). Susceptibility testing was performed with the Kirby–Bauer disk diffusion test, and the results were interpreted according to CLSI (formerly NCCLS) standards [7]. Testing of *E. coli* isolates for susceptibility to nitrofurantoin and fosfomycin was introduced in January 2009. All wound swabs were screened for MRSA, with a biplate consisting of mannitol salt agar 4% (Oxoid, Hampshire, UK) and oxacillin screen agar containing 6 μg of oxacillin/mL (BioMérieux, Croponne, France). Cefuroxime-resistant *Enterobacteriaceae* were screened for ESBL according to the CLSI ESBL recommendations for disk diffusion, including ceftriaxone, ceftazidime, and aztreonam. The second screening criterion was visible inhibition by clavulanic acid (amoxicillin–clavulanic acid placed between aztreonam and ceftazidime on screening plates). The presence of ESBL was confirmed by the double-disk test [8]. Significant bacteriuria was defined as a concentration of ≥1000 CFU/mL for *E. coli* and *Staphylococcus saprophyticus*, and a concentration of ≥10 000 CFU/mL for all other microorganisms, according to the European guidelines [9].

Statistical analysis

Samples that would have been collected by physicians for diagnostic purposes independently of the study were designated as 'routine samples', and all others as 'solicited samples'. In *E. coli*, 'dual resistance' was defined as resistance to norfloxacin and trimethoprim–sulphamethoxazole, and 'multiresistance' was defined as resistance to three or more of norfloxacin, trimethoprim–sulphamethoxazole, amoxicillin–clavulanic acid, and cefuroxime axetil.

Data were analysed with Epi info Version 3.4.3 (CDC, Atlanta, GA, USA). Proportions were compared by use of the chi-square test or Fisher's exact test as appropriate.

Results

Antimicrobial resistance prevalence in urinary tract isolates

In total, 1018 urine samples were provided by a total of 124 physicians, who account for 13% of all practising physicians in the ambulatory setting in the Canton of Berne (http://www.fmh.ch). Each physician recruited a median number of three patients. Of the 1018 urine samples, about half (n = 525, 51.6%) represented 'routine samples' and 428 (42.0%) 'solicited samples' (information was missing for 65