Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/medici

Original Research Article

Antimicrobial usage among hospitalized children in Latvia: A neonatal and pediatric antimicrobial point prevalence survey

Inese Sviestina [a,b,*], *Dzintars Mozgis* [c]

[a] *University Children's Hospital, Riga, Latvia*
[b] *Faculty of Pharmacy, Riga Stradins University, Riga, Latvia*
[c] *Public Health and Epidemiology Department, Riga Stradins University, Riga, Latvia*

ARTICLE INFO

Article history:
Received 14 June 2013
Received in revised form
3 July 2014
Available online 13 August 2014

Keywords:
Hospitalized children
Point prevalence survey
Third-generation cephalosporins
Parenteral antibiotics

ABSTRACT

Background and objective: The point prevalence survey was conducted as part of the Antibiotic Resistance and Prescribing in European Children (ARPEC) Project. The study aimed at analyzing pediatric and neonatal antimicrobial prescribing patterns in Latvian hospitals, to identify targets for quality improvement.
Materials and methods: A one day cross-sectional point prevalence survey on antibiotic use in hospitalized children was conducted in November 2012 in 10 Latvian hospitals, using a previously validated and standardized method. The survey included all inpatient pediatric and neonatal beds and identified all children receiving an antimicrobial treatment on the day of survey.
Results: Overall 549 patients were included in the study; 167 (39%) patients admitted to pediatric wards and 25 (21%) patients admitted to neonatal wards received at least one antimicrobial. Pediatric top three antibiotic groups were third-generation cephalosporins (55 prescriptions, 28%), extended spectrum penicillins ($n = 32$, 16%) and first-generation cephalosporins ($n = 26$, 13%). Eleven pediatric patients (85%) received surgical prophylaxis more than 1 day; 143 pediatric patients (86%) received antibiotics intravenously. Lower respiratory tract infections were the most common indications for antibiotic use both in pediatric ($n = 60$, 35.9%) and neonatal patients ($n = 9$, 36%). The most used antibiotics for neonatal patients were benzylpenicillin ($n = 12$, 32%), and gentamicin ($n = 9$, 24%).
Conclusions: We identified a few problematic areas, which need improvement: the high use of third-generation cephalosporins for pediatric patients, prolonged surgical prophylaxis, predominant use of parenteral antibiotics and an urgent need for local antibiotic guidelines.

* *Corresponding author at*: Vienibas 45, Riga 1004, Latvia.
E-mail address: inese.sviestina@bkus.lv (I. Sviestina).
Peer review under responsibility of Lithuanian University of Health Sciences.

ELSEVIER Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.medici.2014.08.005
1010-660X/

1. Introduction

Antibiotics are among the most common medicines given to children [1,2]. According to some studies, 60% of the children receive at least one antibiotic during their hospital stay [3]. There is been a lot of discussion about the rational use of antibiotics because wrongly used they can become a risk factor for the development of resistant bacteria and extra costs for both hospitals and patients [4–6]. There are limited reliable data on antibiotic use in neonates and children in hospitals but without such information it is difficult to "develop strategies for the prevention of infections and the containment of resistant pathogens" [7] and to improve antibiotic prescribing practices. According to Zarb et al. one of the best ways to monitor antibiotic prescribing would be through monitoring electronic prescribing in hospitals that is still not available in many hospitals in Europe (including Latvian hospitals). The alternative is point prevalence surveys (PPSs) that is also a useful tool for this purpose and allows identifying priorities for quality improvement [8]. There are well-established surveillance methodologies developed by The European Surveillance of Antimicrobial Consumption (ESAC) Project but these PPSs have focused mainly on adults [9]. PPSs have been used in hospitals not only at the European level but also undertaken at the national and individual hospital level [10,11]. There are some studies on antibiotic use in pediatric population using PPSs [12] but methodology was adopted from adult PPSs and it was not specifically designed for children. This study was a part of the "Antibiotic Resistance and Prescribing in European Children" (ARPEC) project. The aim of this particular study was to analyze the use of antibiotics among children at hospitals in Latvia to identify targets for quality improvement.

