Antibiotic Use in 3 European University Hospitals

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The use of antibiotic drugs was studied in university teaching hospitals in Tartu, Estonia, Huddinge, Sweden and Badajoz, Spain. Data on drug deliveries to hospital wards during 1992 are presented in defined daily doses (DDD) per 100 bed-days (DDD/100 bed-days). In addition, the time trends of antibiotic use in Tartu University Hospital from 1992 to 1995 are shown. The total amount of antibiotic drugs used for systemic treatment in 1992 was similar in the 3 hospitals, 41 DDD/100 bed-days in Tartu vs. 51 DDD/100 bed-days in Badajoz and 47 DDD/100 bed-days in Huddinge. The antibiotics used most frequently were tetracyclines and aminoglycosides in Tartu, broad-spectrum penicillins and cephalosporins in Badajoz and narrow-spectrum penicillins and cephalosporins in Huddinge. Injectable preparations accounted for one-half of the antibiotics used. Among the medical departments, the total use of antibiotics varied up to 3-fold (from 19 to 61 DDD/100 bed-days), less than among the surgical departments (18–94 DDD/100 bed-days). The frequency of antibiotic use was very similar in departments of similar profile in the 3 hospitals (i.e. in departments of neurology, urology, etc.). The use of antibiotic drugs in intensive care units was twice as high in Huddinge (243 DDD/100 bed-days) as in Badajoz (106 DDD/100 bed-days) and Tartu (135 DDD/100 bed-days) in 1992. In conclusion, the international differences in the use of antibiotics in hospital were not in the frequency of use, but in the predominant prescription preferences in the hospital.

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INTRODUCTION

The in-hospital use of antibiotic drugs has been a major concern in the last few decades for several reasons. For the purchasers of health care services and administrators, antibiotic drugs account for a major proportion of the escalating drug budget, especially in hospitals (1). The overuse and misuse of antibiotic drugs is considered to be one of the reasons for increasing resistance among various pathogens (2, 3). These worries have led to the implementation of strict antibiotic policies in hospitals in many countries, with different strategies and different outcomes.

Monitoring of drug use is essential in order to follow the effects of, and adherence to, the hospital’s antibiotic policies. Patient medical records may be reviewed for this purpose, but this method can be quite exhaustive. Instead, the defined daily dose (DDD) methodology, based on pooled data of drug deliveries to individual wards, may be used to determine the probability of treating a patient with a particular drug (4–6). This method is inadequate for monitoring drug use in 1 hospital only, as the interdepartmental differences in drug use may be determined by the medical profile. Therefore, comparisons with other hospitals and between departments in which similar medical disorders are treated, should be included in the evaluation of the quality of pharmacotherapy.

This study was initiated by the recent observation of large differences in the consumption of antibiotics between the Nordic countries and Estonia during the 1980s (7) and among the countries of central and eastern Europe in 1989–1992 (8). The question arose: to what extent do the drug use patterns in Estonia reflect those of the University Teaching Hospital, which is the training centre of the only medical school in Estonia. To answer this question, antibiotic drug use was followed in Tartu University Hospital from 1992 to 1995 and 2 university hospitals from the European Union were used for comparison.

MATERIALS AND METHODS

Study centres

The data were collected from the Tartu University Maarjamõisa Hospital (Tartu, Estonia), Hospital Infantia Cristina of the University of Extremadura (Badajoz, Spain) and Huddinge University Hospital (Huddinge, Sweden). These 3 hospitals serve as centres of secondary and tertiary care in most medical specialities for a defined population in the corresponding catchment area (Table I). All of these hospitals have departments of infectious diseases and oncology, but for the purposes of this study, and in order to minimize the impact of specific infections of the geographical area and of immunocompromised patients, the data from these departments were excluded from comparison. The departments of gynaecology, dermatology and psychiatry were also excluded from this survey. Thus, the specialities of cardiology, gastroenterology, internal medicine, nephrology, neurology and rheumatology were included in the comparison of medical departments, and the specialties of general surgery, neurosurgery, orthopaedics, traumatology, urology and vascular surgery were included in the comparison of surgical departments from each of the 3 hospitals. Data from the departments of general surgery and internal medicine and the intensive care units (ICU) were selected for presentation, because of the similar patient profile and size (Table I).

