RĪGAS STRADIŅA UNIVERSITĀTE

Inese Sviestiņa

COMPARATIVE ANALYSIS OF ANTIBIOTIC CONSUMPTION AMONG HOSPITALIZED CHILDREN IN MOSTLY COMMON SURGICAL CASES

Summary of the Doctoral Thesis
for obtaining the degree of a Doctor of Pharmacy

Speciality – Clinical Pharmacy

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Doctoral thesis is available in the library of RSU and RSU homepage: www.rsu.lv

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LIST OF ABBREVIATIONS

AAP – American Academy of Pediatrics

AB – antibiotics

ACCP – American College of Clinical Pharmacy

ARIKK – Coordination Committee for Antimicrobial Resistance Limitation (abbreviation from Latvian, *Antimikrobās rezistences ierobežošanas koordinācijas komisija*)

ARPEC – Antibiotic Resistance and Prescribing in European Children

ATC – Anatomical Therapeutic Chemical classification system

BARN – Baltic Antibiotic Resistance collaborative Network

BD – bed days

BNFC – British National Formulary for Children 2013–2014

CI – confidence interval

DDD – defined daily dose

DDD/100 GD – defined daily dose per 100 bed days

DDD/100 patients – defined daily dose per100 treated patients

90%DU – antibiotics, which accounted for 90% of the total volume of use (drug utilization)

EAHP – European Association of Hospital Pharmacists

ECDC – European Centre for Disease Prevention and Control

ESBL – Extended spectrum beta lactamase

ESCP – European Society of Clinical Pharmacy

ESPID – European Society for Paediatric Infectious Diseases

FIP – International Pharmaceutical Federation (abbreviation from French, *Federation Internationale Pharmaceutique*)

HMA – Heads of Medicines Agencies

Hospital Recommendations – UCH Recommendations for surgical prophylaxis

I88 – Nonspecific lymphadenitis

ICD – International Classification of Diseases, 10th revision

IM - intramuscular

INESSS – National Institute for Health and Social Services Excellence (abbreviation from French, *Institut national d'excellence en santé et en services sociaux*)

IV – intravenous

HAI – healthcare-associated infections

K35 – acute appendicitis

kg – kilograms

Lexi – Pediatric and Neonatal Dosage Handbook

mg – milligrams

NICE – National Institute for Health and Clinical Excellence

NICU – Neonatal Intensive Care Unit

O – oral

PICU – Paediatric Intensive Care Unit

PPS – point prevalence survey

QTR – quarter

RSU – Rīga Stradiņš University

S42 – Fracture of shoulder and upper arm

S52 – Fracture of forearm

S62 – Fracture at wrist and hand level

S72 – Fracture of femur

S82 – Fracture of lower leg, including ankle

S92 – Fracture of foot, except ankle

SAAGAR – South Australian expert Advisory Group on Antibiotic Resistance

SAM – State Agency of Medicines of the Republic of Latvia

SCHTA – Swedish Council on Health Technology Assessment

SD – standard deviation

SFAR – French Society of Anaesthesia and Intensive Care (abbreviation from

French, *Société Française d’Anesthésie et de Réanimation*)

SIGN – Scottish Intercollegiate Guidelines Network

SPC – Summary of Product Characteristics

SSI – Surgical Site Infection

UCH – University Children’s Hospital, Riga

USA – United States of America

USG – ultrasonography

WHO – World Health Organization

WHOCC – WHO Collaborating Centre for Drug Statistics Methodology

INTRODUCTION

Growing antimicrobial resistance has been recognized as a worldwide threat to public health (*McLoughlin et al.*, 2005, *Raveh et al.*, 2007). This is why new solutions are needed to improve AB use. According to some studies up to 60% of AB are used incorrectly in hospitals (e.g., the use of broad–spectrum AB instead of narrow–spectrum AB, the administration of intravenous AB instead of use of or switch to oral AB) (*Davey et al.*, 2005). One of the latest WHO reports of AB resistance states that "there are significant gaps in surveillance, and a lack of standards for methodology, data sharing and coordination" (*WHO*, 2014). The Ministry of Health of the Republic of Latvia has founded the "Coordination Committee for Antimicrobial Resistance Limitation" (*Veselības ministrijas rīkojums Nr. 100*, 2013), which aim is to introduce the National plan on AB resistance, as well as correct and rational use of AB in Latvia (*ARIKK*, 2015). It is impossible to introduce correct and rational use of AB without identification of current situation in AB consumption.

There are limited amount of reliable data available on AB use in children in hospitals if to be compared with adult data, but AB are among the most frequently medicines administered to children (*de Jong et al.*, 2009, *Schindler et al.*, 2003). AAP guidelines (*Dellit et al.*, 2007) states that only few of studies have focused on hospitalized newborns, children, as well as adolescents. The study performed in 40 paediatric hospitals across America established that during their hospital stay up to 60% of children received at least one antibiotic (*Gerber et al.*, 2010). The study concludes that children at some hospitals were undertreated with AB and thus could be exposed to the risk of mistreatment, or that some hospitalized children have received excessive AB therapy and thus were unnecessarily exposed to the risk of developing AB resistant infections. The study performed in five children's hospitals in China during the period of time from 2002 to 2006 established that the most frequently used AB were the 3rd generation cephalosporins, the extensive use of which could create preconditions for the developing antimicrobial resistance (*Zhang et al.*, 2008a). It was only in 2012 when Europe had its first European-wide PPS on AB use in hospitalized paediatric patients (*Versporten et al.*, 2013). Latvia was represented by nine hospitals and the author of this thesis collected AB consumption data from all participating hospitals. Systematic PPS was never conducted at the UCH. Therefore there was lack of comprehensive information on AB usage tendencies at the hospital.

The use of surgical antibiotic prophylaxis in children is not well described despite the fact that the study performed in the USA in 1982 (*Kesler et al.*, 1982) established that AB prophylaxis was administered incorrectly. Since this study there have not been any significant changes. The authors still believe that almost half of all procedures of the surgical prophylaxis was not performed under the guidelines in. Most often than not the prophylaxis was unnecessary prolonged (*Voit et al.*, 2005).

There were numerous audits performed in order to evaluate the appropriateness of the use of AB in surgical prophylaxis in adult populations, but there is still shortage of data regarding paediatric surgery (*Hing et al.*, 2005). The study performed in 12 paediatric hospitals in Turkey establishes that inappropriate use of AB was the most common in surgery wards (*Ceyhan et al.*, 2010). Similar conclusions were deduced from the study completed in Europe in 32 hospitals across 21 country (*Amadeo et al.*, 2010). Rangel et al. have concluded that many children still do not receive prophylaxis when indicated, and an even greater proportion receives it when there is no indication (average 40%; 10–83%) (*Rangel et al.*, 2011). Many of current guidelines are based on adult data (*Rangel et al.*, 2011), but there is not enough evidence suggesting that these data could be used in children without any appropriate studies regarding this particular population (*Tönz et al.*, 2000). Appropriate surgical antimicrobial prophylaxis could prevent post-operative SIS. However, inappropriate use of AB could increase the antimicrobial resistance, as well as costs for patients and hospitals (*Paterson*, 2006). Another fundamental problem is a common and well-known practice of AB off–label use especially in the paediatric population that mostly is related to the doses and indications (*Porta et al.*, 2010).

Aim of the study

To examine AB consumption general tendencies in the UCH and to describe AB use in the surgical prophylaxis and treatment in hospitalized children receiving most common surgical treatment.

Objectives of the study

1. To identify AB consumption and to determine the most fundamental AB consumption tendencies in the UCH.
2. To analyse AB surgical prophylaxis in most common surgical cases (appendicitis, mesadenitis, and upper and lower extremity injuries) at the UCH Paediatric Surgery Clinic.
3. To analyse prescribed AB and AB doses to patients in most common surgical cases at the UCH Paediatric Surgery Clinic.
4. To analyse AB off–label use in most common surgical cases at the UCH Paediatric Surgery Clinic.

Hypotheses of the study

1. The UCH has the high rate of the high risk AB consumption that could lead to the development of antimicrobial resistance.
2. The strategy of AB use in children in most common surgical cases at the UCH Paediatric Surgery Clinic differs from what is stated in the international guidelines.
3. Wrong AB doses are most frequently prescribed to children under the age of 12 years.

Scientific novelty of the study

Until now in Latvia data on AB consumption in hospitalized children was never analysed separately from the data covering adult population. Also, this study is the first, which provides analysis on AB use in surgical prophylaxis and treatment of hospitalized children in most common surgical cases.