2. Materials and methods

A one-day cross-sectional point prevalence survey (PPS) was conducted at those hospitals in Latvia with pediatric and neonatal wards which had agreed to participate in the study. A previously validated and standardized ARPEC methodology was used [13–15]. Each hospital was registered in the ARPEC database providing the name, geographic location and type of hospital (primary, secondary, tertiary level and specialized hospital and teaching versus nonteaching hospital). Seven major pediatric ward types (general pediatric medicine, four types of specialized pediatric medicine wards, pediatric surgery and pediatric intensive care unit (PICU)) and four major neonatal wards were defined (three levels of neonatal intensive care units (NICUs) and a general neonatal medical ward) [14,15]. The survey was undertaken during November 2012. The survey days were following: hospital No. 1296, November 30; hospital No. 1312, November 28; hospital No. 1288, November 14 and 20; hospital No. 1291, November 12, 19, 20, and 28; hospital No. 1937, November 30; hospital No. 1324, November 1, 5, 6, 7, 12, 13, 15, 21, 22, 27, and 29; hospital No. 1281, November 27; hospital No. 1323, November 22; hospital No. 1311, November 27 and 29; and hospital No. 1098, November 14. In this study, all neonates and children who were younger than 18 years (from 0 days of life till 17 years 11 month 29 days) and who were present at 8 am on the day of survey (and present since midnight at least) were included. Detailed data were recorded only for patients with active antimicrobial prescriptions at 8 am on the day of survey. Prescriptions that became active after 8 am on the day of the survey were excluded. Day-case patients, out-patients, emergency admissions after midnight and patients in psychiatry clinics were excluded. Children younger than 18 years admitted on an adult ward were excluded. Also adults older than 18 years admitted on a pediatric ward together with their child were excluded from the survey. Pediatric surgical wards were not audited on a Monday in order to gather information about prophylaxis during the previous 24 h (duration of prophylaxis was either 1 dose, 1 day, or >1 day). None of wards were audited on holidays and weekend days. The actual data collection was performed using paper forms: a department form, a pediatric and a NICU form [14,15]. The following data were collected: the patients' age, gender, weight, antimicrobial agent (ATC classes J01, J02, J05, J04A, A07AA, D01BA, P01AB), dose per administration, number of doses per day, route of administration, underlying diagnosis, anatomical site of infection or target for prophylaxis according to the list of provided reasons for treatment and the indication for therapy (community acquired versus hospital acquired infection or prophylaxis) [14,15]. The reason for the treatment for pediatric patients was divided into twenty one category, e.g., "Treatment for surgical disease: proven or suspected infection, e.g., peritonitis, appendicitis, abscess, epididymitis, any case of acute abdominal problem admitted under the surgical team, mediastinitis, etc.", "Sepsis (includes cases of suspected sepsis syndrome or presumed bacteremia/septicemia), etc." [14]. The reason for the treatment for neonatal patients was divided into eighteen categories [15]. For each antimicrobial it was allowed to select only one category. Underlying diagnosis had to be completed in the case of a chronic pre-existing disease. If choices had to be made, those underlying diagnoses related to hospital admission and/or the antibiotic treatment were taken. Underlying diagnoses groups for pediatric patients were divided into 14 subgroups and it was allowed to select a maximum of three diagnoses out of fourteen categories. For neonatal patients there were also 14 subgroups of underlying diagnoses and it was allowed to select a maximum of three diagnoses out of 14 categories. As denominator data, the number of admitted patients and the number of total available beds in each department was used. Six routes of administration had to be entered: parenteral oral, rectal, inhalation, intramuscular, intrathecal and intraperitoneal. Topical use applied on "skin", "oral" topical administration (e.g., oral gel) was excluded. Targeted treatment was based upon microbiological culture and/or sensitivity testing, the action of the remedies given are directed against the cause of the disease (e.g., positive blood or sputum culture). Besides data needed for the ARPEC protocol additional information was collected, i.e., whether or not patient received intravenous antibiotics more than 48 h on the day of the PPS and was there a reason for this written down in medical records. After data collection on wards and hospitals, participants sent that information to the local country administrator who used the ARPEC-webPPS program, a web-based application for data-entry and reporting as designed by the Laboratory of Medical Microbiology of the University of Antwerp, Belgium (http://app.esac.ua.ac.be/arpec_webpps/). Online validation procedure was used to validate data entry.

Data entry was validated using the online validation procedure which helped to discover errors or provided warnings (e.g., departments without entered patients' data). Descriptive statistics (SPSS 20) was used to characterize pediatric patients. Ethics approval was obtained from Riga Stradins University Ethics Committee and hospitals were also individually responsible for ascertaining the need for local ethical approval.