Data source and coding

The data on drug use available in the university hospitals in Tartu, Estonia, and Badajoz, Spain, were expressed in the statistics of the
hospital pharmacies in terms of cost and volume (number of packages) of drug deliveries to different departments on a daily and monthly basis. These raw data had to be coded, classified and transformed manually before comparisons could be performed. Drugs were classified and the volume data were transformed into DDD according to the Anatomical–Therapeutic–Chemical classification and the DDD valid in 1992. The data from Huddinge University Hospital, Sweden, were available in DDD. Preparations of antibiotic drugs for local treatment and drugs for the treatment of tuberculosis were excluded from the study. The data are presented as the number of DDD/100 bed-days. Drug consumption, evaluated according to the DDD methodology and expressed in number of DDD/bed-day has been validated to give a rough estimate of the number of in-patients exposed to a given drug (4).

RESULTS

Average use in the hospital

The total amount of antibiotics used for systemic treatment in 1992 was similar in the 3 hospitals studied (41 DDD/100 bed-days in Tartu University Hospital vs. 51 DDD/100 bed-days in Badajoz and 47 DDD/100 bed-days in Huddinge). By 1995 the use of antibiotics had increased to 48 DDD/100 bed-days in Tartu. On average, antibiotic drug use was 30–50% higher in the surgical departments than in the medical wards in Tartu and Huddinge, but did not differ in this aspect in Badajoz. The use of parenteral formulations accounted for 22 DDD/100 bed-days (53%) in Tartu in 1992, somewhat higher than the 45% in Badajoz. Data from Huddinge did not distinguish between parenteral and oral formulations.

The top 3 antibiotic drugs accounted for at least one-third, and the top 10 antibiotics for 66% of the total use in each of the hospitals studied (Table II). The most used antibiotics were tetracyclines and aminoglycosides in Tartu, broad-spectrum penicillins and cephalosporins in Badajoz and narrow-spectrum penicillins and cephalosporins in Huddinge. The use of narrow-spectrum penicillins had decreased in Tartu in 1995 compared with 1992. Doxycycline, ampicillin and metronidazole had increased their share in Tartu by 1995, whereas the use of cotrimoxazole had decreased. The subgroup of cephalosporins together with quinolones accounted for 3.3% of the total use of antibacterial drugs in Tartu in 1995, a 2-fold increase from 1992, but still 10 times less than in Badajoz (43%) or Huddinge (35%) in 1992.

Surgical departments

The drugs preferred in the various surgical departments were similar within each hospital. The lowest use of antibiotics among surgical wards of the 3 hospitals was in the Department of Orthopaedics in Tartu (18 DDD/100 bed-days) and the highest in the Department of Urology in Tartu (94 DDD/100 bed-days) in 1992. The Department of Urology was also the highest consumer of antibiotics in Badajoz and Huddinge. In the urology departments, broad-spectrum penicillins and tetracyclines were used most often in Tartu (47% of DDD in 1992), whereas fluoroquinolones were the major antibacterial drugs in both Badajoz (38%) and Huddinge (30%). In the general surgery departments, aminoglycosides dominated in Tartu (45% of DDD in 1992), broad-spectrum penicillins in Badajoz (36%) and narrow-spectrum penicillins in Huddinge (29%; Fig. 1).

Intensive care units

The use of antibiotics in the ICU was twice as high in Huddinge (243 DDD/100 bed-days) as in Badajoz (106 DDD/100 bed-days) and Tartu (135 DDD/100 bed-days) in 1992. The drug selection followed that of the other departments in the hospital (Fig. 2), with more use of aminoglycosides in Tartu (40% in 1992 and 32% in 1995) and of cephalosporins in both Badajoz (42%) and Huddinge (28%).