All the data presented in the study are the result of the author's own research, which was completed under the supervision of the scientific supervisor. The doctoral thesis "Comparative analysis of antibiotic consumption among hospitalized children in mostly common surgical cases" was presented on 20th May 2015 during the faculty meeting at the Department of Pharmaceutical Chemistry, Rīga Stradiņš University.

1. MATERIALS AND METHODS

1.1. Place of the study

The research was conducted at the University Children's Hospital.

1.2. Analysis of antibiotic consumption at the University Children's Hospital

1.2.1. Point prevalence survey

During the period from 1st January 2011 to 31st December 2013 twice a year (in May and November each year) in total there were six PPS conducted. In these PPS protocol developed and validated by ARPEC was used. Every ward was audited once. All beds in each administrative unit (department) were completely audited in a single day in order to calculate correctly the denominator (number of admitted patients). In order to capture information about prophylaxis during previous 24 hours Paediatric Surgical Wards were not to be surveyed on a Monday, but during the period from Tuesday to Friday. Paediatric Medical wards were surveyed during all week (from Monday till Friday). Various (mixed) departments (surgery and therapeutics) had also to be surveyed during the period from Tuesday to Friday. During PPS data on both patients in the ward and patients treated with AB, as well as the total number of beds in the ward were collected. See Figure 1.1. for patient selection criteria.

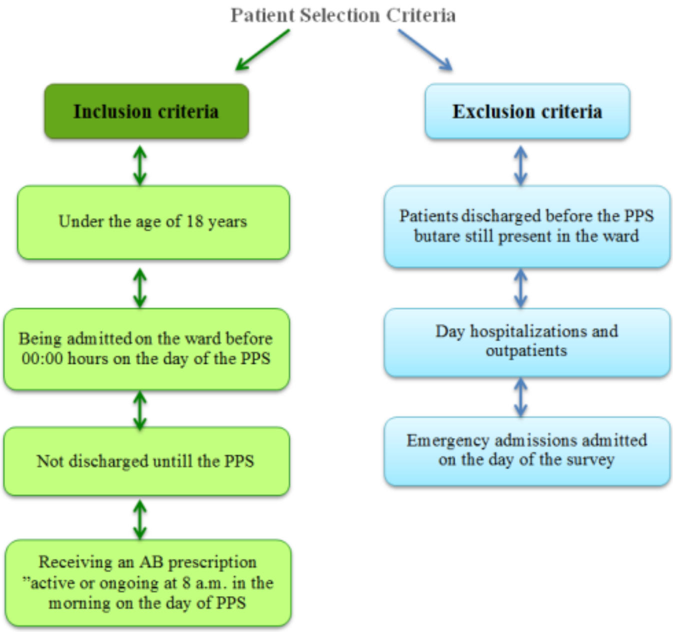

Figure 1.1. **Patient selection criteria**

Three data collection forms were used: Department form, Paediatric patient form and Neonatal patient form. The following data was included in the Department form: date of survey, auditor's code, type of the department – mixed (e.g., therapy plus surgery) or not mixed, activity (medicine, surgery, PICU) – only for mixed departments, total number of admitted inpatients < 18 years old at 8 a.m. on the day of PPS, total number of beds in the ward. The following data was included in the Paediatric patient form and Neonatal patient form: ward's name and activity, patient's age (gestational age of the neonates), weight (birth weight of the neonates), gender, ventilation status, underlying diagnosis, AB name, dose, route, times per day, reason for treatment, indication, type of treatment (empirical versus targeted treatment), notes on the reasons. See Figure 1.2. for AB selection criteria.

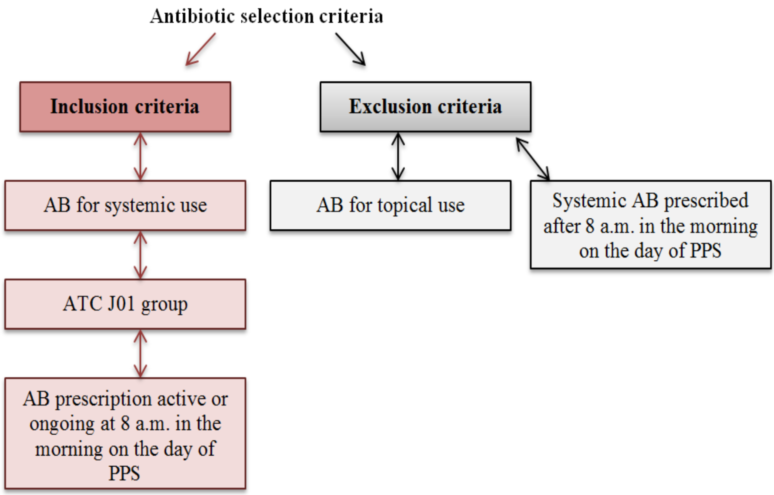

Figure 1.2. **AB selection criteria**

For combinations with two or more active ingredients like Co-trimoxazole the total content was recorded in the patient's form (sulfamethoxazole 200 mg/trimethoprim 40 mg was recorded as 240 mg). For combination with one active ingredient as the main antimicrobial agent, like penicillins with enzyme inhibitors, only the content of active ingredient was recorded in the patient's form (e.g., co-amoxiclav 125/31 suspension (amoxicillin 125 mg and clavulanic acid 31mg as potassium salt) was recorded as prescribed 125 mg).

1.2.2. Antibiotic analysis by using Defined daily dose method

This study contains analysis of the consumption of all AB for systemic use (ATC J01). AB consumption data at the hospital wards were obtained from the hospital pharmacy electronic database. The amount of AB distributed from the pharmacy to the wards was also taken into account. The total amount of every AB used per year and quarter was converted in terms of grams.

Following the ATC/DDD guideline *(WHOCC, Zhang et al.*, 2008a) consumption rates were expressed as DDD, DDD/100 BD and DDD/100 patients. Analysis of AB annual consumption at the UCH hospital "Torņakalns" and Paediatric Surgery Clinic was completed for the period 2006–2013, but quarterly analysis on the whole hospital – for the period 2011–2013. All changes to all three matching indicators (DDD, DDD/100 BD and DDD/100 patients) were considered as important. DDD reflects the true volume of consumption, but the DDD/100 BD and DDD/100 patients – the intensity of use. The number of treated patients and the number of hospital bed-days were used to characterise intensity of patients' treatment. In addition, the analysis considered all data related the average duration of treatment. Information on bed–days, number of treated patients and average duration of the said treatment was obtained from the UCH eHealth and Statistics Department. The day of the patient's hospitalization and as well as discharge was considered as one day. Outpatients, day-stationary patients and emergency department patients were excluded from the study.

1.2.3. Analysis of antibiotic drug utilization (90%DU)

Total consumption of AB at the UCH hospital "Torņakalns" was analysed by using 90%DU method. AB were ranked by amount of DDD. AB, which accounted for 90% of the total volume of use, were specifically noted (*Dimiņa*, 2013, *Zhang et al.*, 2008b).

1.3. Analysis of perioperative AB prophylaxis and treatment in patients with most common surgical cases

1.3.1. Patient selection

This study analysis patients under the age of 18 years with diagnoses code I880, K35, S42, S52, S62, S72, S82, S92 (according to ICD) hospitalized at the Paediatric Surgery Clinic. Study period: 1st January 2001 – 31st December 2003 and 1st January 2011 – 31st December 2013. A historical control group of patients with the same diagnoses treated between years 2001–2003 was used for the comparison. All data on patients were obtained from the patients' medical records, as well as from the UCH software "Andromeda" (patients hospitalized from 1st January 2011 – 31st December). Arrangement according to the age groups was completed by using *Gerber et al.* (2010) classification: under the age of 1 month, from 1 month to 1 year, from 1 year to 5 years, from 5 years to 12 years and from 12 years to 18 years. In the AB dosage analysis patients were arranged into two age groups: under the age of 12 years and from 12 years to 18 years.

1.3.2. Analysis of surgical prophylaxis

Quality indicators used in the analysis of the perioperative AB prophylaxis

In order to evaluate surgical prophylaxis at the Paediatric Surgery Clinic several ECDC surgical quality indicators were used (*ECDC*, 2013):

$$1^{st}\text{ indicator} = \frac{\text{Number of prophylaxis administered within 60 minutes before incision}}{\text{Number of all surgeries where prophylaxis was indicated and administered}}$$

$$2^{nd}\text{ indicator} = \frac{\text{Number of surgeries with appropriate choice of prophylaxis}}{\text{Number of all surgeries when prophylaxis was indicated before incision}}$$

$$3^{rd}\text{ indicator} = \frac{\text{Number of surgeries where prophylaxis was administered when there was an indication}}{\text{Number of all surgeries when prophylaxis was indicated}}$$

$$4^{th}\text{ indicator} = \frac{\text{Number of PAP discontinued within 24 hours post-surgery}}{\text{Number of all surgeries when PAP was indicated}}$$

Surgical prophylaxis analysis criteria

See Figure 1.3. for the timing of AB administration criteria.

