Research articles

REPEATED PREVALENCE STUDIES ON ANTIBIOTIC USE IN LATVIA, 2003-2007

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Antibiotic resistance and nosocomial infections have recently been recognised as a growing threat in Latvian hospitals. We used a modified point prevalence study design to gain accurate information on the antibiotic prescription pattern and the prevalence of nosocomial infections in different hospital departments. A given department was observed on a given day in a given month (May) five years in a row. All antibiotic treatments, dose and route of administration were recorded, in addition to demographic data. The most commonly used antibiotic groups were first generation cephalosporins (35.6-38.9%), broad-spectrum penicillins (17.5-23.0%), fluoroquinolones (8.4-14.5%) and aminoglycosides (7.7-12.6%). Cefazolin was the most commonly used antibiotic. Antibiotics were predominantly used intravenously. The proportion of oral administration varied from 15.1% to 21.8%. A large proportion (13.3%) of the antibiotics was administered without clear reason. The crude prevalence rate of infection treated with antibiotics was 19.3%. The average prevalence of nosocomial infections was found to be 3.6%. These prevalence studies provided an opportunity to compare hospitals and outline variations and problem areas. They indicated the main problems in antibiotic prescription: large interhospital variations in the choice of an antibiotic for the most common infections, frequent antibiotic use without clear reason, and predominant intravenous administration.

Introduction

Antibiotics are one of the most frequently used drugs in outpatient and inpatient care and their use is considered to be an important risk factor for the development and spread of antimicrobial resistance [1]. During the past two decades, resistance to antibiotics has become a major public health concern due to the rapid spread of multiresistant bacterial clones and decreasing availability of new antibacterial drugs [2,3].

Consumption in hospital care accounts for only 5-15% of the total exposure to antibiotics in European countries [4,5]. Nevertheless, hospitals are considered to be the centre of antimicrobial resistance due to high density of broad-spectrum antibiotic use in a particularly vulnerable patient population.

Therefore efforts to encourage prudent antibiotic use are a high priority. Benchmarking of antibiotic use is an important prerequisite for the control of antibiotic use.

Repeated point prevalence studies of nosocomial infections have been performed in several countries [6-11]. In spite of its shortcomings, this methodology is used as a tool for internal quality control and often preferred over prospective surveillance or aggregated data collection. In several recent studies, the point prevalence approach, simply selecting the patients that received an antibiotic therapy, was used to assess the prevalence of antibiotic use and to evaluate how appropriate the therapy was [12-15]. This simplified approach was less time consuming and, in addition, provided an opportunity to collect individual patient data on the prevalence of treated infections, dose of antibiotic, administration route, frequency, indication and main demographic data.

The aim of this study was to estimate the prevalence and pattern of antibiotic use in the largest Latvian hospitals. Internet-based software provided an opportunity for each hospital to get immediate feedback on their hospital data.

Methods

Five consecutive point prevalence studies were repeated annually from 2003 to 2007. We performed repeated point prevalence studies on antibiotic use in 16 selected Latvian hospitals. All hospitals participated on a voluntary basis and considered the study as an opportunity for quality control. In each hospital, the study was carried out by the same trained physician. Data were collected on Tuesdays, Wednesdays and Thursdays in May. Each department had to be surveyed on one day. All patients who were hospitalised at 8 am of the survey day and prescribed an antibiotic were included in the study. The patient charts were reviewed and anonymous data were collected using a standardised protocol which contained ward level and patient level data sheets. Ward level data included speciality of the ward, number of beds, the number of hospitalised patients and number of patients receiving antibiotics. Demographic data and duration of stay in hospital was collected for

each patient. The following prescription-related data were entered in the protocol: type of antibiotic, quantity (dose), frequency and route of administration, and indications or conditions for which antibiotics were given. If there was no evidence of infection or surgical prophylaxis was prolonged for more than 24 hours, the reason for antibiotic use was defined as unclear. The main source of information was the patient chart. If necessary, physicians and nurses were interviewed.

The percentage of antibiotic usage was calculated by the number of patients receiving an antibiotic per total number of hospitalised patients on the study day. Antibiotics were grouped according to the Anatomical Therapeutic Chemical (ATC) classification. Third and fourth generation cephalosporins, carbapenems, aminoglycosides and glycopeptides were additionally defined as hospital-specific antibiotics (HSA).

Infections were defined by the trained physician carrying out the survey according to clinical presentation and did not have specific definition criteria [12]. The prevalence of treated infections was calculated as a percentage of number of infections per total number of the hospitalised patients on the study day. Nosocomial infections were defined as infections that occurred more than 48 hours after hospitalisation. The study questionnaire and protocol were available on the study website (<http://www.abresistance.lv/imed/login.jsp>) and did not change over the study period.

