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CLINICAL AND EPIDEMIOLOGICAL STUDY

Comparison of hospital-wide and unit-specific cumulative antibiograms in hospital- and community-acquired infection

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Abstract

Background Empirical antibacterial therapy in hospitals is usually guided by local epidemiologic features reflected by institutional cumulative antibiograms. We investigated additional information inferred by aggregating cumulative antibiograms by type of unit or according to the place of acquisition (i.e. community vs. hospital) of the bacteria. **Materials and methods** Antimicrobial susceptibility rates of selected pathogens were collected over a 4-year period

in an university-affiliated hospital. Hospital-wide antibiograms were compared with those selected by type of unit and sampling time (<48 or >48 h after hospital admission). **Results** Strains isolated >48 h after admission were less susceptible than those presumably arising from the community (<48 h). The comparison of units revealed significant differences among strains isolated >48 h after admission. When compared to hospital-wide antibiograms, susceptibility rates were lower in the ICU and surgical units for *Escherichia coli* to amoxicillin-clavulanate, *enterococci* to penicillin, and *Pseudomonas aeruginosa* to anti-pseudomonal beta-lactams, and in medical units for *Staphylococcus aureus* to oxacillin. In contrast, few differences were observed among strains isolated within 48 h of admission. **Conclusions** Hospital-wide antibiograms reflect the susceptibility pattern for a specific unit with respect to community-acquired, but not to hospital-acquired strains. Antibiograms adjusted to these parameters may be useful in guiding the choice of empirical antibacterial therapy.

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Keywords Antibiogram · Bacterial sensitivity tests ·
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Introduction

Prompt initiation of effective antibiotic therapy has been associated with better survival in severe hospital- or community-acquired infections [1–3]. As microbiological documentation of infection is usually obtained within 24–48 h of symptom manifestation, the choice of empirical antibiotic therapy is crucial in the early management of severe infections. Such an empirical therapy should provide the optimized antibacterial spectrum that ensures coverage of the

most common pathogens while avoiding the unnecessary selection of resistant bacteria [4, 5]. The use of hospital cumulative antibiograms (summary report of the percentages of susceptible strains of a given pathogen for the antibiotics routinely tested in an institution) to guide the choice of empirical antibiotic therapy has been identified as a key strategy to prevent and control the spread of resistant microorganisms in hospitals [4–6]. However, standardized guidelines for the generation of these reports are currently lacking [6]. Antimicrobial susceptibility patterns may vary between hospitals, and differences between units within a same institution have also been reported [7–12]. Similarly, differences have been observed between hospital- and community-acquired strains [13, 14].

The aim of this study was to investigate the additional information inferred from aggregating cumulative antibiograms by sampling time (< or \geq 48 h from admission) and type of unit within one hospital.

Materials and methods

The study was carried out at the Centre Hospitalier Universitaire Vaudois (Lausanne, Switzerland), an 850-bed university-affiliated hospital. Data of in vitro susceptibility testing were collected from the microbiological laboratory over a 4-year period (2003–2006). The identification of bacterial species and in vitro susceptibility testing were performed according to the criteria of the American Society for Microbiology (ASM) [15] and the breakpoints definitions of the Clinical and Laboratory Standards Institute (CLSI, Wayne, PA) [16], respectively. Antibacterial susceptibility testing for the antibiotics most commonly used for a given microorganism were routinely performed for all potential pathogens isolated from any sample site. According to the microbiological laboratory's policy, this testing was not repeated when a microorganism was isolated more than once in the same patient within 4 days. Thereafter, it was performed every 4 days (if applicable). All isolates for whom antibacterial susceptibility testing had been performed were recorded in a computer-generated database. This system automatically excludes redundancies of strains (same microorganism with the same antibiotic susceptibility pattern detected in a separate isolate from a same patient). Using this database, cumulative antibiograms were retrospectively calculated for each year from 2003 to 2006 for the most frequent Gram-positive and -negative bacteria and the antibiotics most commonly prescribed in the institution. Some microorganisms were selected for their prevalence and the relevance of their susceptibility pattern in the choice of empirical antibacterial therapy: *Escherichia coli* (with respect to amoxicillin/clavulanate, ciprofloxacin, ceftriaxone), *Pseudomonas aeruginosa* (ceftazidime, cefepime,

imipenem, meropenem, piperacillin/tazobactam ciprofloxacin), *Staphylococcus aureus* (oxacillin) and *enterococci*, including *Enterococcus faecium/faecalis* and other *Enterococcus* spp. (penicillin; of note, no *enterococci* non-susceptible to vancomycin were documented during the study period). Antibiograms were extracted for the whole institution and for the following units: internal medicine, general surgery, adult intensive care (ICU) and medical paediatrics. A distinction was made between strains isolated <48 h or \geq 48 h from admission (presumably community- and hospital-acquired, respectively) [17].