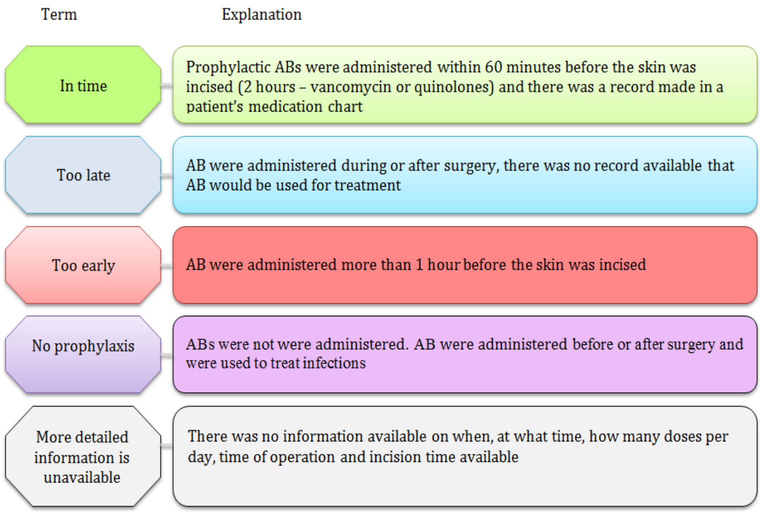

Figure 1.3. **Timing of administration criteria**

Duration of perioperative AB prophylaxis was analysed as follows: 1 dose, multiple doses within 24 hours, > 24 hours and the patient's medication chart contained no accurate data on the duration of the prophylaxis.

1.3.3. Analysis of prescribed AB doses in the Paediatric Surgery Clinic and dosing errors in AB prescribed for surgical patients

The author used four information resources for the analysis of dosing errors: the hospital Recommendations (*Zavadska et al.*, 2013), SPC (if the brand name AB was registered in the SAM register (e.g., *Rocephin* (2010), it was used as a reference document), BNFC (*BNFC*, 2013) and Lexi (*Taketomo*, 2011). Such approach was used because the hospital's Recommendations approved by the hospital's General Board became effective on September 2013. Previously there were not official recommendations, which could be used as a reference for AB dosages. Patients whose body weight did not match the patient's medical record were excluded from the analysis. If AB had a dose range, e.g., cefazolin 20–30 mg/kg (*Taketomo*, 2011), the doses were considered as incorrect if they were lower or higher the lowest or highest dose following a particular information source.

The following SPC were used:

1) ampicillin – *Pamecil* (2008) and *Pan–Ampicillin* (2010);
2) cefazolin – *Cerfazolin–IPP* (2014), *Cefazolin–Hospira* (2014), *Cefazolin–BCPP* (2010) and *Pan–Cefazolin* (2010);
3) ceftriaxone – *Rocephin* (2010);
4) cefuroxime – *Axetine* (2011) and *Cefuroxime MIP*;
5) gentamicin – *Gentamicin Krka* (2011) and *Gentamicin Sopharma* (2014);
6) metronidazole – *Metronidazole B. Braun* (2014) and *Metronidazole Fresenius* (2014).

1.3.4. Antibiotic off–label use

All cases when AB was used in a way that was different from that described in the SPC, e.g., not for particular age group, indication (prophylaxis), in another dose, doses per day or route of administration were considered as off–label use (*Neubert et al.*, 2008).

1.4. Statistical analysis

The statistical analysis was performed by using IBM SPSS Statistics Version 20.0 statistical software package (IBM SPSS Statistics Version 20, SPSS inc., USA) and Microsoft Excel programs. Patients' data were analysed by using descriptive statistical methods (percentage proportion, median, mean and standard deviation, mode, interquartile range, skewness and kurtosis). Nominal data were described as the quantity (n) and percentage with 95% CI. Categorical data were analysed with Chi–square test (2 × 2 tables). Categorical (qualitative) data were also described as the quantity and percentage proportion. Data with value below 0.05 were regarded as statistically significant. Non-interrupted time series analysis was used for the analysis of the relative changes in AB consumption (DDD method). Relation between analysed period (year and quarter) and the dependent variable (AB consumption) was analysed by means of correlation and linear regression method. Pearson' and Spearman's correlations were used to examine the relationship between two variables (*Ansari et al.*, 2010, *Dimiņa*, 2013, *MacKenzie et al.*, 2006, *Teibe*, 2007). The Kolmogorov–Smirnov test was used to determine, whether sample data were normally distributed. The study protocol was approved by the RSU Ethics Committee on 6th October 2011.

2. RESULTS

2.1. Results of point prevalence surveys

2.1.1. Results of point prevalence surveys at the University Children's Hospital

See Table 2.1. for patients' characteristics

Table 2.1.

UCH patients' characteristics (2011-2013)

Year	**2011**		**2012**		**2013**	
Month	**May**	**November**	**May**	**November**	**May**	**November**
Patients	**N (%) [95% CI]**	**N (%) [95% CI]**	**N (%) [95% CI]**	**N (%) [95% CI]**	**N (%) [95% CI]**	**N (%) [95% CI]**
Total number	418	424	395	358	335	320
Boys	230 (55.0) [50.2–59.8]	225 (53.1) [48.4–57.9]	215 (54.4) [49.5–59.3]	196 (54.7) [49.5–59.9]	178 (53.1) [47.8–58.4]	159 (49.7) [44.2–55.2]
Girls	188 (45.0) [40.2–49,8]	199 (46.9) [42.2–51.7]	180 (45.6) [40.7–50.5]	162 (45.3) [40.1–50.5]	157 (46.9) [41.6–52.2]	161 (50.3) [44.8–55.8]
Patients on AB	**125 (29.9) [25.5–34.3]**	**159 (37.5) [32.9–42.1]**	**128 (32.4) [27.8–37.0]**	**130 (36.3) [31.3–41.3]**	**88 (26.3) [21.6–31.0]**	**111 (34.7) [29.5–39.9]**
Chi–square test	p = 0.101		p = 0.430		p = 0.087	
Median age (months)	33	41	33	48	43	41
Gender:						
Male	**63 (50.4) [41.6–59.2]**	**90 (56.6) [48.9–63.3]**	59 (46.1) [37.5–54.7]	**74 (56.9) [48.4–65.4]**	**47 (53.4) [43.0–63.8]**	**57 (51.4) [42.1–60.7]**
Female	62 (49.6) [40.8–58.4]	69 (43.4) [35.7–51.1]	**69 (53.9) [45.3–62.5]**	56 (43.1) [34.6–51.6]	41 (46.6) [36.2–57.0]	54 (48.6) [39.3–57.9]
Chi–square test	p = 0.215	p = 0.258	p < 0.05	p = 0.532	p = 0.952	p = 0.664
Age groups:						
0 – < 1 month	20 (16.0)	19 (12.0)	10 (7.8)	12 (9.2)	10 (11.4)	19 (17.1)
≥ 1 month – < 1 year	14 (11.2)	24 (15.1)	27 (21.1)	21 (16.2)	13 (14.8)	20 (18.0)
≥ 1 – < 5 years	**52 (41.6)**	**54 (34.0)**	**33 (25.8)**	**36 (27.7)**	**32 (36.4)**	24 (21.6)
≥ 5 – < 12 years	27 (21.6)	33 (20.8)	29 (2.7)	35 (26.9)	14 (15.9)	**27 (24.3)**
≥ 12 – < 18 years	12 (9.6)	29 (18.2)	29 (22.7)	26 (19.5)	19 (20.0)	21 (18.9)

Any of PPS did not have normal distribution of patients (Kolmogorov–Smirnov test).

Antibiotic groups used in point prevalence surveys

The most commonly used AB group in all PPS, except on May and November 2011, was other β-lactam AB (J01D) (See Figure 2.1.).

