Point Prevalence Survey on Antibiotic Use in a Croatian Infectious Disease Hospital

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Abstract:

Antibiotic use is the driving force for increasing antibiotic resistance. A large proportion of antibiotics in hospitals are used inadequately. The objective of this study was to evaluate antibiotic use at the Hospital for Infectious Diseases through point-prevalence surveys conducted in 2006, 2008 and 2009.

Point prevalence surveys were part of the European Surveillance on Antimicrobial Consumption (ESAC) Hospital Care Subproject and patients` data were collected following ESAC protocol. Additionally, the adequacy of antimicrobial therapy and

administration of the first line antibiotic according to the local guidelines were assessed by an infectious disease doctor and a clinical microbiologist.

In the study period among the 599 patients admitted to hospital, 352 (58.8%) received antibiotics. Out of 448 antimicrobial treatments, 313 (69.9%) were administered parenterally and 135 (30.1%) orally. Altogether in years 2006, 2008 and 2009 the most commonly prescribed antibiotics were ceftriaxone (19.9%), co-amoxiclav (15.4%), ciprofloxacin (12.3%), narrow spectrum penicillins (6.5%) and penicillinase resistant penicillins (5.6%). Most (82.6%) of the treated infections were community acquired infections. The predominating diagnoses were urinary tract infections and infections with no primary site defined, followed by skin, soft tissue and bone and joint infections. The overall adequacy of antimicrobial therapy was > 90% and the first line antibiotic according to the local guidelines was administered with high frequency for central nervous system and cardiovascular infections (100%), and low for ear, nose and throat infections, urinary tract infections, lower respiratory tract and bone and joint infections (23.0%, 51.6%, 52.5%, 65.0%, respectively) which indicates a significant overuse of antibiotics for diagnoses listed.

The results of an individual PPS provided reliable and representative data for the hospital.
Point-prevalence surveys proved to be a valuable method for detecting targets for antibiotic prescribing improvement and they clearly showed that our local hospital guidelines offered too many choices of antibiotic treatment for each clinical indication and needed revision.

Keywords: Antimicrobial consumption; Croatia; Point prevalence surveys

Introduction

Irrational and extensive antibiotic use is one of the factors that has led to an increase in antibiotic resistance which became a major public health challenge at local, national and international levels [1,2,3,4]. It was reported that 20 – 50 % of antimicrobial use in human population is inappropriate [5,6], and estimated that more than 50% of antibiotic prescriptions in the United States may be inappropriate considering the drug choice, dose adequacy, duration of therapy or route of administration [2,7,8]. Although hospital antibiotic consumption accounts for 5 – 15 % of the overall antibiotic exposure in the European countries, hospitals are held responsible for the increase of resistance due to high use of broad spectrum antibiotics [9,10,11,12,13].

Antimicrobial resistance control measures are commonly perceived to lead to an improvement in quality of prescribing, cost-effectiveness and reduction in resistance. Several different approaches have been proposed to reduce antibiotic resistance. Besides continuous education of physicians, control of antibiotic prescribing and better infection control practices are thought to be the most important measures. One of the frequently used surveillance methods for internal quality control in antibiotic prescribing is a point prevalence survey (PPS) of antibiotic use in hospitals. It is used to evaluate the prevalence of antibiotic use and the appropriateness of antibiotic therapy [14,15,16,17,18,19].

The aim of this study was to evaluate the prevalence and patterns of antimicrobial prescribing for main indications at the Zagreb University Hospital for Infectious Diseases. We also tried to assess the adequacy of antimicrobial treatment and compliance with local guidelines for the management of infectious diseases.

Materials and methods

The Hospital

The University Hospital for Infectious Diseases is a 232 – bed hospital with seven medical and three paediatric wards. It is the national referral hospital for infectious diseases, in particular for patients with AIDS, hepatitis, urinary tract infections and tropical and travel diseases. It is also the reference center for antibiotic resistance surveillance. The hospital has one 12- bed adult intensive care unit (AICU) and one seven bed paediatric intensive care unit (PICU). The AICU also contains six post intensive care beds and antibiotic consumption data are reported for the combined ICU and post ICU ward. PICU is also a part of the 21- bed paediatric ward and antibiotic consumption data for PICU cannot be separated from the rest of this paediatric ward. The number of admissions for the whole hospital was 7599 in 2006, 7351 in 2008 and 7198 in 2009, and bed occupancy was 69651 in 2006, 70106 in 2008 and 68855 in 2009.