Data from 2003 and 2004 were entered using EpiData 3.02 software. In 2005, a web-based database was designed. Since then all data have been entered online, and the hospital level results were available immediately after data entry. Each hospital was responsible for data entry themselves. Before complete analysis for

TABLE 1

Characteristics of the 16 hospitals participating in the study, Latvia, 2003-2007

Hospital	Participation in prevalence studies	Number of patients [mean $\pm$ (SD)]	Level	proportion of surgical patients [%]	proportion of intensive care patients [%]
A	2003-2007	914.4 (38.1)	Tertiary	40.3 ^c	4.80 ^c
B	2005-2007	656.3 (96.7)	Tertiary	39.2 ^c	3.01 ^c
C	2005	136	Regional	47.1 ^b	ND
D	2003-2005	486 (23.6)	Regional	43.1	4.15
E	2003-2007	356 (24.2)	Regional	35.3 ^c	2.60 ^c
F	2004-2006	414.3 (104.6)	Specialised	5.7 ^b	0.44 ^b
G	2003-2005, 2007	272.5 (42.2)	Regional	38.1 ^c	5.08 ^c
H	2005	257	Regional	35.8 ^b	3.9 ^b
I	2005, 2007	130 (7.1)	Specialised	0 ^c	1.60 ^c
J	2003-2007	250.4 (31.4)	Specialised	99.2 ^c	0.80 ^c
K	2003-2005, 2007	504.5 (100.8)	Children	33.2 ^c	10.05 ^b
L	2003-2005, 2007	397 (83.0)	Specialised	0 ^c	0 ^c
M	2007	131	Specialised	20.6 ^c	0.76 ^c
N	2007	191	Specialised	45.0 ^c	0.52 ^c
O	2007	160	Children	0 ^c	2.50 ^c
P	2004	122	Regional	40.2 ^a	1.6 ^a

Data from year ^a2004, ^b2005, ^c2007.

ND: not determined; SD: standard deviation.

TABLE 2

Summary of antibiotic treatment and prevalence of infection for all study sites, Latvia, 2003-2007

	2003	2004	2005	2006	2007
No. of hospitals involved	7	9	12	5	11
No. of patients admitted	3,150	3,774	4,800	2,657	3,843
No. of patients with antibiotics (%) (95% CI)	845 (26.8) (25.3-28.4)	938 (24.8) (23.5-26.2)	1,385 (28.6) (27.3-29.9)	690 (26.0) (24.3-27.7)	1,038 (27.0) (25.6-28.4)
No. of antibiotics used per 100 patients (95% CI)	34.8 (33.2-36.5)	32.7 (31.2-34.2)	38.4 (37.0-39.8)	33.5 (31.7-35.3)	34.5 (33.0-36.1)
Prevalence of infections (95% CI)	17.3 (16.0-18.7)	19.8 (18.6-21.1)	22.0 (20.8-23.2)	16.4 (15.0-17.8)	18.8 (17.6-20.1)
Prevalence of community-acquired infections (95% CI)	13.4 (12.3-14.6)	15.9 (14.7-17.1)	18.8 (16.3-21.4)	12.7 (11.4-14.0)	15.3 (14.2-16.4)
Prevalence of nosocomial infections (95% CI)	3.9 (3.3-4.6)	4.0 (3.4-4.6)	3.1 (2.7-3.7)	3.7 (3.0-4.5)	3.5 (3.0-4.2)

CI: confidence interval.

scientific publication, a data check was done by an independent data manager.

Data were analysed using the SPSS 15.0 software package. Trends over time were examined using linear regression analysis. The study protocol was accepted by the local ethical committee.

Results

Five annual point prevalence studies were performed since 2003. The characteristics of the study hospitals are displayed in Table 1. The number of participating hospitals was not constant throughout the study period and varied from 7 hospitals in 2003 to 12 hospitals in 2006. A total of 18,226 patients were surveyed

during the studies and their number varied from 2,657 to 4,800 by year (Table 2).

Across all study hospitals and all years, 6,389 antibiotic doses/courses were prescribed for 4,883 patients. The proportion of patients on antibiotics varied among all patients from 24.8% in 2004 to 28.6% in 2005 with high variability between hospitals (Table 1, Figure 1). On average 35.1 antibiotic treatments per 100 patients (median 38.0) were prescribed. Most patients received one antibiotic (72.7% in 2003, 71.2% in 2004, 69.1% in 2005, 71.3% in 2006, and 73.7% in 2007). The rest received a combination therapy of two or more antibiotics.