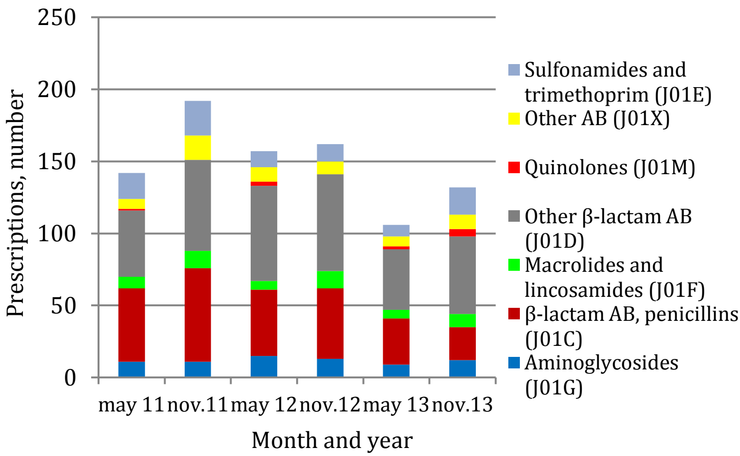

Figure 2.1. **AB groups used during PPS in 2011–2013**

In β-lactam penicillin (J01C) group the commonly used AB were penicillins of the extended–spectrum (J01CA): from 49.0% (CI 41.3–56.7) of all β-lactam AB in the PPS in November of 2012 up to 70.6% (CI 63.1–78.1) in May 2011 (average 58.7%: 62.3% in May's PPS and 55.2% in November's PPS). The Chi–squared test showed that statistically seasonal changes (May – November) did not have significant influence on the use of the extended-spectrum penicillins ($p > 0.05$). In cephalosporin group the most commonly used AB were the 3rd generation cephalosporins: from 54.5% (CI 46.0–63.0) in the PPS in November 2013 up to 72.6% (CI 66.3–78.9) in November of 2011 (average 62.7%: 63.0% in May's PPS and 62.4% in November's PPS) (See Figure 2.2.).

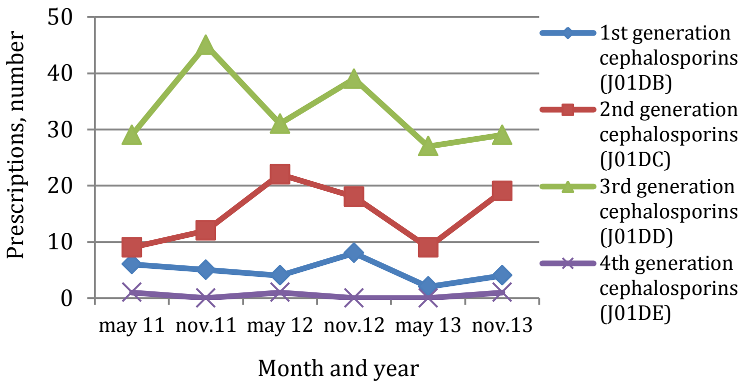

Figure 2.2. **Cephalosporin consumption in PPS during the period of 2011–2013**

A consumption of particular antibiotics in point prevalence surveys during the period of 2011–2013

There were 21 AB used in May 2011 and 20 AB – in November 2011, 23 AB – in May 2012 and 20 AB – November 2012, and 21 AB in both May and November 2013. Ampicillin was the most commonly used AB in May 2011: 25 (17.6%; CI 11.3–23.9) prescriptions, but in November 2013 ampicillin shared the 7^{th}–9^{th} place with gentamicin and amikacin: 6 (4.5%; CI 1.0–8.0) prescriptions. Ceftriaxone was the fifth most frequently used AB in May 2011: 12 (8.5%; CI 3.9–13.1) prescriptions, but in November 2013 it became the most often used AB: 23 (17.4%; CI 10.9–23.9) prescriptions.

Route of administration

There were only IV and O route of administration. IV route of administration dominated in all PPS. The lowest number of IV prescriptions was registered in November 2013 – 75.8%, but the highest – 86.2% in May 2013 (See Figure 2.3.).

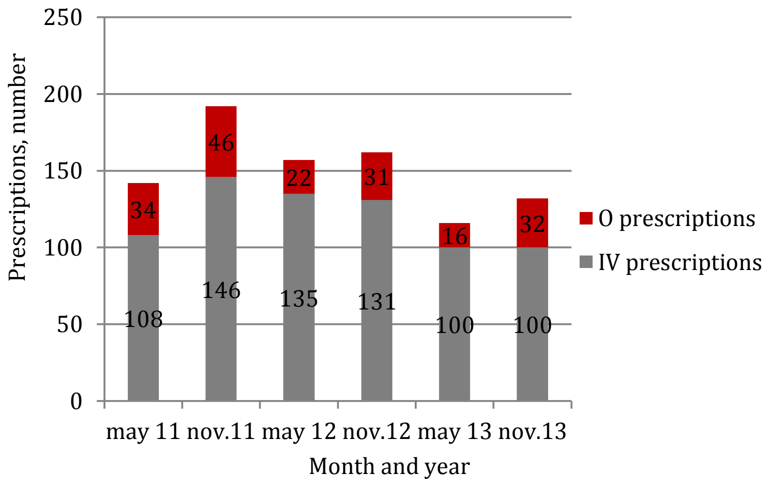

Figure 2.3. **Number of IV and O prescriptions in PPS during the period of 2011–2013**

Surgical prophylaxis – paediatric patients

All PPS had low number of surgical prophylaxis prescriptions: from 4 (4.5%, CI 0.2–8.8) prescriptions in May 2013 to 13 (9.1%, CI 4.4–13.8) in November 2012. Most patients received prophylactic AB for more than one day: from 50.0% (4 prescriptions) in November 2011 to 100% (7 prescriptions) in May 2011 and 100% (12 prescriptions) in November 2012. In total there were 9 AB used in PPS. The most commonly prescribed AB was cefuroxime: 20 (42.5%) prescriptions in all PPS. The second most frequently used AB was ceftriaxone – 12 (25.5%) prescriptions. All AB were prescribed in monotherapy, except for one ampicillin and gentamicin combination in May 2011.

2.1.2. Antibiotic consumption at Latvian hospitals

In November 2012 the PPS was conducted as a part of the ARPEC study. Nine hospitals from Latvia participated in this PPS. Five hundred forty nine patients were included in the study. AB was received by 192 (35.0%, CI 31.0–39.0) patients: 167 (87.0%, CI 82.2–91.8) children and adolescent and 25 (13.0%, CI 8.2–17.8) neonates. Patients hospitalized at the UCH hospitals "Torņakalns" and "Gaiļezers" represented 67.0% of all patients receiving AB. The highest number of patients was in the group of 5–12 years old – 53 (28.0%, CI 21.3–33.9): 33 (17.1%, CI 11.8–22.4) boys and 20 (10.4%, CI 6.1–14.7) girls.

Used antibiotics

The most commonly used AB group in paediatric patients was other β-lactam AB (J01D) – 101 (50.8%; CI 43.9–57.8) prescription, but the second most commonly used AB group was β-lactam AB, penicillins (J01C) – 52 (26.1%; CI 20.0–32.2) prescriptions. Ceftriaxone was the most commonly prescribed AB – 41 (20.6%; CI 15.0–26.2) prescription.

2.2. Antibiotic consumption by using defined daily dosage method

2.2.1. Antibiotic consumption in the hospital

At the UCH hospital "Torņakalns" the number of treated patients decreased from 26055 patients in 2006 to 22211 in 2013 ($r = -0.89$, $p < 0.05$), and the number of bed–days – from 149125 in 2006 to 92575 ($r = -0.99$, $p <$

0.05). The average duration of treatment decreased from 5.7 days in 2006 to 4.2 days in 2013. In total there were 91 AB formulations used during the period of 2006–2013: 44 (48.4%) IV and 47 (51.6%) O formulations (Figure 2.4.).

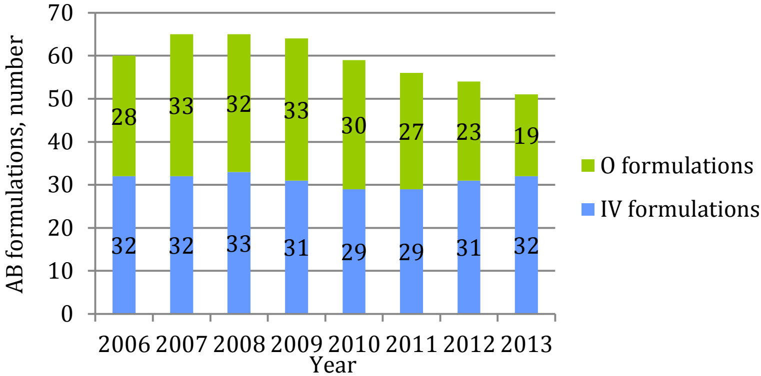

Figure 2.4. **Number of IV and O formulations at the UCH hospital "Torņakalns" in 2006–2013**

The total AB consumption (in DDD) decreased from 58847 DDD in 2006 to 45406 DDD in 2013 ($r = -0.77$, $p < 0.05$). The total number of AB substances equalled 29 in 2012 and 36 in 2006 and 2007 respectively. There was a strong positive correlation (Spearman's rank correlation coefficient r_s = 0.92) between available active substances and AB consumption in DDD/100 BD). The total AB consumption in DDD/100 BD increased by 25.1%: from 39.5 DDD/100 BD in 2006 till 49.4 DDD/100 BD in 2013. AB consumption (DDD/100 patients) slightly decreased: from 225.9 DDD/100 patients in 2006 till 204.4 DDD/100 patients in 2013 but it was not statistically significant (p = 0.08).