Data collection

The PPS on antibiotic consumption was done in 2006, 2008 and 2009, as a part of the European Surveillance on Antimicrobial Consumption (ESAC)-2 and ESAC-3 Hospital Care Subproject. In 2006 the software used for data entry was based on Swedish STRAMA software whilst in 2008 and 2009 the ESAC web-based survey program (WebPPS) was developed by ESAC. The protocol used in ESAC-2 survey was similar to that used in ESAC-3 PPS 2008 and ESAC-3 PPS 2009 [20]. The survey in our hospital was carried out by a microbiologist and an infection control nurse who collected the required data by examining patients' notes available at the ward. For the purpose of this study the adequacy of applied treatment as well as the proportion of treatments matching the first line antibiotic recommended by the local guidelines were assessed. This was evaluated by a team consisting of an infectious disease doctor and a clinical microbiologist. Therapy was recorded as adequate if it covered an expected or proven pathogen at the specific site of infection. The use of the first choice antimicrobial according to the local guidelines was used as a marker of compliance with the local guidelines. Compliance with the first line antibiotic according to the local guidelines was assesed administratively irrespective of the presence or absence of conditions that might require second line antibiotics.

All inpatients receiving antimicrobials for treatment or prophylaxis present at 8 am in the hospital on the day of the audit were included in the survey. It took two days for each PPS to audit all wards. Antibiotics belonging to the J01, J02, P01AB and J04AB02 according to The Anatomical Therapeutic Chemical（ATC) classification by the WHO Collaborating Centre for Drug Statistics were recorded and included in the survey [21]. Rifampicin was recorded for any indication but tuberculosis.

For each patient receiving antibiotic treatment, demographic data, antibiotic treatment, dosage and route of administration, anatomical site of infection or target for prophylaxis according to the list of provided diagnosis groups, indication for therapy (community or hospital acquired infection, medical or surgical prophylaxis) and indication for given therapy stated in medical records was recorded on the patient form. The existence of relevant culture before therapy was recorded in 2006 and 2008.

Guidelines for antibiotic use

In the year 2000 a pocket formulary for prophylaxis and treatment of infectious diseases was issued by the Croatian Society for Chemotherapy [22]. The manual was distributed to every physician in the hospital and was used as the reference guideline in our survey. The formulary includes recommendations for the first and second line antibiotics for defined clinical indications.

Statistics

Descriptive statistical methods were used in order to assess frequency distributions, and cross tabulations. For testing the statistical significance of the difference of categorical variables' distributions between two groups, non-parametric chi-square analytic tests were performed. In case of three or more groups, the Kruskal-Wallis non-parametric test was performed. Furthermore, where needed (the number of cases less than 5 in a number of strata) the Fisher`s exact test was performed.

Results

Patients

Altogether in three PPSs, performed in the years 2006, 2008 and 2009, a total of 599 patients were evaluated (471 adults and 128 children). Out of them, 352 (58.8%) received antimicrobials with 271 (76.9%) receiving one, 68 (19.3%) receiving two, 11 (3.1%) receiving three, and two (0.6%) patients receiving four antimicrobials. Their mean age was 51,23 (CI= 48.81-53.66), and median age 57 years. Out of 352 patients receiving antimicrobials, 186 (52.8%) were males. There were no statistically significant yearly differences according to sex (chi-square=2.030, df=2, p=0.362). Out of the total of 352 patients receiving antibiotics, 144 (40.9%) patients were ≥65 years old, 144 (40.9%) patients were aged between 18-64 years and 64 (18.2%) patients were <18 years old.

Antibiotic use

Out of 98 patients treated in ICU, 37 (37.8%) received antibiotics. In medical wards 304 (64.5%) out of 471 adult patients were given antibiotics. Out of 128 patients admitted to paediatric wards, 48 (37.5%) received antimicrobials. In PICU 16 (37.2%) out of 43 children underwent antibiotic therapy.

Out of 448 antimicrobial treatments, 313 (69.9%) were administered parenterally and 135 (30.1%) orally. The proportion of patients receiving antibiotics per type of department and per year is shown in Table 1 together with characteristics related to antibiotic treatment, such as route of administration, percentage of monotherapy, the existence of relevant culture before therapy and explained reasons for the given therapy recorded in patients' notes.

Table **1**. Patients` data.