The pattern of antibiotic use

More than 40 different antibiotics were used. Twelve antibiotics in 2003, 15 in 2004, 14 in 2005, 11 in 2006 and 16 in 2007 constituted 90% of all antibiotic use.

The cephalosporins (35.6-38.9%), penicillins (17.5-23.0%) fluoroquinolones (8.4-14.5%) and aminoglycosides (7.7-12.6%) were the most commonly used antibiotic groups. The most common antibiotic subgroups were first generation cephalosporins (J01DB) (22% of all administered antibiotics), broad-spectrum penicillins (J01CA) (12.9%), other aminoglycosides (J01GB) (10.7%), third generation cephalosporins (J01DD) (10.6%), metronidazole (J01XD) (10.3%) and fluoroquinolones (J01MA) (10.2%). Cefazolin was the single most commonly used antibiotic in general. In some hospitals, ampicillin, co-amoxiclav or ceftriaxone were the most frequently prescribed drugs.

Use of hospital-specific antibiotics (HSA)

A total of 1,549 (24.2%, 95% confidence interval (CI): 23.2-25.2) prescriptions recorded during the study period were classified as prescriptions of HSA. There was a significant increase in consumption of over that period. The number of HSA prescribed per 100 patients increased from 7.4 in 2003 to 9.5 in 2007 ($p < 0.05$). The proportion of HSA among all prescribed antibiotics increased from 21.4% in 2003 to 27.6% in 2007 ($p < 0.05$).

Indications for antimicrobial therapy

Infection

The most frequent indication for antibiotics was infection (69%). The prevalence of infections treated with antibiotics varied from 17.0% to 22.0% ($p < 0.05$) across the study years, with the highest prevalence in 2005 (see Table 2).

The mean percentage of nosocomial infections treated with antibiotics was 3.6% (median 3.0%), but in five hospitals, the prevalence of nosocomial infections exceeded 6%. The highest mean prevalence of nosocomial infections were found in the large multidisciplinary teaching hospitals (4.5%, 95% CI: 4.0-5.0) and paediatric hospitals (4.0%, 95% CI: 3.4-4.5) (Figure 2). The most frequently reported nosocomial infections were lower respiratory tract infections 23.1% (20.3-30.0%) and surgical site infections 26.5% (19.1-32.0%). Fever of unknown origin with significantly increased C-reactive protein levels accounted for 13.9% of nosocomial infections. Nosocomial urinary tract infection, gastrointestinal infection and bacteriologically confirmed bloodstream infection were recorded in lower numbers (9%, 4% and 7%, respectively).

FIGURE 1

Mean number of patients receiving antibiotics with maximal and minimal annual variations, Latvia, 2003-2007

Hospitals C, H, M, N, O and P participated in the study only once.

FIGURE 2

Prevalence of treated infections and variations between hospitals according to hospital size and specialisation, Latvia, 2003-2007

Surgical prophylaxis

Of the total of 6,389 antibiotic courses, 785 (12.3%; 95% CI: 10.34-14.23) were prescribed for surgical prophylaxis. Cefazolin was the most commonly used drug and accounted for 58.6-80.5% of all prescriptions for surgical prophylaxis per year. Cefuroxime (5.2-11.7%), gentamicin (4.51-11.0%) and metronidazole (3.01-10.1%) were also used frequently.

Unclear use

Only a small proportion of antibiotics were used for medical prophylaxis. According to the investigators' observations, a large proportion, 13.3% (95% CI: 11.3;15.3), was administered without clear reason (16.9% in 2003, 9.9% in 2004, 9.9% in 2005, 19.4% in 2006, and 14.1% in 2007). Cefazolin was the antibiotic most often used without clear reason (mean 27.2%, 95% CI: 24.2-30.2). Metronidazole, ampicillin, and ceftriaxone were also often used without clear reason. In addition, an increase in the unclear use of ceftriaxone and metronidazole ($p < 0.05$) was reported during the study period.

The route of administration

Antibiotics were most predominantly used intravenously (77.4%, 95% CI: 76.3-78.4) with a much smaller proportion of oral use (17.1%, 95% CI: 16.2-18.0). The proportion of oral use varied from 21.8% of all prescriptions in 2003 to 15.1% in 2006. The total intramuscular administration of antibiotics decreased from 8.2% in 2005 to 1.1% in 2007.

Discussion

Surveillance of antibiotic use and subsequent feedback to the staff could help to increase treatment quality, decrease the risk of antibacterial resistance and reduce unnecessary treatment costs.

The selection of the hospitals could be biased because the presence of a trained specialist in infectious diseases or clinical microbiology was defined as a precondition for participation. Many hospitals in Latvia did not employ such specialists. Nevertheless, nearly all largest regional hospitals participated in the study, and therefore, all regions of the country were represented in the study sample. The same protocol and data entry system was used in all hospitals and the study was performed by the same person over the years. It was therefore possible to compare the data longitudinally as suggested by earlier investigations [16-18].