Antibiotic seasonal consumption

Hospital showed different total results of AB consumption for the different quarters (2011–2013). These differences were not critical (See Figure 2.5.).

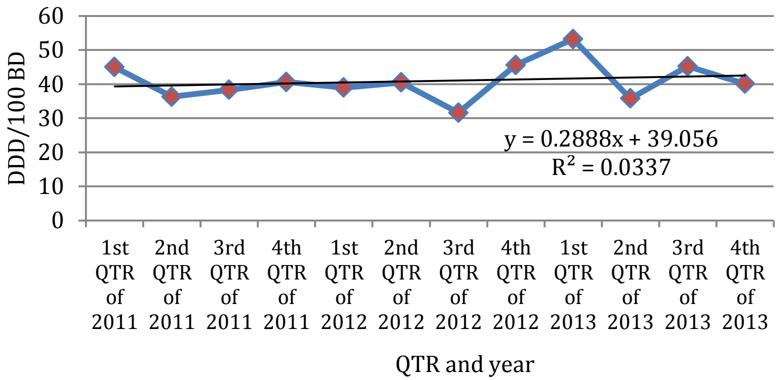

Figure 2.5. **Total AB consumption at the UCH during different quarters for the period of 2011–2013 (DDD/100 BD)**

In 2011 and 2013 the highest AB consumption by indicators (DDD, DDD/100 BD and DDD/100 patients) was registered during the 1st quarter. In 2013 the second highest consumption was registered in summer, although the number of treated patients (4858) and bed–days (26658) was the lowest if to be compared with other quarters in 2013. DDD/100 patients: 53.2 – in the 1st quarter, 35.8 – in the 2nd quarter 45.2 – in the 3rd quarter and 40.1 – in the 4th quarter. While analysing the consumption of different cephalosporin groups (DDD/100 BD), it was established that the 3rd generation cephalosporins had the highest percentage of consumption in all quarters: from 48.6% (6.9 DDD/100 BD) in the 1st quarter of 2013 to 67.8% (6,4 DDD/100 BD) in the 1st quarter of 2011.

Antibiotics used at the UCH "Torņakalns"

During the period of 2006–2013 the most commonly used AB groups were β-lactam AB, penicillins (J01C) and other β-lactam AB (J01D), which combined accounted for 75.5% of the total AB consumption (DDD) registered in 2006 and 73.6% in 2013. A similar trend was also observed in DDD/100 BD (See Figure 2.6.) – from 73.5% of the total AB consumption in 2013 to 77.7% in 2010 and in DDD/100 patients – from 73.6% in 2013 to 77.8% in 2010.

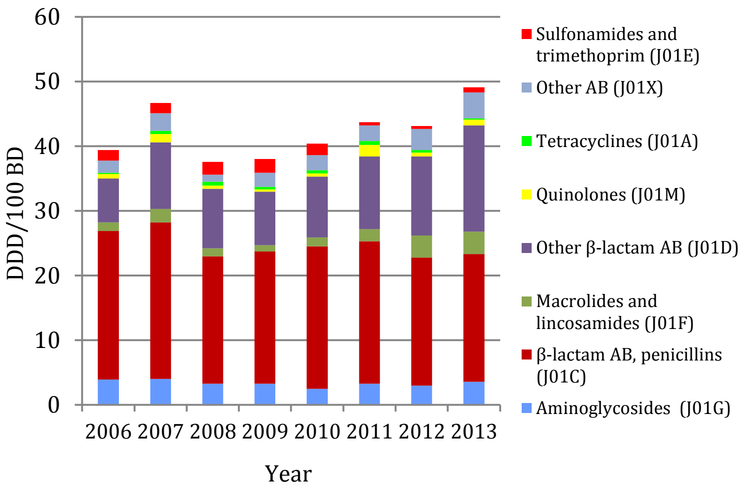

Figure 2.6. **AB groups used at the UCH hospital „Torņakalns" during the period of 2006–2013 (DDD/100 BD)**

B-lactam group antibiotic (J01C) consumption

Total β-lactam AB consumption (in DDD, DDD/100 BD and DDD/100 patients) decreased almost twice (See Table 2.2.).

Table 2.2.

J01C group AB consumption at the UCH hospital "Torņakalns" during the period of 2006–2013

Year	2006	2007	2008	2009	2010	2011	2012	2013
DDD	34279	35425	26830	25454	25999	25647	20212	18194
DDD/100 BD	23.0	24.2	19.7	20.4	22.0	22.0	19.8	19.7
DDD/100 patients	131.6	135.7	111.8	106.7	110.7	90.1	87.9	81.9

Other β-lactam antibiotic (J01D) consumption

Statistically both the total other β-lactam AB and cephalosporin consumption increased significantly only for DDD/100 BD ($r = 0.84$, $p < 0.05$) and ($r = 0.85$, $p < 0.05$). Statistically the 1st generation cephalosporin consumption decreased significantly in respect of all three indicators (DDD/100 BD $r = -0.82$, $p < 0.05$), but the 2nd generation, and especially 3rd generation cephalosporin consumption, statistically significantly increased: ($r = 0.90$, $p < 0.05$) and ($r = 0.92$, $p < 0.05$) respectively. There was no correlation between the decrease of penicillins' consumption and the increase of cephalosporins' consumption neither in DDD ($r = -0.22$, $p = 0.60$) nor DDD/100 BD ($r = -0.40$, $p = 0.32$). Ceftriaxone consumption increased in respect to all three indicators: DDD – 3 times (from 1940 in 2006 – 6243 in 2013), DDD/100 BD – 5 times (from 1.3–6.7), but DDD/100 patients – almost 4 times (from 7.4–28.1).

Antibiotic group (J01A, J01E, J01F, J01G, J01M and J01X) consumption

Statistically none of these groups had significant consumption growth or reduction.

2.2.2. Antibiotic consumption in hospital wards

In 2006 AB consumption at the Paediatric Surgery Clinic equalled 28.0% (16482 DDD) of the total consumption and in PICU – 3.4% (2019 DDD), but in 2013 – 22.8% (10369 DDD) and 3.9% (1761 DDD) respectively. In 2013 the intensity of AB usage (DDD/100 BD) was the highest in oncohematology (92.5 DDD/100 BD), PICU (84.3 DDD/100 BD) and General Paediatric ward of the hospital "Torņakalns" (82.2 DDD/100 BD).

2.2.3. Antibiotic consumption at the Paediatric Surgery Clinic

Total AB consumption for both DDD ($r = -0.80$, $p < 0.05$) and DDD/100 ($r = -0.76$, $p < 0.05$) decreased. It also decreased for DDD/100 BD, but these changes were not statistically significant ($p = 0.16$). The most commonly used AB groups were β-lactam AB, penicillins (J01C) and other βlactam AB (J01D). These two groups together equalled 76.1% of the total AB consumption (DDD) in 2011 to 83.3% in 2007. Similar tendency was identified for DDD/100 BD – from 76.2% of the total AB consumption in 2011 to 83.7% in 2007. The consumption of the 1st generation cephalosporins decreased from 807 (31.0%) DDD in 2006 to 770 (21.0%) DDD of the total cephalosporin consumption in 2013, but the consumption of the 3rd generation cephalosporins increased from 685 (26.0%) DDD in 2006 to 1547 (43.0%) in 2013. There was no correlation between the decrease of the 1st generation consumption and the increase of the 3rd generation consumption ($r = -0.13$, $p > 0.05$).

2.3. Antibiotic consumption 90%DU analysis

During the period of 2006–2013 the total number of used AB ranged from 36 AB (in 2006) to 30 AB (in 2012). Ninety percent of all used AB equalled 13.8 AB in average. The lowest number of 90%DU AB was registered in 2007 – 38.9%, but the highest – 45.2% in 2011. Starting from 2008, amoxicillin (J01CA04) was the most commonly used AB at the hospital. During the studied period it was also the only AB that was among five most frequently used AB (See Figure 2.7.). Amoxicillin consumption increased from 12.3% in 2006 to 23.1% in 2013. Although ampicillin (J01CA01) was among 90%DU AB, during the studied period the ampicillin usage decreased significantly: from 20.5% of the total consumption in 2006 to 5.5% in 2013. The usage of ceftriaxone (J01DD04) increased from 3.3% in 2006 to 13.8% in 2013, and starting from 2010, it became the second most frequently used AB.