	2006	**2008**	**2009**	**Total**	**Difference among study periods *(P<0.05)***
No. of patients admitted	184	227	188	599	
No. of patients on antibiotic (% of patients admitted)	108 (58.7)	132 (58.1)	112 (59.6)	352 (58.8)	0.956
No. of paediatric patients admitted (% of patients admitted)	37 (20.1)	61 (26.9)	30 (15.9)	128 (21.4)	0.023
No. of paediatric patients on antibiotic (% of paediatric patients admitted)	14 (37.8)	20 (32.8)	14 (46.7)	48 (37.5)	0.810
No. of adult	147 (79.9)	166 (73.1)	158 (84.0)	471 (78.6)	0.023

patients admitted (% of patients admitted)					
No. of adult patients on antibiotic (% of adult patients admitted)	94 (63.9)	112 (67.5)	98 (62.0)	304 (64.5)	0.810
No. of patients admitted at PICU* (% of paediatric patients)	10 (27.0)	23 (37.7)	10 (33.3)	43 (33.6)	0.554
No. of PICU patients with antibiotic (% of PICU patients)	6 (60.0)	6 (26.1)	4 (40.0)	16 (37.2)	0.176
No. of patients admitted to AICU** (% of adult patients)	13 (8.8)	27 (16.3)	15 (9.5)	55 (11.7)	0.072
No. of AICU patients with	6 (46.2)	9 (33.3)	6 (40.0)	21 (38.2)	0.726

antibiotic (% of AICU patients)					
Percentage of females*** (%)	61 (56.5)	63 (47.7)	42 (37.5)	166 (47.2)	0.362
Parenteral route (%)	77 (59.7)	131 (74.0)	105 (73.9)	313 (69.9)	0.002
Monotherapy (%)	88 (81.5)	97 (73.5)	86 (76.8)	271 (76.9)	0.341
Relevant culture before therapy (%)	114 (88.3)	127 (71.8)	/	241 (78.8)	<0.001
Reason for therapy stated in patients` notes (%)	96 (74.4)	158 (89.2)	131 (92.3)	385 (85.9)	<0.001

*PICU = paediatric intensive care unit

**AICU = adult intensive care unit

*** of patients receiving antimicrobials

Indication for therapy

Most (82.6%) of the treated infections were community acquired infections. Hospital acquired infections accounted for 12.9% of all infections, and medical prophylaxis accounted for only 4.5%. There were no statistically significant differences in indications for antimicrobial therapy according to year of PPS (chi-square=6.78, df=4, P=0.148) (Table 2).

Table **2**. Indications for antimicrobial therapy.

Indications for therapy	**2006 (%)**		**2008 (%)**		**2009 (%)**		**Total (%)**	
Community acquired infections	107 (82.9)		142 (80.2)		121 (85.2)		370 (82.6)	
HCAI* 1	0	13 (10.1)	4 (2.3)	30 (17.0)	3 (2.1)	15 (10.6)	7 (1.5)	58 (12.9)
HCAI* 2	6		6 (3.3)		1 (0.7)		13 (2.9)	
HCAI* 3	2		0		2 (1.5)		4 (0.8)	
HCAI* 4	0		4 (2.3)		4 (2.8)		8 (1.8)	
HCAI* 5	5		16 (9.0)		5 (3.5)		26 (5.8)	
Medical prophylaxis	9 (7.0)		5 (2.8)		6 (4.2)		20 (4.5)	
Total	129		177		142		448	

*HCAI = health care associated infections

Diagnoses leading to antibiotic use

The proportion of diagnoses leading to antibiotic use is shown in Figure 1.
In 2006, 2008 and 2009 the most frequent diagnosis groups were SSTBJ, UTI and NDS, respectively. The differences in diagnosis group distribution according to year of PPS were statistically significant (chi-square=17.82, df=8, **P=0.022**).

Figure 1. The proportion of diagnoses leading to antibiotic use

The proportion of antibiotics used

As shown in Figure 2, the top five ranking antibiotics for the three PPSs were ceftriaxone (19.9%), co-amoxiclav (15.4%), ciprofloxacin (12.3%), narrow spectrum penicillins - benzylpenicillin, benzathine benzylpenicillin, procaine benzylpenicillin (6.5%) and penicillinase resistant penicillins - cloxacillin, flucloxacillin (5.6%). There were no statistically significant differences between the years when looking at the whole panel of antibiotics used (Kruskal Wallis chi square=0.784, df=2, P=0.676), or the first ten antibiotics (Pearson chi-square=1.131, df=18, P=0.568), or even the top five antibiotics (Pearson chi-square=13.160, df=8, P=0.106).

