Antibiotic usage in German hospitals: results of the second national prevalence study

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Objectives: Data on antibiotic usage (AU) are helpful for improvement of antibiotic stewardship. This study describes findings and targets for quality improvement in German hospitals identified in a national point prevalence survey of healthcare-associated infections and AU.

Methods: The survey was organized by the German National Reference Centre for Surveillance of Nosocomial Infections (NRZ) as part of a pan-European survey organized by the European Centre for Disease Prevention and Control (ECDC). Infection control personnel of participating hospitals were trained in methodology and performed the survey in September and October 2011. Data on the antimicrobials prescribed (e.g. compounds and indications) were analysed by the NRZ. In order to submit national data to the ECDC, a representative sample of 46 hospitals was generated, although other hospitals were invited to participate in the survey if interested.

Results: In total, 41,539 patients were surveyed in 132 hospitals. AU prevalence in these hospitals and in the representative sample did not differ significantly [25.5% (95% CI 24.5%–26.6%) and 23.3% (95% CI 21.3%–25.5%), respectively]. AU rates were higher compared with a previous survey in 1994. Antimicrobials were administered for treatment in 70% and prophylaxis in 30% of cases. Surgical prophylaxis (SP) was prolonged (>1 day) in 70% of cases. Indication was documented in patients’ charts in 73% of administrations. The most frequently used agents were cefuroxime (14.3%), ciprofloxacin (9.8%) and ceftriaxone (7.5%).

Conclusions: The study identified several points for improvement, e.g. the large amount of prolonged SP, the extensive use of broad-spectrum antibiotics and the high percentage of antibiotic administration without documented indication.

Keywords: antibiotic usage, treatment, prophylaxis, Germany

Introduction

Knowledge about antibiotic usage (AU) is a prerequisite for antibiotic stewardship (ABS). The European Surveillance of Antimicrobial Consumption (ESAC) point prevalence surveys (PPSSs) provide a standardized methodology to determine the prevalence of AU in hospitals and to get a snapshot on the quality of antimicrobial use within hospitals and countries.1 Many European hospitals participated in the three prior ESAC hospital PPSSs on antimicrobial use.2 Unfortunately, German hospitals did not participate in these studies.

In 2011, the second German national prevalence study on healthcare-associated infections and AU was performed within the framework of the European PPSS, which was organized by the European Centre for Disease Prevention and Control (ECDC). This study was the first national project to achieve an overview about AU in German hospitals on a large scale.

The prevalence of healthcare-associated infection based on this national prevalence study is published elsewhere; this article describes the major findings concerning AU and provides conclusions for ABS activities in Germany.

Methods

Protocol

For the survey, a standardized study protocol1 including the main variables of the ESAC hospital-PPS protocol was provided by the ECDC. Furthermore, the ECDC trained national contacts in implementing the survey in participating countries. The German National Reference Centre for Surveillance of Nosocomial Infections (NRZ) translated all study materials into...
German national survey on antibiotic usage in hospitals

Setting
Because the ECDC required a representative hospital sample (according to hospital size) of 46 hospitals in Germany, a representative group was generated by random selection of all hospitals listed in the German hospital directory. Hospitals in this representative sample, together with all hospitals participating in the German Krankenhaus Infektions Surveillance System and all other interested German hospitals, were invited to be trained and to participate in the survey.

Data collection
Data collection in the hospitals was performed by local infection control (IC) teams who were trained by NRZ physicians and an information technology specialist during one of six introductory courses.

The survey was undertaken between September and October 2011. IC teams in the participating hospitals had to survey at least one entire ward per study day and record all the necessary information. Ward staff were asked for further details in cases where relevant information was not found in the patients’ charts.