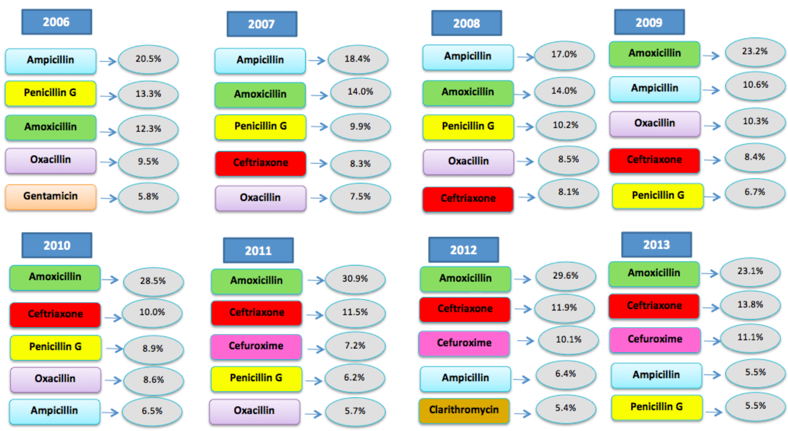

Figure 2.7. **Five most commonly used AB at the UCH hospital "Torņakalns" during the period of 2006–2013 (90%DU)**

2.4. Acute appendicitis: the patients' characteristics and analysis of the antibiotic usage

2.4.1. The patients and surgeries' characteristics and analysis of prophylaxis and treatment

Table 2.3. shows the patients' characteristics included into the study. During the period of 2011–2013 the highest number of patients was patients under the age of 12 years, but in 2001-2003 – at the age of 12–18 years. In 2013 surgery was not performed in 29 (5.6%) patients: 10 (34.5%) girls and 19 (65.5%) boys, but in 2001-2003 the surgery was not performed in 10 (1.3%) patients: 7 (70.0%) girls and 3 (30.0%) boys.

Table 2.3.

Demographic characteristics on the patients with acute appendicitis (2001–2003 and 2011–2013)

Year	2011–2013		2001–2003	
Patients	Total N (%) [95% CI]	Had surgery (%) [95% CI]	Total N (%) [95% CI]	Had surgery (%) [95% CI]
Total number	520	491 (94.4) [92.4–96.4]	773	763 (98.7) [97.9–99.5]
Boys	**311 (59.8) [55.6–64.0]**	292 (59.5) [55.2–63.8]	**449 (58.1) [54.6–61.6]**	446 (58.5) [55.0–62.0]
Girls	209 (40.2) [36.0–44.4]	199 (40.5) [36.2–44.8]	324 (41.9) [38.4–45.4]	317 (41.5) [38.0–45.0]
Mean age (years ± SD)	11.4 ± 4.0	11.4 ± 4.0	11.5 ± 3.7	11.6 ± 3.7
Median age (years)	11.5	11.4	12.1	12.2

The number of patients, who had surgery and to whom AB was or was not administered in 2011–2013 and 2001–2003 is presented in Figure 2.8. Statistically there was significant difference between patients, who had surgery and to whom AB was or was not administered in 2011–2013 and 2001–2003 (Chi–squared test, $p < 0.05$). Perforative appendicitis had 79 (15.2%) patients in 2011–2013 and 110 (14.2%) patients in 2001–2003. Surgery was performed in all these patients.

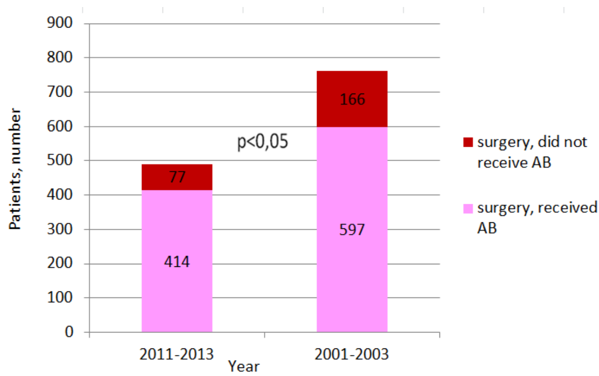

Figure 2.8. **Patients with acute appendicitis, who had a surgery and to whom AB was or was not administered during the period of 2001–2003 and 2011–2013**

In 2011–2013 283 (68.4%, CI 63.9–72.9) patients did not receive AB prophylaxis, 99 (23.9%, CI 19.8–28.0) received but in 32 (7.7%, CI 5.1–10.3) cases there was no detailed information available whether or not the AB usage was initiated before the surgery. In 2001–2003 354 (59.3%, CI 55.4–63.2) patients did not receive AB prophylaxis, 221 (37.0%, CI 33.1–40.9) received, but in 22 (3.7% CI 2.2–5.2) cases there was no detailed information available. Statistically there was significant difference between patients, who received or did not receive AB prophylaxis in 2011–2013 and 2001-2003 (Chi-squared test, $p < 0.05$). In 2011–2013 36 (36.4%) patients had timely prophylaxis, but in 2001–2003 – 25 (11.3%) patients. Reason in notes was not written in 174/414 (42.0%) patient medical charts for those patients who had surgery in 2011–2013. In 2001–2003 such patient medical charts were 392/597 (65.7%). In 2001–2003 44.3% or 58 patients with diagnosis acute phlegmanous or catarrhal appendicitis received AB for longer than 24 hours but in 2011–2013 – 55.8% or 29 patients. The indication of AB administration time was not written in 60.2% or 133 patients' records in 2001–2003 and in 85.9% or 85 records in 2011–2013. Four the most commonly used AB are indicated in Table 2.4.

Table 2.4.

Four most commonly prescribed AB for surgical prophylaxis (2011–2013 and 2001–2003)

Year	**2011–2013**		**2001–2003**	
Total number of prescriptions	165		391	
Antibiotics	Mono therapy N (%)	Combination therapy N (%)	Mono therapy N (%)	Combination therapy N (%)
Ampicillin	**12 (7.3)**	**49 (29.7)**	**45 (11.5)**	**141 (36.1)**
Gentamicin	0	**47 (28.5)**	0	**149 (38.1)**
Metronidazole	0	18 (10.9)	0	21 (5.4)
Ceftriaxone	6 (3.6)	13 (7.9)	4 (1.0)	3 (0.8)

2.4.2. Analysis of the dosages of the most commonly used antibiotics

The Summary contains analysis of ampicillin and gentamicin dosages.

Ampicillin

According to BNFC in 2011–2013 ampicillin doses were correct in 18/61 (29.5%) prescriptions, but too high in 43 (70.5%) prescriptions. According to Lexi and SPC recommendations, doses were correct in 40 (65.6%) prescriptions, but too low in 21 (34.4%) prescriptions. According to BNFC in 2001-2003 doses were correct in 59 (32.8%) prescriptions, too low in 3 (1.7%), but too high in 118 (65.6%) prescriptions. According to Lexi and SPC, doses were correct in 128 (71.1%) prescriptions, but too low in 52 (28.9%) prescriptions.

Gentamicin

According to SPC in 2011–2013 doses were too low in 30/47 (63.8%) prescriptions and in 2001–2003 they were too low in 82 (57.7%) prescriptions.

According to BNFC and Lexi recommendations, gentamicin doses were too low in all prescriptions.

2.4.3. Antibiotic off–label use

Antibiotic prescriptions outside the indication and patient's age

The Summary contains analysis of ampicillin and gentamicin prescriptions only.

Ampicillin

All prescriptions: 61 in 2011–2013 and 180 in 2001–2003 were outside of the indication, prophylaxis listed in the SPC.

Gentamicin

According to *Gentamicin Sopharma* (2014) SPC the usage outside the indication (prophylaxis) was in 47 cases in 2011–2013 and in 142 cases in 2001–2003.

Antibiotic doses that do not correspond to the Summary of Product Characteristics

The Summary does analyse ampicillin, gentamicin and metronidazole off-label doses. AB doses were not prescribed in accordance with SPC in 65/126 (51.6%) prescriptions in 2011–2013 and in 143/343 (41.7%) prescriptions in 2001–2003.

2.5. Mesadenitis: the patients' characteristics and analysis of the antibiotic usage

2.5.1. Patients' characteristics and treatment analysis

Patients' demographic characteristics are presented in Table 2.5.