Figure 2. The ranking of antibiotics used

Antibiotics per clinical diagnosis

There was a statistically significant difference according to year in antibiotic administration for the top three antibiotics used for UTI (Chi-square=16.55, df=6, **P=0.011**). The most frequently used antibiotic in 2006 and 2008 was co-amoxiclav and in 2009 ceftriaxone.

There was no statistically significant difference by year in antibiotic administration for the top three antibiotics used for NDS (Fisher`s exact test P=0.254). The most frequently used antibiotics in all three years were ceftriaxone and co-amoxiclav.

There was no statistically significant difference by year in antibiotic administration for the top three antibiotics used for SSTBJ (Fisher`s exact test P=0.767). The most frequently used antibiotics in all three years were narrow spectrum penicillins.

There was no statistically significant difference by year in antibiotic administration for the top three antibiotics used for GI (Fisher`s exact test P=0.696). The most frequently used antibiotic in all three years were ciprofloxacin and ceftriaxone.

There was no statistically significant difference by year in antibiotic administration for the top three antibiotics used for respiratory tract infections (Fisher`s exact test P=0.462). The most frequently used antibiotics in all three years were co-amoxiclav, azithromycin and ceftriaxone. In respiratory tract infections, as well as in GIT infections we excluded medical prophylaxis (co-trimoxazol and fluconazole, respectively).

Adequacy of antimicrobial therapy and compliance with the local guidelines

Table 3. Adequacy of antimicrobial therapy and administration of the first line antibiotic according to the local guidelines

Diagnosis group* (No.)	First line antibiotic (%)	Adequate (%)
CNS (35)	100	100
ENT (22)	23	40.8
RESP (55)	52.5	98.5
CVS (10)	100	100
GI (59)	71	100
SST (59)	83	91
BJ (24)	65	100
UTI (95)	51.6	100
GUOB (1)	100	100
NDS (88)	34	97.7

* abbreviations are the same as in Figure 1

Discussion

Prevalence studies on antibiotic prescribing in hospitals report different proportions of patients receiving antibiotics with rates varying between 17 - 51% [15,17,18,19,23,24,25,26]. This study analyzed antimicrobial drug use in an infectious disease hospital and a high proportion of patients on antibiotics (approx. 60% in all three PPSs together) was expected. The three PPSs done in the same hospital revealed a very similar structure of patients admitted, a similar proportion of patients on antibiotics (Table 1) and a similar distribution of indications for therapy (Table 2) suggesting that the results of an individual PPS provide reliable and representative data for the hospital.

Like in other reported studies no statistically significant differences by sex were noted [15,16,17,19,28]. A higher proportion of patients on antibiotics was recorded among adult (65%) than among paediatric (37.5%) patients which suggests that childhood viral infections are more common reason for admission to hospital than bacterial infections. Surprisingly the proportion of patients receiving antibiotics in adult ICU (38%) was below the rate for adults in the whole hospital (65%). This suggests that although bacterial infections are a more common reason for admission to our hospital in adult population, viral infections more often require admission to AICU.

The predominance of the parenteral route (70%), as well as the high proportion of monotherapy (77%) is consistent with the findings of other authors and similar surveys [27,28]. Over the years there was an improvement in keeping records of reasons for antibiotic therapy stated in the patients`notes. This might be the consequence of a more detailed administrative tasks imposed by the national health insurance system since 2006. However, no decrease in the use of parenteral antibiotics or increase in relevant culture before therapy (Table 1) were recorded, both of which are continuous recommendations of the hospital professional board.

In this study, the community acquired infections present a higher proportion (83%) than the average recorded in the ESAC PPSs (66% in 2008, 62% in 2006)

[27,28]. Considering hospital profile, the domination of community acquired infections was not unexpected, although our hospital also admits patients for treatment of HCAI acquired in other hospitals. In all three PPSs, the same four diagnoses (UTI, NDS, SSTBJ, GI) were the most frequent diagnoses leading to antibiotic use, with variable ranking among them (Figure 1).

The most commonly prescribed antibiotics were ceftriaxone, co-amoxiclav and ciprofloxacin which is consistent with most of the findings of similar surveys conducted in other European countries [5,15,19,26,27,28,29]. Croatia is a country where penicillins represent the most frequently used antibiotic class in the hospitals and the proportion of the narrow spectrum penicillins is substantial [9]. In our hospital, the narrow spectrum penicillins were mostly used for skin and soft tissue infections.