Overall, in Latvia 10 hospitals participated in this PPS. Three were tertiary-level hospitals, five were regional hospitals, and two were local hospitals. Of them, two were children hospitals and eight adult hospitals with pediatric departments. Nine hospitals surveyed all eligible wards within the hospital; one hospital surveyed only neonatal wards. Two children hospitals accounted for 476 pediatric and neonatal beds (62%). There was observed a wide range of total number of beds: from 10 to 375 (Table 1). Pediatric surgery wards were in three hospitals, one hospital had pediatric surgical beds within the general medical ward. Five hospitals had one or more NICUs and among them large neonatal units – NICU level three were in three hospitals.

3. Results

Table 2 shows the demographic data of patients under antibiotic treatment and prophylaxis. Lower respiratory tract infections (LRTI) were the most common indications for antibiotic use both in pediatric and neonatal patients (Table 3). Top three antibiotics for the LRTI treatment in pediatric patients were ceftriaxone (*n* = 20 prescriptions, 31%), amoxicillin (*n* = 13, 20%), and clarithromycin (*n* = 7, 11%). Six pediatric patients had two diagnoses as a reason for antibiotic use. Twelve neonatal patients (48%) and 29 pediatric patients (17%) received more than one antimicrobial. There were one zidovudine and seven fluconazole prescriptions of 243 antimicrobial prescriptions. The rest of prescribed antimicrobials belonged to J01 group antimicrobials. Patients admitted to pediatric wards received 21 different antibiotic (J01 group), and patients admitted to neonatal wards, 13 different antibiotics. Eight antibiotics accounted for 75% of all antibiotic use in pediatric patients and five antibiotics in neonatal patients. Antibiotic classes used for the treatment and prophylaxis of infection are shown in Table 4. Top five antibiotics for pediatric patients were ceftriaxone (41 prescriptions, 21%), cefazolin (*n* = 24, 12%), amoxicillin (*n* = 22, 11%), cefuroxime (*n* = 18, 9%), and benzylpenicillin (*n* = 14, 7%). Most used antibiotics for neonatal patients were benzylpenicillin (*n* = 12, 32%) and gentamicin (*n* = 9, 24%). In total, there were 15 patients receiving antimicrobial surgical prophylaxis; 13 (87%) received prophylaxis for more than 1 day. The most used antibiotics for surgical pediatric patients were ceftriaxone (*n* = 7, 26%) and metronidazole (*n* = 4, 15%), cefazolin (*n* = 4, 15%), and cefuroxime (*n* = 4, 15%). In three cases, metronidazole was used in combination with ampicillin, amoxicillin or ceftriaxone, ceftriaxone was also used in combination with oxacillin, cefuroxime was used in combination with gentamicin and benzylpenicillin with clindamycin. In total, 143 (86%) of the pediatric patients received antibiotics intravenously for both treatment and prophylaxis, and 91 (64%) of them, more than 48 h.

Table 1 – Bed utilization and proportional use of antimicrobials in hospitals.

Hospitals	Total antimicrobial and antibiotic proportions				Pediatric antimicrobial and antibiotic proportions				Neonatal antimicrobial and antibiotic proportions			
	No. of beds	Bed occupancy (%)	No. of patients	Treated patients all antimicrobials N (%)	No. of beds	Bed occupancy (%)	No. of patients admitted to pediatric wards	Treated patients all antimicrobials N (%)	No. of beds	Bed occupancy (%)	No. of patients admitted to neonatal wards	Treated patients all antimicrobials N (%)
Total	769	71	549	192 (35)	580	74	430	167 (39)	189	63	119	25 (21)
1324	375	73	272	87 (32)	328	75	246	82 (33)	47	55	26	5 (19)
1098	101	73	74	41 (55)	81	77	62	32 (52)	20	60	12	9 (75)
1297	77	53	41	9 (22)	42	60	25	6 (24)	35	46	16	3 (56)
1281	48	81	39	21 (54)	27	107	29	19 (66)	21	48	10	2 (24)
1323	25	68	17	6 (35)	25	68	17	6 (35)	0	0	0	0 (0)
1291	70	50	35	10 (29)	50	54	27	10 (37)	20	40	8	0 (0)
1311	20	60	12	4 (33)	12	58	7	4 (57)	8	62	5	0 (0)
1312	10	100	10	3 (30)	0	0	0	0 (0)	10	100	10	3 (30)
1288	25	112	28	8 (29)	15	113	17	8 (47)	10	110	11	0 (0)
1296	18	117	21	3 (14)	0	0	0	0 (0)	18	117	21	3 (14)

Table 2 – Demographic data of patients under antibiotic treatment.