Table 2.5.

Patients with mesadenitis demographic characteristics (2001–2003 and 2011–2013)

Year	**2011–2013**			**2001–2003**		
Patients	**N (%) [95% CI]**			**N (%) [95% CI]**		
Boys	87 (48.1) **[**40.8–55.4**]**			192 (48.1) **[**43.2–53.0**]**		
Girls	**94 (51.9) [44,6–59.2]**			**207 (51.9) [47.0–56.8]**		
Mean age (years ± SD)	10.4 ± 4.3			11.0 ± 4.3		
Median age (years)	10.5			11.8		
Age groups	Total N (%)	Girls N (%)	Boys N (%)	Total N (%)	Girls N (%)	Boys N (%)
0 – <1 month	0	0	0	0	0	0
≥ 1 month – < 1 year	2 (1.1)	1 (0.6)	1 (0.6)	1 (0.3)	1 (0.3)	0
≥ 1 – < 5 years	24 (13.3)	14 (7.7)	10 (5.5)	42 (10.5)	24 (6.0)	18 (4.5)
≥ 5 – < 12 years	**90 (49.7)**	**51 (28.2)**	39 (21.5)	171 (42.9)	81 (20.3)	90 (22.5)
≥ 12 – < 18 years	65 (35.9)	28 (15.5)	37 (20.4)	**185 (46.3)**	**101 (25.3)**	84 (21.1)

In 2011–2013 USG approved diagnosis in 127 (70.2%) patients, but in 2001–2003 – 15 (3.8%) patients. In 2011–2013 mesadenitis was not approved by USG in 48 (26.5%) patients, but in 2001–2003 – in 243 (60.9%). In 2011–2013 USG was not performed in 6 (3.3%) patients, but in 2001–2003 – 141 (35.3%) patients. In 2011–2013 AB received 39.8% patients: 40 (55.6%; CI

44.1–67.1) boys and 32 (44.4%; CI 32.9–55.9) girls, but in 2001–2003 – 26.6% patients: 54 (50.9%; CI 41.4–60.4) boys and 52 (49.1%; CI 39.6–58.6) girls. In 2011–2013 the most commonly used AB was ampicillin – 61 (51.3%) prescriptions, but in 2001–2003 – 84 (44.5%). In 2011–2013 there were 39 (32.2%) gentamicin prescriptions, but in 2001–2003 – 73 (38.6%). Reason in notes was not written in 22 (30.6%) patients' medical records in 2011–2013 and in 79 (74.5%) patients' medical records in 2001–2003.

2.5.2. Analysis of antibiotics most commonly used in the mesadenitis treatment

The Summary contains analysis of ampicillin and gentamicin prescriptions.

Ampicillin

See Figure 2.9. for the correctness of ampicillin doses.

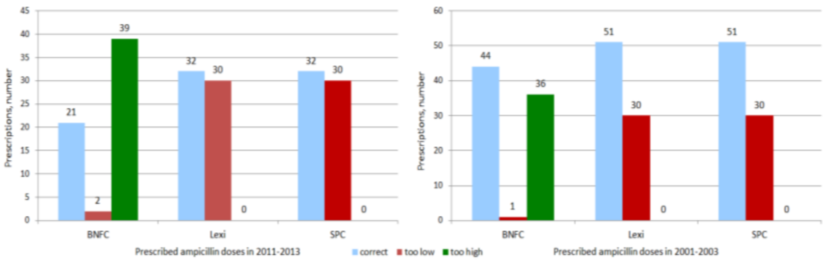

Figure 2.9. **Compliance of the prescribed ampicillin doses with BNFC, Lexi and SPC recommendations as of 2011–2013 and 2001–2003**

Wrong doses were administered most frequently to children under the age of 12 years: according to SPC, such were 30 (81.1%) prescriptions in 2011–2013 and 30 (60.0%) prescriptions in 2001–2003.

Gentamicin

See Figure 2.10. for the correctness of doses.

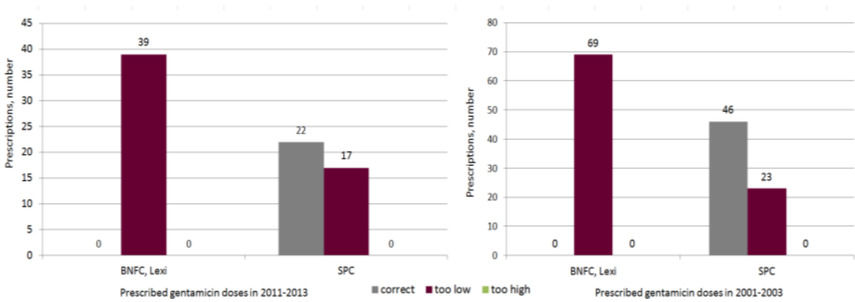

Figure 2.10. **Compliance of the prescribed gentamicin doses with BNFC, Lexi and SPC recommendations as of years 2011–2013 and 2001–2003**

2.5.3. Antibiotic off–label use

The Summary contains analysis of ampicillin and gentamicin off–label use.

Doses not listed in the Summary of Product Characteristics

Ampicillin

In 2011–2013 doses not listed in the SPC were prescribed in 30 (48.4%) prescriptions, but in 2001–2003 – in 30 (37.0%) prescriptions.

Gentamicin

In 2011–2013 doses not listed in the SPC were prescribed in 17 (43.6%) prescriptions, but in 2001–2003 – in 23 (33.3%) prescriptions.

Timing of administration

In 2011–2013 ampicillin had wrong administration in regard of timing in 15 (24.2%) prescriptions, but in 2001–2003 – in 5 (6.0%) prescriptions. Timing for gentamicin timing of administration was every 12 hours according to SPC (*Gentamicin KRKA*, 2011, *Gentamicin Sopharma*, 2014), but not under BNFC and Lexi recommendations.

2.6. Injuries of upper and lower extremities: patients' characteristics and analysis of the antibiotic usage

2.6.1. Characteristics of patients and surgeries, and analysis of the surgical prophylaxis

Both during the period of 2011–2013 and 2001–2003 the number of hospitalized boys exceeded the number of hospitalized girls more than twice. See Figure 2.11. for the characteristics of patients.

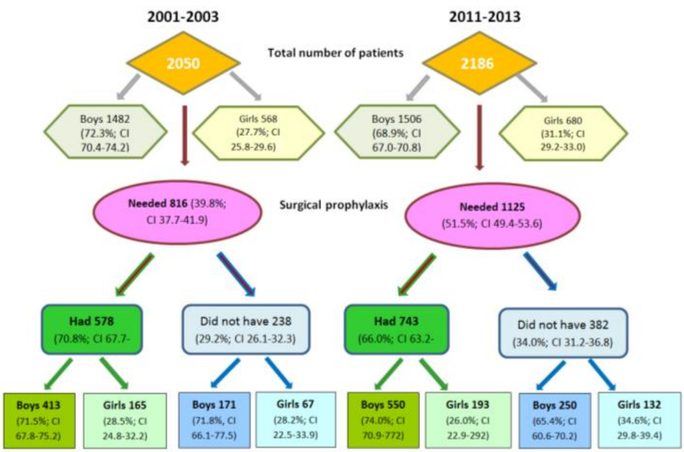

Figure 2.11. **Demographic characteristics for the patients with upper and lower extremities (2011–2013 and 2001–2003)**

In 2011–2013 AB were received by 751 (34.4%; CI 32.4–36.4) patient: 555 (73.9%; CI 70.8-77.0) boys and 196 (26.1%; CI 23.0-29.2) girls, but in 2001-2003 – by 654 (31.9%; CI 29.9-33.9) patients: 472 (72.2%; CI 68.8-75.6) boys and 182 (27.8%; CI 24.4-31.2) girls. During both periods of study (2011-2013 and 2001-2003) the highest number of procedures was the reduction and immobilization without inserting any internal fixation devices (Table 2.6.).

Table 2.6.

Characteristics of surgeries in 2011–2013 and 2001–2003

Year	**2011–2013**	**2001–2003**
Surgery	**N (%) [95% CI]**	**N (%) [95% CI]**
Total number	2116	1907
Reduction and immobilization without internal fixation	**962 (45.5) [43.4–47.6]**	**1016 (53.3) [51.1–55.5]**
Closed reduction with insertion of internal fixation devices	928 (43.9) [41.8–46.0]	639 (33.5) [33.4–37.7]
Open reduction	226 (10.7) [9.4–12.0]	252 (24.8) [22.9–26.7]
Only immobilization (number of patients)	140	212

In 2011–2013 the highest number of patients who received AB prophylaxis was the age of 5-12 years – 347 (46.7%) patients, but in 2001–2003 – from the age of 12-18 years – 293 **(**50.7%) patients. In 2011–2013 there were more patients than in 2001–2003 who did not receive AB prophylaxis although it was indicated by the guidelines: 382 (34.0%) and 238 (29.2%) patients respectively. Statistically this difference was significant (Chi-squared test, $p < 0.05$). Details on the prophylaxis timing and duration are shown in Table 2.7.