Strains were differentiated as “susceptible” and “non-susceptible” (intermediate or resistant) according to the breakpoints definitions of the CLSI [16].

Susceptibility rates were compared between presumably community- and hospital-acquired strains and between the whole hospital and the units mentioned above. Differences between susceptibility rates aggregated by the site of sampling (blood cultures vs. cultures from any other site) were also investigated. Fisher's exact test was used to compare proportions. Two-sided p values <0.05 were considered as statistically significant. Because of the large number of statistical comparisons, Bonferroni corrections for multiple tests were applied.

Results

Of the total number of strains analysed for the whole institution during the study period, 11,485 (44.5% hospital-acquired) were *E. coli* strains, 4,638 (72.6% hospital-acquired) were *P. aeruginosa* strains, 3,405 (65% hospital-acquired) were *enterococci* strains and 8,008 (50.9% hospital-acquired) were *S. aureus* strains.

Annual hospital-wide susceptibility rates of these pathogens remained stable over the 4-year period (<5% variation over time for all of the antibiotics tested). Antibiograms calculated for the 4-year period were thus considered in further analyses.

For the whole institution, susceptibility rates were significantly lower for strains isolated \geq 48 h from admission when compared to those isolated <48 h (p value <0.001 for all pathogen/antibiotic combinations) (Table 1).

Among presumably community-acquired strains (isolated <48 h from admission), antibiograms calculated for specific units displayed few differences when compared to those of the whole institution. The most relevant differences were observed for *P. aeruginosa* susceptibility to ciprofloxacin in medical and surgical units (64 vs. 80%, $p < 0.001$ and 62 vs. 80%, $p = 0.01$, respectively), and to imipenem in surgical units (71 vs. 87%; $p = 0.01$). In contrast, major differences between units were observed among hospital-acquired strains (Fig. 1a, b). *P. aeruginosa*

Table 1 Comparison of the rates of susceptibility to selected antibiotics between presumably community- and hospital-acquired strains

Microorganisms and selected antibiotics to which they showed susceptibility	Community-acquired strains (<48 h from admission)	Hospital-acquired strains (>48 h from admission) ^a
<i>Escherichia coli</i>		
Amoxicillin/clavulanate	5,672/6,370 (89)	4,146/5,111 (81)
Ceftriaxone	6,301/6,372 (99)	4,940/5,113 (97)
Ciprofloxacin	5,860/6,348 (92)	4,342/5,091 (85)
<i>Pseudomonas aeruginosa</i>		
Cefepime	1,179/1,269 (93)	2,807/3,368 (83)
Ceftazidime	1,148/1,269 (90)	2,638/3,368 (78)
Imipenem	1,100/1,269 (87)	2,389/3,368 (71)
Meropenem	1,157/1,269 (91)	2,703/3,367 (80)
Piperacillin/tazobactam	1,215/1,269 (96)	3,039/3,368 (90)
Ciprofloxacin	1,015/1,269 (80)	2,309/3,369 (69)
<i>Staphylococcus aureus</i>		
Oxacillin	3,670/3,931 (93)	3,439/4,077 (84)
<i>Enterococci</i>		
Penicillin	1,151/1,192 (97)	1,904/2,214 (86)

Values are given as the number of susceptible strains/total number of strains, with the percentage of total in parenthesis

^a p value < 0.001 for all comparisons between community- and hospital-acquired strains

susceptibility rates to most anti-pseudomonal beta-lactams were lower in surgical units and ICU than those calculated for the whole institution, while medical and paediatric units displayed similar or higher susceptibility rates (Fig. 1a). In addition, susceptibility of *enterococci* to penicillin was lower in ICU and surgical units (70 vs. 86% for the whole institution, $p < 0.001$) and susceptibility of *E. coli* to amoxicillin/clavulanate was lower in surgical units (70 vs. 81%, $p < 0.001$). The susceptibility of *S. aureus* to oxacillin was lower in medical units (70 vs. 84%, $p < 0.001$) (Fig. 1b).