Patients' characteristics	Total No. of patients under antibiotic treatment N = 192 (%)	Male N = 110 (%)	Female N = 82 (%)
Admitted on neonatal wards	25 (13)	17 (68)	8 (32)
Admitted on pediatric wards	167 (87)	93 (56)	74 (44)
Age (months)			
Mean ± SE	60 ± 5.1	84 ± 7.0	42 ± 7.1
Mode	24	204	36
Skewness	0.564	0.268	1.012
Kurtosis	−1.015	−1.249	−0.201
Age range			
<29 days	23 (12)	15	8
>29 days ≤ 1 year	28 (14)	16	12
>1 year ≤ 5 years	51 (27)	21	30
>5 years ≤ 12 years	53 (28)	33	20
>12 < 18 years	37 (19)	25	12

Table 3 – Reasons for the antimicrobial use in pediatric and neonatal patients.

Diagnosis	Patients admitted to pediatric wards N = 173 (%)	Patients admitted to neonatal wards N = 25 (%)
Lower respiratory tract infections	60 (34.7)	9 (36)
Upper respiratory tract infections	24 (13.9)	0
Prophylaxis for surgical disease	14 (8.1)	1 (4)
Prophylaxis for medical problems	14 (8.1)	0
Acute otitis media	11 (6.4)	0
Urinary tract infections	10 (5.8)	0
Other	9 (5.2)	1 (4)
Lymphadenitis	6 (3.5)	0
Surgical treatment	7 (4.0)	0
Febrile neutropenia/fever in oncologic patients	4 (2.3)	0
Skin/soft tissue infections	6 (3.4)	0
Sepsis	4 (2.3)	5 (20)
Joint/bone infections	4 (2.3)	0
Prophylaxis for maternal risk factors	0	5 (20)
Prophylaxis for newborn risk factors	0	4 (16)

Table 4 – Antibiotic classes used for the treatment and prophylaxis of infection.

Antibiotic classes	Prescriptions for pediatric patients N (%)	Prescriptions for neonatal patients N (%)
Third-generation cephalosporins (J01DD)	55 (27.9)	4 (10.5)
Penicillins with extended spectrum (J01CA)	32 (16.2)	6 (15.8)
First-generation cephalosporins (J01DB)	26 (13.2)	0
Second-generation cephalosporins (J01DC)	18 (9.1)	0
Beta-lactamase sensitive penicillins (J01CE)	14 (7.1)	12 (31.6)
Combinations of sulfonamides and trimethoprim, including derivatives (J01EE)	13 (6.6)	0
Macrolides (J01FA)	9 (4.6)	0
Other aminoglycosides (J01GB)	9 (4.6)	11 (28.9)
Beta-lactamase resistant penicillins (J01CF)	5 (2.5)	0
Lincosamides (J01FF)	5 (2.5)	0
Glycopeptide antibacterials (J01XA)	2 (1.0)	0
Comb. of penicillins, incl. beta-lactamase inhibitors (J01CR)	1 (0.5)	0
Carbapenems (J01DH)	1 (0.5)	2 (5.2)
Other	7 (3.6)	3 (3.9)