Medical departments

The use of antibiotics varied up to 3-fold among the medical departments studied, i.e. less than among the surgical departments. The lowest use of antibiotics was in the Department of Neurology in Tartu (19 DDD/100 bed-days) and the highest in the Department of Lung Diseases in Huddinge (61 DDD/100 bed-days) in 1992. The Department of Neurology was the only department in Tartu where the use of narrow-
Table II. Antibiotics used most frequently in the university teaching hospitals

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<tr>
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<tr>
<td>1</td>
<td>Doxycycline</td>
<td>20.8</td>
<td>Doxycycline</td>
<td>25.8</td>
<td>Amoxicillin</td>
<td>19.7</td>
<td>Cefuroxime</td>
<td>12.2</td>
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<tr>
<td>2</td>
<td>Ampicillin</td>
<td>15.1</td>
<td>Ampicillin</td>
<td>24.0</td>
<td>Ciprofloxacin</td>
<td>12.1</td>
<td>Cotrimoxazole</td>
<td>10.4</td>
</tr>
<tr>
<td>3</td>
<td>Kanamycin</td>
<td>11.9</td>
<td>Gentamicin</td>
<td>12.7</td>
<td>Amoxicillin + clavulanic acid</td>
<td>7.7</td>
<td>Phenoxymethylpenicillin</td>
<td>10.1</td>
</tr>
<tr>
<td>Top 3</td>
<td></td>
<td>48</td>
<td></td>
<td>63</td>
<td></td>
<td></td>
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<td>33</td>
</tr>
<tr>
<td>4</td>
<td>Benzylpenicillin</td>
<td>9.7</td>
<td>Benzylpenicillin</td>
<td>8.1</td>
<td>Erythromycin</td>
<td>4.4</td>
<td>Doxycycline</td>
<td>7.9</td>
</tr>
<tr>
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<td>Cefuroxime</td>
<td>5.1</td>
<td>Metronidazole</td>
<td>6.7</td>
<td>Cefotaxime</td>
<td>4.3</td>
<td>Norfloxacin</td>
<td>7.6</td>
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<tr>
<td>6</td>
<td>Gentamicin</td>
<td>4.6</td>
<td>Ciprofloxacin</td>
<td>3.8</td>
<td>Cefazoline</td>
<td>3.9</td>
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<td>4.4</td>
<td>Streptomycin</td>
<td>3.3</td>
<td>Tobramycin</td>
<td>3.8</td>
<td>Amoxicillin</td>
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</tr>
<tr>
<td>8</td>
<td>Polymyxin</td>
<td>4.1</td>
<td>Kanamycin</td>
<td>2.7</td>
<td>Ceftriaxone</td>
<td>3.7</td>
<td>Cloxacillin</td>
<td>5.8</td>
</tr>
<tr>
<td>9</td>
<td>Streptomycin</td>
<td>3.9</td>
<td>Erythromycin</td>
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<td>Cefixime</td>
<td>3.4</td>
<td>Flucloxacillin</td>
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</tr>
<tr>
<td>10</td>
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<td>3.4</td>
<td>Tetracycline</td>
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<td>Clindamycin</td>
<td>2.8</td>
<td>Metronidazole</td>
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<tr>
<td>Top 10</td>
<td></td>
<td>83a</td>
<td></td>
<td>92b</td>
<td></td>
<td>66c</td>
<td></td>
<td>75d</td>
</tr>
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</table>

a Of total 41.1 DDD/100 bed-days.
b Of total 47.6 DDD/100 bed-days.
c Of total 51.4 DDD/100 bed-days.
d Of total 46.5 DDD/100 bed-days.

Spectrum penicillins increased considerably, from 2.6 (13%) to 9.0 DDD/100 bed-days (32%) during 1992–1995. In the departments of internal medicine, broad-spectrum penicillins and tetracyclines were used most often in Tartu (46% of DDD in 1992), whereas broad-spectrum penicillins were the major antibiotics in Badajoz (31%) and narrow-spectrum penicillins in Huddinge (28%; Fig. 3).

DISCUSSION

The use of antibiotics is frequently reviewed, usually for in-house purposes, in many hospitals in several countries (5, 9). Such reviews have not been conducted before in 2 of the university teaching hospitals included in this study, Tartu and Badajoz. The total use of antibacterial drugs for systemic use in the 3 study hospitals was similar in 1992—approximately 50% of all patients may have received an antibiotic daily. These figures (41–51 DDD/100 bed-days) are up to 25% higher than those reported for Denmark (6), Germany and The Netherlands, at the same level as Belgium (9) and significantly lower than 74 DDD/100 bed-days, which was the reported average of the 450 hospitals in the USA in 1981 (5).