In our study, 26.8% of hospitalised patients received antibiotics. This was less than reported in prevalence studies in Brazil [19], China [20], Greece [6], Italy [7,21], Malaysia [22], and Turkey [23] but significantly more than in German hospitals (17.7%) [18]. The proportion of patients on antibiotics in the study was similar to observed rates in Estonia [13], Lithuania [13] and the Netherlands [9], Scotland [24] Sweden [12]. Antibiotic consumption rates in hospitals in Latvia would therefore appear to be similar to what is observed in Northern and Central European countries.

There was a very high variability in the rates of antibiotic use between the hospitals investigated (see Figure 1). In 2007 for example, the proportion of patients on antibiotics varied from 5.3 to 44.4%. This variation could be due either to a different mixture of patients or to different treatment practices.

Cephalosporins were most commonly used antibiotic group in Latvian hospitals, with cefazolin being the most commonly used antibiotic. We could not find any clear explanation for its

widespread use in Latvia because it did not provide any obvious cost benefit or treatment rationale.

The use of HSA was higher in Latvia than observed in other European countries (average 10%) [4] and increased from 21.4% in 2003 to 27.6% in 2007. Previously published studies indicate that extensive use of HSA may facilitate the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA), extended spectrum beta-lactamase (ESBL)-producing Gram-negative bacteria and selected resistance in *Streptococcus pneumoniae* [2,25].

Almost 70% of all antibiotics were prescribed for treatment of infection, but 13.3% were used without defined reason. 12.3% of the antibiotics were used for surgical prophylaxis and that was similar to the proportion observed in other studies (14-42%) [12,13,22,26].

The crude percentage of infections treated with antibiotics was 19.3%. The prevalence of nosocomial infections was 3.6%, which is similar to other studies with comparable study design: In Swedish hospitals, the prevalence of all infections in 2003 and 2004 was found to be 17% and 18%, respectively [12], and in the Netherlands in 2004 it was 16.7% [9]. Nevertheless, the prevalence of nosocomial infections in those years was higher in Swedish studies (9.2% and 9.4%) than in our study. The overall prevalence of nosocomial infections was lower in our study than in most other studies [6,10,15,23,26]. This difference could be explained by differences in patient profile, length of hospitalisation and local health systems. We also observed significant variations of nosocomial infection rates over the years in some hospitals (Figure 2) for which we could not find an explanation.

Our study had several limitations regarding the detection of nosocomial infection. The approach of studying patients that receive antibiotics could have a relatively low sensitivity in finding nosocomial infections in certain patient populations [27,28]. Case definitions did not contain specific criteria and contained information only on what organs were affected. We relied only on the participating physician and his judgement. However, the study was performed by a well trained consultant specialist, and it was always the same person who collected the data over the years. Therefore, we believe in the consistency and good quality of their judgement. In addition, our first Latvian prevalence study for nosocomial infections that was performed on all hospitalised patients in 2001 using British National Survey definitions revealed very similar results [29].

Relatively low prevalence rates of nosocomial urinary tract and bloodstream infection compared with the high percentage of fever of unknown origin with significantly increased C reactive protein levels could indicate an insufficient clinical and laboratory capacity to identify these infections.

Oral use of antibiotics has been considered as a sufficient alternative even in hospitalised patients. It also reduces the risk of catheter-related infections, staff labour and costs. The proportion of intravenous use antibiotics found in Latvian hospitals was alarmingly high. Educational interventions to reduce intravenous and intramuscular use were taking place in several hospitals during the study period, but our data did not report any improvement except for a reduction in intramuscular use. Nevertheless, we can conclude that point prevalence studies can be used as simple approach to assess the efficacy of such educational interventions.

Each hospital could obtain an analysis of their data in the form of graphs immediately after the data entry was done. This option provided immediate feedback for the participants to plan educational activities based on the results of the study. Several interventions that were aimed at better antibiotic prescription and prevention of nosocomial infections were implemented during the study period in the participating hospitals. Nevertheless, our data did not reveal any significant improvements in our study endpoints after the period of five years. However, all participating hospitals achieved significant reductions in MRSA bacteraemia rates (EARSS, unpublished individual Latvian hospital data) over the study period, which might be partly related to the impact of repeated point prevalence surveys.

Point prevalence studies were considered mainly as a quality control exercise, but at the same time they provided useful information for further studies and targeted interventions. We consider point prevalence studies as an efficient, cheap and not very time-consuming measure for evaluation of antibiotic use in hospitals.

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