4. Discussion

This study provides an analysis of antibiotic use in hospitalized pediatric and neonatal patients. The study is important because the use of antibiotics in Latvia according to some studies is the highest among the European countries [16] and it is important to analyze reasons behind such high usage of antibiotics. The study indicates several problematic areas: first of all, the high use of the third-generation cephalosporins in pediatric population and especially ceftriaxone that was the top one antibiotic used in pediatric patient group. In November 2011 the PPS was done in four hospitals (two of them University hospitals, one regional and one local hospital) and results were almost similar with last November results, i. e., pediatric top three antibiotic groups were penicillins with extended spectrum ($n = 39$, 40%), the third generation cephalosporins ($n = 38$, 23%), and combinations of sulfonamides and trimethoprim, incl. derivatives ($n = 22$, 13%) – the last group was due to a high number of oncohematology patients who received co-trimoxazole for medical prophylaxis. Top three antibiotics for pediatric patients were amoxicillin ($n = 23$; 14%), co-trimoxazole ($n = 22$; 13%), and ceftriaxone ($n = 21$; 13%). In May 2012 the PPS was done in four hospitals (two of them University hospitals, two regional) and top three antibiotic groups were the third-generation cephalosporins ($n = 37$, 25%), penicillins with extended spectrum ($n = 31$, 21%) and the second-generation cephalosporins ($n = 21$, 14%). Top three antibiotics for pediatric patients were ceftriaxone and cefuroxime both ($n = 21$, 14%) and amoxicillin ($n = 20$, 13%). These results show that in all PPS the third-generation cephalosporins were among the mostly used antibiotic groups for pediatric patients and ceftriaxone was among top three antibiotics in this patient group. The use of the third-generation cephalosporins can lead to the increase of resistant bacterial strains and should be reduced as a result [17,18]. Some European countries have reported high increase of the third-generation cephalosporin-resistant *Escherichia coli* in their hospital wards [19]. At the same time some countries such as UK have succeeded in decreasing of the use of the third-generation cephalosporins with both publications from the Department of Health recommending good antimicrobial stewardship, e.g., the ''Start Smart then Focus'' approach [20] and a policy of restricting cephalosporin prescription and this approach helped to decrease the use of cephalosporins, for example, in the Children Hospital in Birmingham [21]. Currently there are almost no local and also national recommendations for antibiotic use in hospitals except one University Hospital with a maternity ward that has local recommendations for adults and the University Childrens' Hospital that has local recommendations for bronchiolitis, epiglottitis, croup and community acquired pneumonia treatment. This situation indicates an urgent need for recommendations both on national and local (hospital) level.

Another problematic area is the high use of intravenous antibiotics. A total of 143 pediatric patients (86%) received intravenous antibiotics, and 91 (64%), for more than 48 h; 107 patients (85%) received antibiotics intravenously in May 2012 and 112 patients (74%) in November 2011. In this study, we did not evaluate the appropriateness of the route of therapy or the initial diagnosis. One explanation of such high use of intravenous antibiotics could be due to social acceptance that intravenous antibiotics are ''stronger'' than oral antibiotics in treating an infection during hospital stay. Some antibiotics (e.g., aminoglycosides) are not available in oral form although sometimes have off-label oral use [22]. Alternatively, some oral antibiotics are not available on the Latvian market, e.g., flucloxacillin and penicillin Whilst some infections (e.g., central nervous system infections) or patients groups (e.g., neonates) require parenteral use there are other patient groups (e.g., children, adolescent) and/or diagnoses where the disproportionately high use of intravenous antibiotics should be reduced at hospitals in Latvia. In some situations (e.g., community acquired pneumonia or some cases of acute pyelonephritis), switch to oral antibiotics allow reducing the stay at the hospital and has potential benefits because can decrease the risk of needle-borne infections, need for referral or admission, administration costs, and family-related costs [23–25]. Our results are similar with the study done in pediatric antimicrobial prescribing in 32 hospitals of 21 European countries where parenteral route was more commonly used than the oral route for both prophylactic and therapeutic indications [12].

Antibiotic prophylaxis for surgical patients was not focused on this study. However, further analysis would be beneficial in the choice of agents, if prophylaxis is appropriately prescribed and especially duration of treatment. Surgical prophylaxis in general and unnecessary prolonged prophylaxis (>1 day) in particular are areas were serious improvements are needed. Although there were a small number of patients receiving a surgical prophylaxis in our study, the tendency was that the duration of the surgical prophylaxis appeared to be longer than recommended in a high proportion of the cases: 11 patients of 13 received prophylaxis longer than one day. These findings are similar with results of other studies [12,26–28]. Some of studies show that many children may not receive antibiotics were proven benefit and could receive antibiotics when there is no clear indication for it [29]. The appropriate use of antibiotics could lead to essential saving not only for the hospital and patient but also for the health care system [30] and can help to decrease the incidence of the surgical site infection and hospital related costs. At the same time overuse of antibiotics can lead to the emergence or resistant microorganisms [13].