The distinction according to the site of sampling (blood vs. any site) showed no differences above 5% in susceptibility rates, with the exception of *P. aeruginosa* susceptibility to piperacillin/tazobactam (85 vs. 92% for blood cultures and cultures from any site, respectively, $p = 0.015$) and ciprofloxacin (86 vs. 72%, $p = 0.001$), and *enterococci* susceptibility to penicillin (82 vs. 90%, $p = 0.002$).

Discussion

The results of our analysis revealed significant differences in antimicrobial susceptibility rates between presumably hospital- and community-acquired strains. These differences were particularly relevant for *P. aeruginosa*. The comparison between different units showed similar susceptibility rates among community-acquired strains, whereas important differences were observed among hospital-acquired strains, especially for *P. aeruginosa* and *enterococci* and with respect to the prevalence of

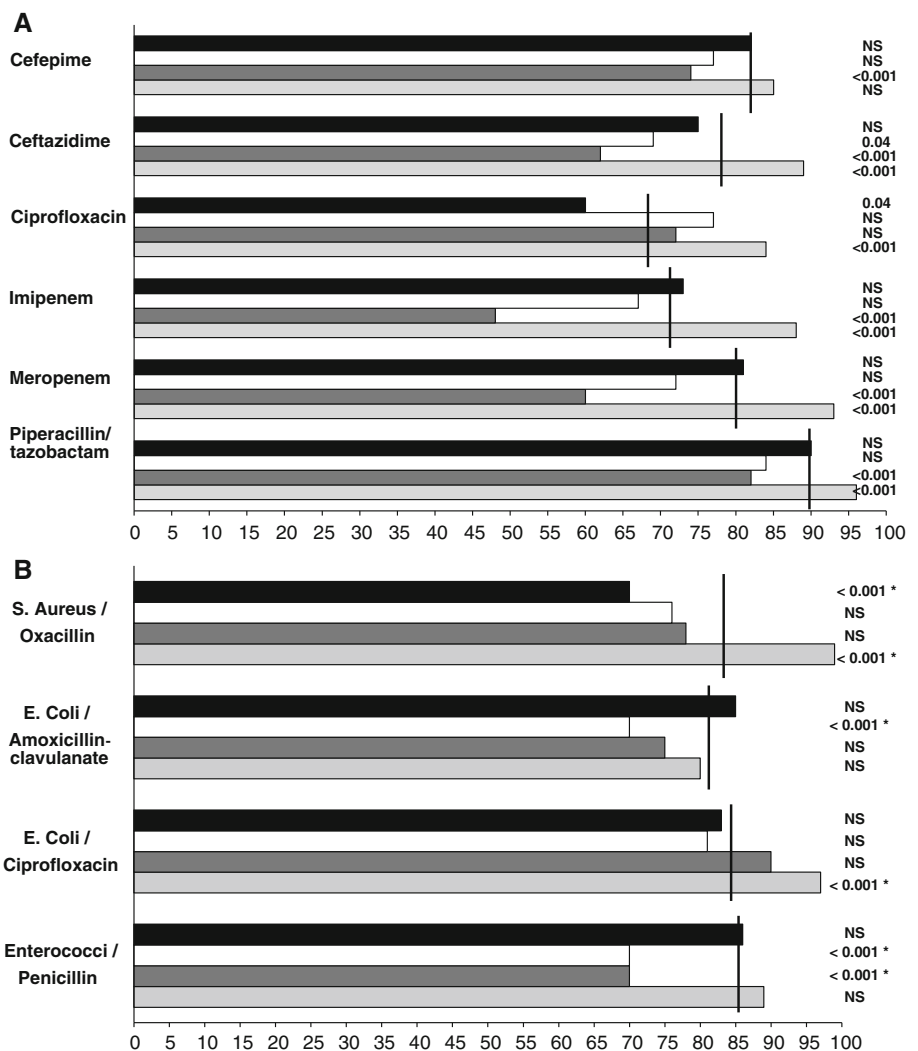
methicillin-resistance in *S. aureus* (MRSA). However, stratification according to the site of sampling for cultures added little additional relevant information. These findings may have an impact on the choice of empirical antibiotic therapy, although it is limited to a subset of clinical situations and specific for the hospital where the data were collected.