During the PPS audit the most time consuming task was assessing the appropriateness of antibiotic therapy and it required a high level of expertise from the auditor. According to diagnosis and/or results of relevant cultures, it was possible to estimate if the therapy was adequately covering an expected or proven pathogen. However, reasons why first line antibiotics were not used were rarely stated in the notes. Hence, full compliance with the guidelines that offer numerous options for different kind of patients was difficult to assess without an interview with the attending physician which is even more time consuming and was not feasable in this study. Considering that all antibiotics were prescribed by infectious disease doctors it is not surprising that the rates of adequate treatment were very high for all categories of diagnosis. However, compliance with recommendations for first line antibiotic was low for some clinical indications, such as upper respiratory tract infections (ENT) (23%) and infections with no defined site (NDS) (34%) in particular, followed by lower respiratory tract and urinary tract infections (52% each) (Table 3). Ceftriaxone was largely used for the upper respiratory tract infections (50%) although this treatment option was not in the local guidelines at all. A shift towards a greater use of ceftriaxone was also recorded for UTI. This is a reflection of a general trend towards the increase in hospital use of the third generation cephalosporins in most European countries [9].

We also expected a greater proportion of narrow spectrum penicillins in the treatment of lower respiratory tract infections which would be in accordance with the local guidelines for patients with pneumonia < 65 years old and admitted to the hospital. The weakness of this study is that based on the methodology of data collection it was difficult to assess to what extent the deviation from the first line treatment was clinically justified. The majority of other similar studies have also showed low compliance rate with the local guidelines [17], but in the studies carried out in Norway, Switzerland or Israel the appropriateness of antibiotic use was reported at high rates (96% with positive bacteriological samples and 84% without; 71% and 80+/-9%, respectively) [26,30,31].

National guidelines on antibiotic use may be of great help for individual hospitals when writing or updating local guidelines. In 2007 the Croatian Intersectorial Coordination Mechanism (ICM) for antibiotic resistance control (Interdisciplinarna sekcija za kontrolu antibiotika, ISKRA) started writing national guidelines on prudent antibiotic use. This action was undertaken following the MATRA Pre-Accession Programme (MPAP) project „Antimicrobial resistance surveillance in human medicine" financed by the Dutch Ministry of Foreign Affairs. This project enabled a close collaboration between ISKRA and the Dutch Working Party on Antibiotic Policy (Stichting Werkgroep Antibiotica Beleid, SWAB) in the field of writing evidence based guidelines. So far, the Croatian national guidelines on MRSA treatment and control, urinary tract infections, sore throat and surgical prophylaxis have been published [32,33,34,35]. New ISKRA guidelines covering other clinical topics are underway. Based on the experience of PPSs conducted at the University Hospital for Infectious Diseases, ISKRA plans to extend a nationwide PPS on antibiotic use in hospitals. This study demonstrates that PPS is a useful tool for selecting areas that need improvement and performed nationwide could point out the topics that should have a priority in national guideline writing. Also PPS can be used as a tool to monitor the effect of interventions such as the introduction or revision of local or national guidelines [18,36].

Despite limitations of the study considering data on compliance, PPSs conducted in our hospital clearly revealed targets for quality improvement. It is important to find a way of data collection that is relatively simple and feasible in practice, so that a PPS can be conducted regularly as a simple and inexpensive method for monitoring and evaluation of antibiotic prescribing and use.

We conclude that there was no significant undertreatment of patients receiving antibiotics in our hospital but considering very low proportion of patients receiving first line antibiotic for upper respiratory tract infections, lower respiratory tract infections, infections with no defined site and urinary tract infections we presume there is a significant overuse of antibiotics for these indications. Therefore we intend to conduct a more detailed survey focusing on this problem. We also conclude that local guidelines for our hospital should be revised as they are offering too many choices of antibiotic treatment for each clinical indication.

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References

[1]Loeffler JM, Garbino J, Lew D, Harbarth S, Rohner P. Antibiotic consumption, bacterial resistance and their correlation in a Swiss university hospital and its adult intensive care units. *Scand J Infect Dis* 2003;35:843-50.

[2]Cooke FJ, Bryony DF, Lawson W, Jacklin A, Holmes A. Multidisciplinary hospital antibiotic stewardship: a West London model. *Clinical Governance: An International Journal* 2004;9:237-43.

[3]Goossens H, Ferech M, Vander Stichele R, Elseviers M, ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005;365:579–87.

[4]Bronzwaer SL, Cars O, Buchholz U, et al. A European study on the relationship between antimicrobial use and antimicrobial resistance. *Emerg Infect Dis* 2002;8:278-82.