The strength of this study is that all hospitals in Latvia used the same standardized protocol that was also used in hospitals in other countries and was tested in two ARPEC pilot studies in 2011 and also in two local pilot studies in four hospitals in Latvia in November 2011 and in May 2012. One common method used in all those studies allows comparing data not only at the country level, but also among the institutions from different countries. PPS are not expensive, but at the same time efficient method that allows to identify antibiotic prescribing trends and areas for improvement. Such a methodology was chosen as a study design for the ARPEC study of antibiotic prescribing analysis in pediatric and neonatal patients (both authors of this article participated in this ARPEC pilot study) [13]. There are PPS conducted in hospitals in Latvia focusing on adult patient [11], but for the first time a PPS was conducted only in so many pediatric and neonatal wards and analyzed separately from adult patients.

Limitations of this study are associated with the study design – a cross sectional design allows capturing only particular numbers of patients. We have to analyze all results bearing in mind that they may represent only situation in the particular time period and patients with individual conditions [13]. In some hospitals only few patients received antimicrobial treatment. This was a reason why hospitals' results were not compared, but only general tendencies were analyzed. Nevertheless, these results are important because children are not small adults and we need more information about the use of medications, e.g., antibiotics in pediatric population in order to provide better care for them. Participation in the survey was voluntary and none of participants was paid for it. Invitations were sent to all hospitals in Latvia with pediatric and/or neonatal wards. Some hospitals did not respond to several invitation letters or declined participation. It is the main reason why this study does not contain information, for example, about tuberculosis treatment in pediatric population: tuberculosis is treated in a specialized clinic in one of the adult University hospitals which also has a pediatric ward. At the same time the University Children's Hospital participated in the survey and those specialists from hospitals who participated were very motivated and interested in the survey and its results. The PPS as a surveillance tool is the first step in auditing the antimicrobial use in hospitals and allows identification of priorities for quality improvement what was the main aim of this study.

5. Conclusions

We identified few problematic areas, which need improvement: the high use of third-generation cephalosporins for pediatric patients, prolonged surgical prophylaxis, predominant use of parenteral antibiotics and an urgent need for local antibiotic guidelines.

Conflict of interest

The authors state no conflict of interest.

Acknowledgments

The authors of this article wish to thank I. Berzina, M. Brice, E. Dimina, R. Irbe, I. Kaleja, M. Kula, A. Mironovska, and I. Ozola, who participated in this study and kindly agreed to complete our study questionnaires.

REFERENCES

[1] Spyridis N, Sharland M. The European Union Antibiotic Awareness Day: the paediatric perspective. Arch Dis Child 2008;93:909–10.

[2] de Jong J, van den Berg PB, Visser ST, de Vries TW, de Jong-van den Berg LT. Antibiotic usage, dosage and course length in children between 0 and 4 years. Acta Paediatr 2009;98 (7):1142–8.

[3] Gerber JS, Newland JG, Coffin SE, Hall M, Thurm C, Prasad PA, et al. Variability in antibiotic use at children's hospitals. Pediatrics 2010;126:1067–73.

[4] Frank U, Kleissle EM, Daschner FD, Leibovici L, Paul M, Andreassen S, et al. Multicentre study of antimicrobial resistance and antibiotic consumption among 6780 patients with bloodstream infections. Eur J Clin Microbiol Infect Dis 2006;25:815–7.

[5] Hulscher ME, Grol RP, van der Meer JW. Antibiotic prescribing in hospitals: a social and behavioural scientific approach. Lancet Infect Dis 2010;10(3): 167–75.

[6] European Parliament resolution of 11 December 2012 on the Microbial Challenge – Rising threats from Antimicrobial Resistance. Available from http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P7-TA-2012-0483+0+DOC+XML+V0//EN (cited 29.01.13).

[7] Council of the European Union. Council recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC). Off J Eur Commun L34 2002;45:13–6. Available from http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2002:034:0013:0016:EN:PDF (cited 11.05.12).

[8] Zarb P, Amadeo B, Muller A, Drapier N, Vankerckhoven V, Davey P, et al. Identification of targets for quality improvement in antimicrobial prescribing: the web-based ESAC Point Prevalence Survey 2009. J Antimicrob Chemother 2011;66(2):443–9.

[9] Zarb P, Goossens H. European Surveillance of Antimicrobial Consumption (ESAC): value of a point-prevalence survey of antimicrobial use across Europe. Drugs 2011;71(6):745–55.

[10] Malcolm W, Nathwani D, Davey P, Cromwell T, Patton A, Reilly J, et al. From intermittent antibiotic point prevalence surveys to quality improvement: experience in Scottish hospitals. Antimicrob Resist Infect Control 2013;2(1):3.