The main finding in this study was that the international differences in the hospital use of antibiotics were not in the intensity of use, but in the prescription preferences. The wards of similar medical specialities used similar total amounts of antibiotics, but from different pharmacological subgroups and, thus, with different microbiological activities. Ideally, the selection of antibiotic drugs should be based on the microbiological data on bacterial sensitivity and on prevalence of resistance in the respective hospitals. This consensus is well recognized, but difficult to adhere to, as illustrated by the empirical initial treatment with antibiotics in 85% of infection cases shown in a recent survey in the 5 largest European countries (10).

The patients in all study centres were treated with a relatively limited number of antibiotics, as illustrated by the increase of the impact of the 10 most prescribed antibiotics from 83% to 92% during 1992–1995 in Tartu. This is noteworthy because, so far, the university hospitals in Tartu and Badajoz have no restrictive hospital formulary, but the concept is followed without formal recognition. Nevertheless, the content of the top 10 list should be critically evaluated in all 3 hospitals. The increased use of metronidazole in Tartu and the very frequent use of cephalosporins in Badajoz and Huddinge are suitable topics for discussion on rational antibiotic pharmacotherapy in the respective clinics. One of the encouraging findings of this study was that injectable preparations in the study hospitals (45–53%) were used considerably less often than was reported for Germany (65%) and Italy (80%), but more often than in the UK (40%) (10). The proportion of parenteral formulations in Tartu had decreased from 53% to 48% by 1995.

Broad-spectrum antibiotics dominated in all departments in each of the 3 hospitals. Tetracyclines and aminoglycosides were the antibiotics used most commonly in Tartu, broad-spectrum penicillins and cephalosporins in Badajoz and narrow-spectrum penicillins and cephalosporins in Huddinge. The subgroup of cephalosporins together with or Huddinge, which could explain the high use of aminoglycosides in Tartu. This was a major difference between the...
hospitals studied, which can be attributed to the limited financial resources available in Estonia.

The increase in antibiotic consumption in Tartu from 41 to 48 DDD/100 bed-days from 1992 to 1995 is in line with the worldwide yearly increase in the use of pharmaceuticals by 8–10% (1). The most popular antibiotic drugs in the Tartu University Hospital were doxycycline and ampicillin, which ranked first and second respectively throughout the study years. This is in accordance with the data from national use of drugs in countries of central and eastern Europe (8), where doxycycline headed the lists in Bulgaria, Estonia and Hungary, and ampicillin ranked between third and fifth in all countries studied in 1992.

Frequent use of aminoglycosides in Tartu University Hospital (accounting for 19–24% of antibiotics in 1992–1995) is in line with their proportion of 5% among all antibiotics used in Estonia during the years under study (unpublished data). High aminoglycoside consumption has been known to select multiresistant bacteria (2, 11), which might be of concern for the university hospital in Tartu, Estonia. Significant associations have also been established between the consumption of cephalosporins and methicillin resistance in staphylococci (12), a potential problem for the university hospital in Tartu. Estonia. Significant associations have also been established between the consumption of aminoglycosides and methicillin resistance in staphylococci (12), a potential problem for the university hospitals in Badajoz and Huddinge. In addition, development of fluoroquinolone resistance in staphylococci and Pseudomonas aeruginosa has been reported (3). No access to microbiological data was available in this study and thus the antibiotic selection preferences could not be compared with the bacterial sensitivity patterns. Nevertheless, it is difficult to believe that different selection patterns of antibiotic drugs in the study hospitals could be based on microbiological data only.

The use of the DDD methodology provides data that are standardized to allow comparisons between various drugs and among different wards, hospitals or countries. This method is useful when direct data from patient records are difficult to obtain or when rapid estimation is desirable. Certain problems with the data presented here are apparent. It has been estimated that up to one-third of hospitalized patients receive therapy with 2 or more antibiotics at the same time (5, 10). The DDD method does not give any information on the possible combination strategies, which may be of importance in the context of possible misuse and overuse of antibiotics. Thus, the data presented here cannot be used alone to judge the clinical appropriateness of antibiotic therapy. Despite these limitations, this approach allows a general overview of antibiotic use in a hospital setting, i.e. estimation of the risk of selecting resistant bacteria. The information concerning the use of antibiotics over time can help to identify inconsistencies, improve awareness of drug use and serve as a basis for more in-depth or intervention studies.

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