Variability in the susceptibility rates between units in a same hospital has been reported previously [7–12]. Most differences were observed between the ICUs and non-ICUs. However, little data are available on the comparison of cumulative antibiograms between wards other than ICUs and according to the sampling time in terms of being able to distinguish presumably nosocomial from community-acquired infections [7, 13, 14]. The study presented here proposes an integration of these easily available parameters. The potential impact of such a focused approach on the control of the emergence of resistance has been suggested in earlier studies [5, 18]. It should, however, be specified that the use of cumulative antibiograms aggregated according to ward or sampling time would only be possible if they are derived from a large enough number of isolates to reach statistical significance (provided that susceptibility rates remain stable over the time needed to obtain this number of isolates). Statistical significance is not enough, however, and unit- or sampling time-specific data should only be provided if they show clinically relevant gaps in antibiotic susceptibility. It may be the task of a hospital antibiotic committee to assess this relevance.

Resistance of *P. aeruginosa* to carbapenems is an important problem in ICUs and has been associated with exposure to this class of antibiotics [19–21]. Similarly,

Fig. 1 Comparison of susceptibility rates between units within a same hospital for selected microorganism/antibiotic combinations in hospital-acquired strains (culture drawn >48 h from admission). *x* axis Percentage of susceptible strains, *black bars* medical units, *white bars* surgical units, *dark-grey bars* intensive care units, *light-grey bars* pediatric units, *black vertical lines* susceptibility rate for the whole hospital. *Numbers on the right* *p* value (Fisher's exact test with application of Bonferroni corrections for multiple tests) for the comparison between unit-specific and hospital-wide susceptibility rates, *NS* not significant ($p > 0.05$).

a *Pseudomonas aeruginosa* and cefepime, ceftazidime, ciprofloxacin, imipenem, meropenem and piperacillin/tazobactam, **b** *Staphylococcus aureus* and oxacillin, *Escherichia coli* and amoxicillin/clavulanate and ciprofloxacin, *enterococci* (*Enterococcus faecalis/faecium* and other *enterococci* species) and penicillin



a low susceptibility rate of *P. aeruginosa* to carbapenems was observed among ICU isolates in our analysis. Data on antimicrobial consumption in our institution revealed that the use of carbapenems was particularly high in the ICU [22 defined daily dose (DDD)/100 bed-days for both imipenem and meropenem when compared to 4.5 for piperacillin/tazobactam, whereas carbapenems consumption in the whole institution was only 4 DDD/100 bed-days] [22]. The use of amoxicillin and amoxicillin/clavulanate in surgical units was also higher than that in medical units (22.4 and 14.3 DDD/100 bed-days, respectively), which may contribute to the lower susceptibility rate of *enterococci* to penicillin in the former setting.

This analysis has several limitations. First, it was conducted in a single centre. As such, these results may not be reproducible in other countries or institutions depending on potential differences in case-mix and epidemiologic characteristics. Differences observed in the prevalence of MRSA may particularly result from variations in the case-mix between units or from possible cross-infections. In

addition, individual risk factors for infections with resistant microorganisms, such as the duration of hospital stay, underlying diseases or previous antibacterial therapy, are not taken into account by such an approach based on aggregated data from the microbiology lab. However, the utility of cumulative antibiograms for guiding local empirical antibiotic strategies and preventing the emergence of resistance has been clearly established despite this intrinsic limitation [5]. Second, the 48-h cutoff was chosen according to the Centers for Disease Control standard definitions of nosocomial infections [17]. However, the incubation period of infection may vary according to the type of pathogen or the patient's underlying conditions, making the distinction between hospital- and community-acquired infections difficult to determine in some cases [17]. This may be of particular relevance for *P. aeruginosa*. Third, our data do not allow differentiating bacteria isolated in true infections from those considered to be colonizers or contaminants. However, such a distinction should not have resulted in significant differences in susceptibility

rates. Finally, the repetition of antimicrobial susceptibility testing for a same strain isolated in a same patient may have been a source of bias despite the use of selection criteria to avoid such redundancies in our electronic database. One of the consequences is the impossibility to distinguish between primary or secondary acquired resistance.

In conclusion, the results of the analysis reported here suggest that hospital-wide cumulative antibiograms reflect the actual susceptibility pattern for a specific unit with regard to community-acquired infection, but not with regard to hospital-acquired infections. Institutional policies for the report of cumulative antibiograms should thus be adapted to these parameters that are easy to obtain. Such an approach may be useful in guiding the choice of empirical antibacterial therapy.

Conflict of interest statement None.

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