[5]Usluer G, Ozgunes I, Leblebicioglu H, Turkish Antibiotic Utilization Study Group. A multicenter point-prevalence study: antimicrobial prescription frequencies in hospitalized patients in Turkey. *Ann Clin Microbiol Antimicrob* 2005;4:16.

[6]Hecker MT, Aron DC, Patel NP, Lehmann MK, Donskey CJ. Unnecessary use of antimicrobials in hospitalized patients. *Arch Intern Med* 2003;163:972-8.

[7]Jarvis WR. Preventing the emergence of multidrug-resistant microorganisms through antimicrobial use controls: the complexity of the problem. *Infect Control Hosp Epidemiol* 1996;17:490-5.

[8]Marr JJ, Moffet HL, Kunin CM. Guidelines for improving the use of antimicrobial agents in hospitals: a statement by the Infectious Diseases Society of America. *J Infect Dis* 1988; 157:869-76.

[9]Vander Stichele RH, Elseviers MM, Ferech M, Blot S, Goossens H, European Survaillance of Antibiotic Comsuption (ESAC) Project Group. Hospital consumption of antibiotics in 15 European countries: results of the ESAC Retrospective Data Collection (1997–2002). *J Antimicrob Chemother* 2006;58:159–67.

[10] Vander Stichele RH, Elseviers MM, Ferech M, Blot S, Goossens H, ESAC Project Group. European Surveillance of Antimicrobial Consumption (ESAC): Data Collection Performance and Methodological Approach. *Br J Clin Pharmacol* 2004;58:419–28.

[11]de With K, Bergner J, Bühner R, et al. Antibiotic use in German university hospitals 1998–2000 (Project INTERUNI-II). *Int J Antimicrob Agents* 2004;24:15–20.

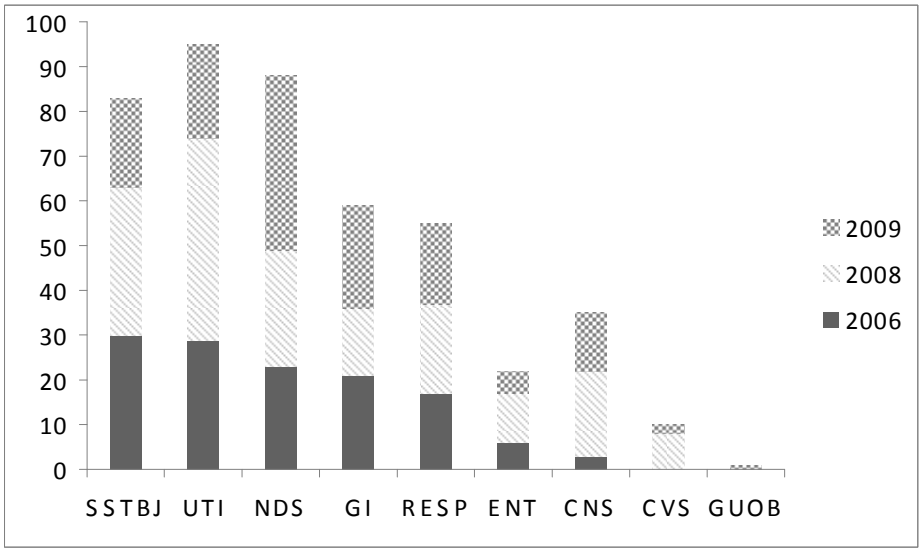
[12]Müller-Pebody B, Muscat M, Pelle B, Klein BM, Brandt CT, Monnet DL. Increase and change in pattern of hospital antimicrobial use, Denmark, 1997–2001. *J Antimicrob Chemother* 2004;54:1122–6.

[13]Kritsotakis EI, Gikas A. Surveillance of antibiotic use in hospitals: methods, trends and targets. *Clin Microbiol Infect* 2006;12:701–4.