All patients admitted to the ward before or at 8:00 AM and not discharged from the ward at the time of the study were surveyed. Patients undergoing same-day treatment or surgery were excluded from the survey. A data collection form was filled out for every patient receiving at least one antimicrobial agent on the survey day. In each case, the following information was obtained: antimicrobial name converted into the WHO ATC5 (Anatomical Therapeutic Chemical Classification of drugs) code, the route of administration (parenteral, oral, rectal or inhalation) and the indication for antimicrobial use (treatment intention or prophylaxis). In the case of patients receiving antibiotics for treatment, the corresponding infections were classified as community, long-term care facility or hospital acquired. In addition, the diagnosis group by anatomical site was recorded for each infection.

Prophylaxis was categorized into surgical prophylaxis (SP) and medical prophylaxis. The duration of SP was grouped as: (i) single dose, (ii) 1 day or (iii) >1 day. Data on SP were to be collected retrospectively for the 24 h prior to the time of the survey in order to code the duration accordingly.

In every case, it was asked whether the reason for the antimicrobial use was documented in the patient’s chart.

All data were anonymous and were collected in accordance with German recommendations for good epidemiological practice with respect to data protection. Ethical approval and informed consent were not required, since all hospitals are obliged to collect and analyse data on the prevention and management of infectious diseases in humans according to the German Protection Against Infection Act (Infektionsschutzgesetz 23). Completed study forms were sent to the study centre and entered in the study database by an optical character recognition technique (Teleform). Datasets were sent back to all participating hospitals for a plausibility check. Finally, the study centre double-checked all data prior to analysis.

Data analysis
For the analysis of the prevalence of AU, aggregated denominator data (all patients present in the ward at 8:00 AM and not discharged at the time of the survey) were collected for each ward. The AU prevalence was calculated as the ratio of patients receiving at least one antimicrobial drug to all patients present during the time of the survey.

For calculating the 95% CI of the AU prevalence, the ‘cluster effect’ caused by individual hospitals was taken into account by analysing a factor for overdispersion according to the methods described by Spiegelhalter. The factor of 2.16 was calculated as the square standardized Pearson residuals of the units’ observed AU.

Results
A total of 132 hospitals participated in the study and surveyed 41539 patients. The representative sample, whose data were sent to ECDC, consisted of 46 hospitals with 9626 patients. The overall AU prevalence was 25.5% and did not differ significantly between all participating hospitals and the representative sample. Table 1 shows the data for both groups in comparison with the data from the previous national prevalence study, which was performed in 1994.

The distribution of AU rates among hospitals is shown in Figure 1. In most of the 132 participating hospitals, the prevalence of AU was between 20% and 35%. The mean AU rate in intensive care units (ICUs) was 50.5% (95% CI 47.2%–54.1%) compared

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<td>AU prevalence (%) (95% CI)</td>
<td>25.5 (24.5–26.6)</td>
<td>23.3 (21.3–25.5)</td>
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Table 1. Study characteristics and prevalence of AU in all hospitals and in the representative sample in comparison with the representative sample of hospitals in the national prevalence study from 1994.

Figure 1. Distribution of hospitals according to AU prevalence categories. AU, patients receiving at least one antibiotic/100 patients.

aPatients receiving at least one antibiotic/100 patients.
with 25.2% (95% CI 24.7%–25.7%) in other parts of the hospital. Among specialties, surgery had the highest AU prevalence (29.8%), followed by internal medicine (28.1%) and paediatrics (23.9%).

Among all patients with known indication for antimicrobial use, the majority received antibiotics for treatment (70%), particularly to treat community-acquired infection (44.3%) or hospital-acquired infection (18.3%). Infections associated with long-term care facilities were seen in only 5.4% of patients. Due to this small share, antibiotic use for long-term care facility-acquired infection will not be further described in detail.

A substantial number of patients received antibiotics for prophylaxis (30%) and the data showed prolonged administration for SP in more than two-thirds (70%) of cases, as shown in Figure 2.

Sixty-four percent of antimicrobial agents were administered parenterally and 36% orally. The indication for antibiotic therapy was documented in the patient’s chart in only 73% of all patients administered antimicrobials.