[11] Dimiņa E, Kūla M, Caune U, Vīgante D, Liepiņš M, Zeidaka L, et al. Repeated prevalence studies on antibiotic use in Latvia, 2003–2007. Euro Surveill 2009;14(33). pii: 19307.

[12] Amadeo B, Zarb P, Muller A, Drapier N, Vankerckhoven V, Rogues AM, et al. European Surveillance of Antibiotic Consumption (ESAC) point prevalence survey 2008: paediatric antimicrobial prescribing in 32 hospitals of 21 European countries. J Antimicrob Chemother 2010;65 (10):2247–52.

[13] Versporten A, Sharland M, Bielicki J, Drapier N, Vankerckhoven V, Goossens H, for the ARPEC Project Group Members. The antibiotic resistance and prescribing in European children project: a neonatal and pediatric antimicrobial web-based point prevalence survey in 73 hospitals worldwide. Pediatr Infect Dis J 2013;32(6): e242–53.

[14] Pediatric Point Prevalence Survey (ARPEC). Available from http://links.lww.com/INF/B548 (cited 21.06.13).

[15] Neonatal Point Prevalence Survey (ARPEC). Available from http://links.lww.com/INF/B549 (cited 21.06.13).

[16] European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2010. Stockholm: ECDC; 2013.

[17] European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2010. Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: The Centre; 2011.

[18] Meyer E, Gastmeier P, Deja M, Schwab F. Antibiotic consumption and resistance: data from Europe and Germany. Int J Med Microbiol 2013;303(6–7):388–95.

[19] Meyer E, Schwab F, Schroeren-Boersch B, Gastmeier P. Dramatic increase of third generation cephalosporin-resistant *E. coli* in German intensive care units: secular trends in antibiotic drug use and bacterial resistance, 2001 to 2008. Crit Care 2010;14:R113.

[20] Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI). Antimicrobial stewardship: ''Start Smart – then Focus''. Guidance for antimicrobial stewardship in hospitals (England). London: Department of Health; 2011.

[21] Sviestina I, Aston J, Mozgis Dz. Comparison of antimicrobial prescribing between two specialist paediatric centres in the UK and Latvia. Eur J Hosp Pharm 2013;20:180–4.

[22] Malik BA, Xie YY, Wine E, Huynh HQ. Diagnosis and pharmacological management of small intestinal bacterial

overgrowth in children with intestinal failure. Can J Gastroenterol 2011;25(1):41–5.
[23] Rojas MX, Granados C. Oral antibiotics versus parenteral antibiotics for severe pneumonia in children. Cochrane Database Syst Rev 2006;2:CD004979.
[24] Lorgelly PK, Atkinson M, Lakhanpaul M, Smyth AR, Vyas H, Weston V, et al. Oral versus i.v. antibiotics for community-acquired pneumonia in children: a cost-minimisation analysis. Eur Respir J 2010;35(4): 858–64.
[25] Vouloumanou EK, Rafailidis PI, Kazantzi MS, Athanasiou S, Falagas ME. Early switch to oral versus intravenous antimicrobial treatment for hospitalized patients with acute pyelonephritis: a systematic review of randomized controlled trials. Curr Med Res Opin 2008;24(12): 3423–34.
[26] Voit SB, Todd JK, Nelson B, Nyquist AC. Electronic surveillance system for monitoring surgical antimicrobial prophylaxis. Pediatrics 2005;116(6):1317–22.
[27] Ceyhan M, Yildirim I, Ecevit C, Aydogan A, Ornek A, Salman N, et al. Inappropriate antimicrobial use in Turkish pediatric hospitals: a multicenter point prevalence survey. Int J Infect Dis 2010;14(1):e55–61.
[28] Robert J, Péan Y, Varon E, Bru J-P, Bedos J-P, Bertrand X, et al. Point prevalence survey of antibiotic use in French hospitals in 2009. J Antimicrob Chemother 2012;67:1020–6.
[29] Rangel SJ, Fung M, Graham DA, Ma L, Nelson CP, Sandora TJ. Recent trends in the use of antibiotic prophylaxis in pediatric surgery. J Pediatr Surg 2011;46:366–71.
[30] Hing WC, Yeoh TT, Yeoh SF, Lin RT, Li SC. An evaluation of antimicrobial prophylaxis in paediatric surgery and its financial implication. J Clin Pharm Ther 2005;30(4):371–81.