[14]Ansari F, Erntell M, Goossens H, Davey P. The European surveillance of antimicrobial consumption (ESAC) point-prevalence survey of antibacterial use in 20 European hospitals in 2006. *Clin Infect Dis* 2009;49:1496-504.
[15]Dimiņa E, Kūla M, Caune U, et al. Repeated prevalence studies on antibiotic use in Latvia, 2003-2007. *Euro Surveill* 2009;14:19307.
[16]Vlahovic-Palcevski V, Dumpis U, Mitt P, et al. Benchmarking antimicrobial drug use at university hospitals in five European countries. *Clin Microbiol Infect* 2007;13:277–83.
[17]Yilmaz GR, Bulut C, Yildiz, Arslan S, Yetkin MA, Demiröz AP. Examining Antibiotic Use at an Education and Research Hospital in Turkey: Point Prevalence Results. *Turk J Med Sci* 2009;39:125-31.
[18]Seaton RA, Nathwani D, Burton P, et al. Point prevalence survey of antibiotic use in Scottish hospitals utilising the Glasgow Antimicrobial Audit Tool (GAAT). *Int J Antimicrob Agents* 2007;29:693–9.
[19]Ciofi Degli Atti ML, Raponi M, Tozzi AE, Ciliento G, Ceradini J, Langiano T. Point prevalence study of antibiotic use in a paediatric hospital in Italy. *Euro Surveill* 2008;13:19003.
[20]ESAC3 Hospital Care Subproject - Protocol Pan European Point Prevalence Survey 2009. http://app.esac.ua.ac.be/public/. Published 2010. Accessed September 2011.
[21]WHO Collaborating Centre for Drug Statistics Methodology. http://www.whocc.no/. Published 2011. Accessed September 2011.
[22]Schönwald S, Barsic B, Beus A, et al. *Priručnik za liječenje i sprečavanje infektivnih bolesti: džepni vodić*. Zagreb: Tisak; 2001.
[23]Fonseca LG, Conterno LO. Audit of Antibiotic Use in a Brazilian University Hospital. *Brazil J Infect Dis* 2004;8:272-80.
[24]Lee MK, Chiu CS, Chow VC, Lam RK, Lai RW. Prevalence of hospital infection and antibiotic use at a University Medical Center in Hong Kong. *J Hosp Infect* 2007;65:341-7.
[25]Gikas A, Pediaditisy J, Papadakis JA, et al. Prevalence study of hospital-acquired infections in 14 Greek hospitals: planning from the local to the national surveillance level. *J Hosp Infect* 2002;50:269-75.
[26]Berild D, Ringertz SH, Lelek M. Appropriate Antibiotic Use According to Diagnoses and Bacteriological Findings: Report of 12 Point-prevalence Studies on Antibiotic Use in a University Hospital. *Scand J Infect Dis* 2002;34:56-60.
[27]The ESAC PPS of patterns of antibiotic use in 50 European hospitals in 2008.
http://www.blackwellpublishing.com/eccmid19/abstract.asp?id=73988.
Published 2010. Accessed September 2011.
[28]Erntell M, Ansari F, Goossens H, Davey P. ESAC II Hospital Care Subproject 2005-2007: Patterns of Antibiotic Use in Relation to Diagnose in 19 European Hospitals in 2006, Point Prevalence Study (PPS). In: 17th European Congress of Clinical Microbiology and Infectious Diseases; March 31-April 4, 2007; Münich, GE. Abstract O166.