The most frequently administered antibiotic groups were second-generation cephalosporins (14.6%) and fluoroquinolones (14%), followed by penicillins with β-lactamase inhibitors (12.6%) and third-generation cephalosporins (10.6%). Figure 3 shows the cumulative use of antibiotic groups according to indication. The high use of second-generation cephalosporins is mainly explained by their use for SP. Figures 4–6 are corresponding figures for the treatment of lower respiratory tract infections (Figure 4), sepsis (Figure 5) and urinary tract infections (UTIs) (Figure 6). Interestingly, many patients with community-acquired pneumonia (CAP) received piperacillin with a β-lactamase inhibitor or carbapenems. Patients with sepsis were most often treated with carbapenems followed by penicillins with a β-lactamase inhibitor, fluoroquinolones, glycopeptide antibiotics and third-generation cephalosporins. The most administered substances for sepsis were vancomycin (11%), meropenem (10.8%) and ciprofloxacin (10%), followed by piperacillin with an enzyme inhibitor (7.2%) and ceftriaxone (6.7%).

The most frequently administered agents in general were cefuroxime (14.3%) followed by ciprofloxacin (9.8%), ceftriaxone (7.5%), metronidazole (5.3%), ampicillin with an enzyme inhibitor (4.9%) and piperacillin with an enzyme inhibitor (4.1%).

Figure 2. Indications for antibiotic use. MP, medical prophylaxis; SP, surgical prophylaxis.

Figure 3. Cumulative AU for the most frequently used antibiotic groups for therapy and prophylaxis [community-acquired infection (CI), n = 4915; hospital-acquired infection (HI), n = 2100; prophylaxis, n = 3363]. 2ndGC, second-generation cephalosporins; FLQ, fluoroquinolones; PENβlacI, penicillins with β-lactamase inhibitor; 3rdGC, third-generation cephalosporins; Carb, carbapenem; ExtSpPEN, extended-spectrum penicillins; Macrol, macrolides; Lincosam, lincosamides; 1stGC, first-generation cephalosporins; SXT, sulfamethoxazole/trimethoprim.

Figure 4. Cumulative AU for therapy of lower respiratory infections [community-acquired infection (CI), n = 1274; hospital-acquired infection (HI), n = 458]. PENβlacI, penicillins with β-lactamase inhibitor; 3rdGC, third-generation cephalosporins; FLQ, fluoroquinolones; Macrol, macrolides; Carb, carbapenem; 2ndGC, second-generation cephalosporins; ExtSpPEN, extended-spectrum penicillins; GlycopAB, glycopeptide antibiotics; SXT, sulfamethoxazole/trimethoprim; Tetracyc, tetracyclines.
**Discussion**

The first German national prevalence study to determine the prevalence of nosocomial infections and AU was performed in 1994. However, that survey focused only on the administration of antibiotics and the indication in general, but not on antibiotic groups or substances. Therefore, the current study provides not only updated data about AU, but also a much more intensive and comprehensive overview.

Compared with 1994, the overall prevalence of AU increased from 17.7% to 23.3%, focusing on the representative sample of hospitals, or 25.5%, focusing on all participating hospitals. For comparison, some methodological differences between the two study protocols have to be considered, but the main principles and definitions are identical. During the last 17 years, patients’ risk factors for infection and resulting AU may have increased: according to the data of German Health Statistics, the average age of hospitalized patients increased from 2001 to 2008, from 51.8 to 53.2 years.

In the same time, the average length of hospital stay decreased significantly (from 11.9 days in 1994 to 7.9 days in 2010).

Today, patients often receive antibiotics until the last day of their hospital stay, whereas in previous years many patients remained in hospital for several days after the end of antibiotic treatment. Interestingly, no changes were observed in the distribution of categories for which antimicrobials were administered. In 1994, 48% of patients received antibiotics for the treatment of community-acquired infection, 17% for the treatment of hospital-acquired infection and 35% for prophylaxis.