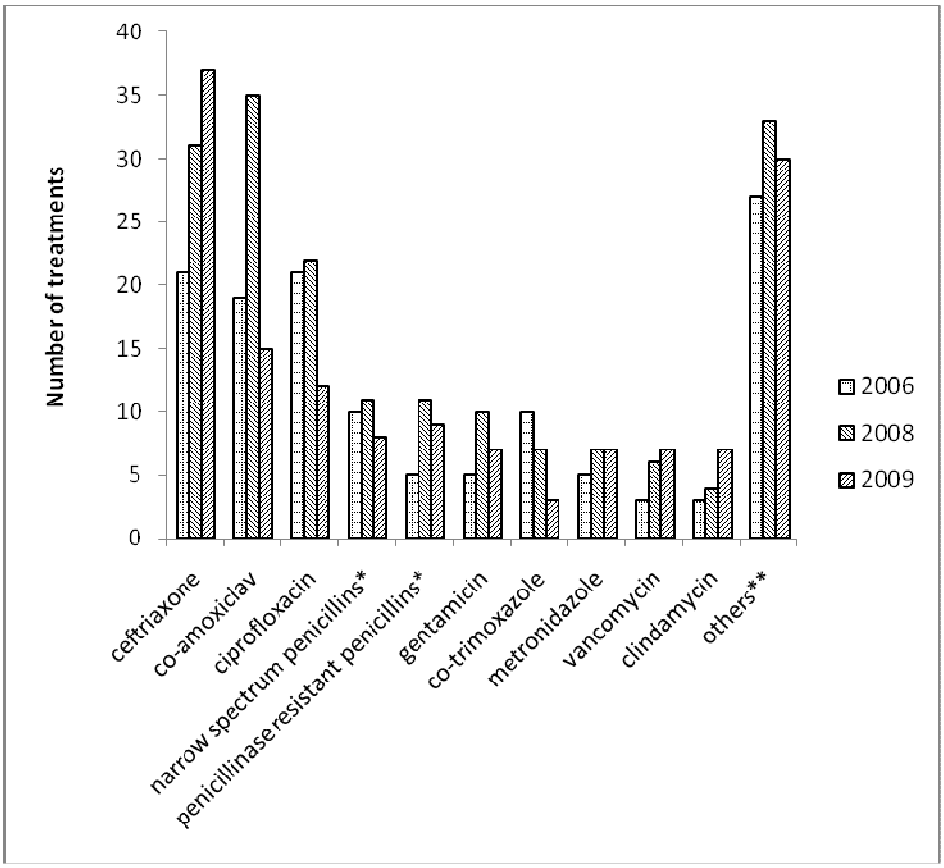
[29]Kanerva M, Ollgren J, Lyytikainen O. Antimicrobial Use in Finnish acute care hospitals: data from national prevalence survey, 2005. *J Antimicrob Ther* 2007;60:440-4.
[30]Raveh D, Levy Y, Schlesinger Y, Greenberg A, Rudensky B, Yinnon AM. Longitudinal surveillance of antimicrobial use in the hospital. *Q J M* 2001;94:141-52.
[31]Di Giammarino L, Bihl F, Bissig M, Bernasconi B, Cerny A, Bernasconi E. Evaluation of prescription practices of antibiotics in medium-sized Swiss hospital. *Swiss Med Wkly* 2005;135:710-4.
[32]Tambic Andrasevic A, Baudoin T, Vukelic D, et al. ISKRA guidelines on sore throat: diagnostic and therapeutic approach-Croatian national guidelines. *Lijec Vjesn* 2009;131:181-91.
[33]Skerk V, Tambic Andrasevic A, Andrasevic S, et al. ISKRA guidelines on antimicrobial treatment and prophylaxis of urinary tract infections – Croatian national guidelines. *Lijec Vjesn* 2009;131:105-18.
[34]Kalenic S, Payer Pal M, Vlahovic Palcevski V, et al. Guidelines for prevention, control and treatment of infections caused by methicillin-resistant Staphylococcus aureus (MRSA). *Lijec Vjesn* 2008;130(Suppl.1):7-32.
[35]Francetic I, Sardelic S, Bukovski S, et al. ISKRA guidelines for antimicrobial prophylaxis in surgery – Croatian national guidelines. *Lijec Vjesn* 2010;132:203-17.
[36]Dean B, Lawson W, Jacklin A, et al. The use of serial point-prevalence studies to investigate hospital anti-infective prescribing. *Int J Pharm Pract* 2002:10:121-5.

Figure 1. The proportion of diagnoses leading to antibiotic use



SSTBJ skin and soft tissue together with bone and joint infections; UTI urinary tract infections; NDS no defined site infections (bacteriaemia with no clear anatomical site, or systemic inflammatory response with no clear anatomical site, and completely undefined site with no systemic inflammation); GI gastro intestinal infections (prophylaxis in neutropenic patients, GI infections, intra - abdominal sepsis); RESP respiratory infections (pneumonia, bronchitis, prophylaxis of respiratory pathogens); ENT ear, nose, throat infections; CNS central nervous system infections; CVS cardiovascular infections (cardiovascular infections, endocarditis); GUOB obstetric or gynaecological infections (sexually transmitted diseases (STD) in women, prostatitis, epididymo-orchitis and STD in men – GUM.

Figure 2. The ranking of antibiotics used



*narrow spectrum penicillins – benzylpenicillin, benzathine benzylpenicillin, procaine benzylpenicillin

*penicillinase resistant penicillins – cloxacillin, flucloxacillin

**others = azithromycin, fluconazole, imipenem/cilastatin, meropenem, doxycycline, piperacillin/tazobactam, cefazolin, cefixime, moxifloxacin, netilmicin, amphotericin B, moxifloxacin, cefepime, cefuroxime, doripenem, nitrofurantoin, rifampicin, amikacin, cefalexin, cefotaxim, ceftazidim, ceftibuten, ertapenem, etambutol, isoniazid B6, clarithromycin, norfloxacin, pyrazinamide