During the study in 1994, external investigators visited the hospitals to survey hospital-acquired infection and AU, whereas this time, hospitals’ IC teams themselves undertook the survey. A validation study evaluating 200 cases in two hospitals showed a 96% sensitivity (95% CI 91%–98%) surveying AU and comparing local IC teams with a trained observer (the gold standard). Due to the methodology, an analysis of specificity was not possible.

Overall, about one-quarter of hospitalized patients and half of the patients in ICUs received an antibiotic. About half of the patients received an antibiotic because of a community-acquired infection, about one-third received antibiotics for prophylaxis and less than one-fifth received antibiotics because of a hospital-acquired infection. The extensive use of antibiotics for prolonged SP is particularly problematic. The duration of antibiotic prophylaxis for surgery (SP not continued for >24 h) is one quality indicator for AU described by Ansari et al. In the meantime, more research has been initiated on the identification of valuable indicators for the adequate realization of SP.

Further quality indicators identified were the documentation of antibiotic indication in the patients’ chart and compliance with guidelines for antimicrobial usage. The rate of documentation of indication found in this survey is consistent with the rates described in previous ESAC surveys, but indicates that documentation is not the rule in 27% of cases. This percentage may be even higher, since the methodology of the survey also permitted the discussion of patients’ data with the ward personnel and some surveying IC teams may have interpreted information in the charts in connection with information from the ward personnel as indication for antimicrobial use. In the future, hospitals should be encouraged to document indications distinctly and in a standardized way.

Regarding the consistency with evidence-based guidelines, antibiotics used for therapy of CAP were mainly in accordance with the
recommendations of the German CAP guidelines. However, in ~20% of cases, antibiotics active against *Pseudomonas* spp. were used (piperacillin with a β-lactamase inhibitor and carbapenems). This is not indicated because *Pseudomonas* spp. normally do not play a role in the pathogenesis of CAP. Also, the treatment of sepsis was principally analogous to the German sepsis guidelines.

The high use of vancomycin for septic patients may be explained by an incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia of 4.8%/100,000 inhabitants, which is higher than the reported incidences from other European countries. Another reason may be seen in the general awareness about this topic as discussed by Meyer et al. The authors analysed data from 55 German ICUs and identified an increasing consumption of newly approved anti-MRSA drugs—mainly linezolid—without increasing MRSA in these ICUs.

The compliance of treatment of UTIs was not assessed, because national guidelines only describe the treatment of uncomplicated UTIs and PPS data did not allow for differentiation between uncomplicated and complicated infections.

The increasing trend in the incidence of *Clostridium difficile*-associated infection (CDI) was also observable in the survey of healthcare-associated infections in the participating hospitals: 6.6% of all healthcare-associated infections were CDI. The incidence density of nosocomial CDI in German hospitals was 0.47 per 1000 patient-days in 2010. This high burden may explain why metronidazole was the fourth most frequently administered substance in the hospitals.

Compared with other European countries, the total prevalence of AU in German hospitals seems to be relatively low. However, the study was able to identify several points for improvement: the large amount of prolonged SP, the extensive use of broad-spectrum antibiotics and the high percentage of antibiotics administered without documentation of indication.

The adoption of national guidelines on antibiotic prescribing is not mandatory for German hospitals. In a questionnaire survey conducted in 355 German ICUs, only 76% reported having access to guidelines on antimicrobial therapy. Antibiotic policy measures in these ICUs were the routine access to unit-based reports on bacterial resistance data (83%) and restrictive prescribing practice, i.e. the assignment of personal responsibilities for the prescription of antibiotics (84%) (P. Gastmeier, Charité—Universitätsmedizin Berlin, personal communication). Since 2010, the German ABS training initiative is educating physicians and pharmacists—who are the key stakeholders in ABS in German hospitals—in designing and implementing ABS on a voluntary basis.

In addition, the German Infection Prevention Act meanwhile requires prospective ongoing recording of AU in all German hospitals on a hospital-based level. This will stimulate ABS activities in German hospitals in the future and possible additional surveys on AU may show further improvement in the critical use of antimicrobial agents.

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**Transparency declarations**

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**References**