Table 2.7.

Surgical prophylaxis during the period of 2011–2013 and 2001–2003

Year	2011–2013	2001–2003
Information about prophylaxis	**N (%) [95% CI] (number of prescriptions)**	**N (%) [95% CI] (number of prescriptions)**
Too late	146 (19,6)	30 (5,2)
Too early	184 (24,7)	9 (1,5)
On time	370 (49,7)	10 (1,7)
No information about timing	44 (5,9)	532 (91,2)
1 dose	546 (73,4)	196 (33,7)
Multiple doses administered in 24 h	153 (20,6)	326 (56,1)
> 24 h	41 (5,5)	52 (9,0)
No correct information available	4 (0,5)	7 (1,2)

Analysis of surgical prophylaxis according to ECDC quality indicators (Figure 2.12).

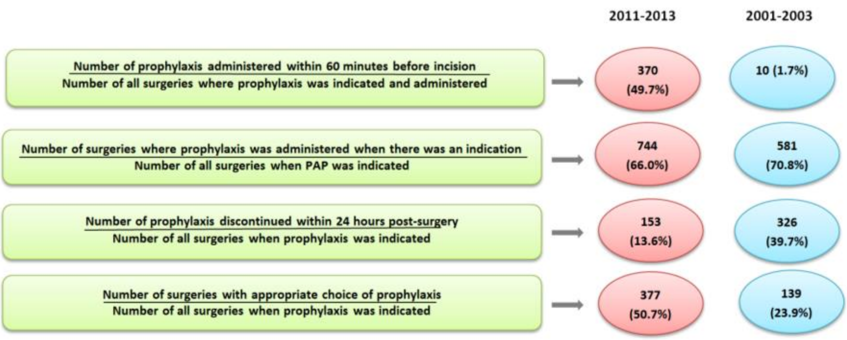

Figure 2.12. Surgical prophylaxis according to ECDC quality indicators during the period of 2011–2013 and 2001–2003.

2.6.2. Analysis of the most commonly used antibiotics for surgical prophylaxis

In 2011–2013 6 AB were used for prophylaxis, but in 2001–2003 – 4 AB. The most frequently used AB are indicated in Table 2.8. In 2011-2013 doses were not analysed in 20 (2.7%) prescriptions – the patient's medical charts did not contain any data on the patient's weight. Cefazolin was used in 9 cases, cefuroxime – in 6 and ceftriaxone - in 5. Ampicillin, amoxicillin and oxacillin each was used in one prescription.

Table 2.8.

Three most frequently used AB during the period of 2011–2013 and 2001–2003

Year	**2011-2013**		**2001-2003**	
Antibiotic	**N (744)**	**%**	**N (581)**	**%**
Cefazolin	**377**	**50.7**	139	23.9
Cefuroxime	155	20.8	**432**	**74.4**
Ceftriaxone	209	28.2	0	0

Analysis of cefazolin doses

According to the hospital's Recommendations in 2011-2013 cefazolin doses were not correct in 217 (59.0%) prescriptions, but according to Lexi they were not correct in 160 (43.5%) prescriptions and according to the SPC – in 120 (32.6%) prescriptions. According to the hospital's Recommendations in 2001-2003 cefazolin doses were not correct in 35 (34.7%) prescriptions, but according to Lexi – in 22 (21.8%) prescriptions and according to the SPC – in 23 (22.8%) prescriptions. AB doses were not correct most often in children under the age of 12 years: according to the hospital's Recommendations during the period of 2011–2013 in 152 (80.4%) prescriptions and during the period of 2001–2003 – in 23 (88.4%) prescriptions.

Analysis of cefuroxime doses

According to BNFC and Lexi recommendations, in 2011–2013 cefuroxime doses were not correct in 121 (81.2%) prescriptions and according to the SPC – in 45 (30.2%) prescriptions, but according to BNFC and Lexi recommendations, in 2001–2003 – in 124 (35.6%) prescriptions and according to the SPC – in 92 (26.4%) prescriptions. Statistically the difference was significant for BNFC and Lexi recommendations ($p < 0.05$), but was not significant for the SPC (Chi–squared test, $p = 0.588$).

Analysis of ceftriaxone doses

According to the SPC, in 2011-2013 doses were correct in 160 (78.4%) prescriptions, but according to BNFC recommendations – only in 88 (43.1%) prescriptions.

2.6.3. Antibiotic off–label use

Antibiotic prescriptions outside the indication and patient's age

In 2011–2013 AB were used for the indications not listed in the SPC in 418 (56.2%) prescriptions and in 2001–2003 – in 283 (48.7%) prescriptions.

Antibiotic doses, which do not match the Summary of Product Characteristics

In 2011–2013 antibiotic doses did not match the SPC in 210 (28.2%) prescription and in 2001–2003 – in 123 (21.2%) prescriptions.

3. DISCUSSION

3.1. The usage of point prevalence surveys in the antibiotic consumption analysis

In 2003, 2005, 2007 and 2011 there have been conducted several national level PPS in Latvia (*Dimiņa*, 2013). Nevertheless, the usage of AB in hospitalized paediatric patients as a separate notion has been analysed only since 2011 as a part of these doctoral thesis. After the development of the ARPEC PPS protocol it became easier to compare the UCH PPS results with the results from hospitals in other countries. Literature provided studies, where the PPS methodology is used, but paediatric patients were quite often analysed together with adults (*Ansari et al.*, 2009, *Ansari et al.*, 2010, *Dimiņa et al.*, 2009, *Thu et al.*, 2012) or there were different nuances in PPS protocols, e.g., information about AB doses were not collected (*Thu et al.*, 2012, *Xie et al.*, 2014). The aim of the PPS conduction at the UCH was to find out general trends of AB usage at the hospital, while focusing on AB usage trends at the Paediatric Surgery clinic. PPS results show that there is the high use of the 3rd generation cephalosporins, especially ceftriaxone consumption in the UCH in general (Figure 2.1.). More and more cephalosporin and quinolone use has been linked to development of resistance, as unnecessary use of them may contribute to the development of selection pressure. These are broad-spectrum AB, which reaches high concentrations in the body and are excreted for relatively long time. The most appropriate is AB of the narrow-spectrum penicillin group. PPS methodology does not provide explanation for the high use of cephalosporins. The UCH results are similar to the results obtained from other Latvian hospitals where the 3rd generation cephalosporins were among the most frequently used AB (previously these were the 1st generation cephalosporins) (*Dimiņa*, 2013, *Dimiņa et al.*, 2009). Similar trends were observed in the PPS performed in

Latvian paediatric hospitals and wards in November 2012 – other β-lactam AB (and especially the 3rd generation cephalosporins) were the most frequently prescribed AB group – in 101 (50.8%) prescriptions. Nevertheless, it should be noted that 66.7% of all analysed patients were the UCH patients.

The route of AB administration is also one of the quality indicators of the AB usage. There was the high number of parenterally administrated AB at the UCH (Figure 2.3.). The switch from parenteral to oral AB depends from the individual choice made by the physician – the hospital does not provide any general recommendations on when such switch should be performed. The usage of parenteral AB also indicates that the necessity of the AB usage is not always evaluated after the period of 48-72 hours (*Public Health England*, 2015).

Strength and limitations of the method

In PPS necessary information is obtained from the patients' medical documents. Therefore there is less possibility of collecting wrong data than in the case of DDD method were data are obtained from the pharmacy. In addition, unlike the DDD method, where aggregated data (hospital in general or particular ward) are used, in PPS individual (patient specific) data are used. The PPS methodology is useful in situations, when it is necessary to obtain information on AB use for a specific time period or on AB usage tendencies (if PPS are repeated). This method could also be used to obtain information on spectrum of used AB in the hospital in general or in a specific ward in particular. This method does not require substantial financial investment and the PPS protocol is not very complicated, which is important when thinking about specialists who will use this protocol. The PPS has also some limitations, e.g., analysis is performed only on the patients in the PPS who receive AB at a specific point in time, but it is impossible to obtain information on patients, who should receive AB but do not receive them. The PPS does not provide information on the total AB consumption in a longer period, because it records the situation at a particular point in time. Cross-sectional studies, that also include the PPS, do not allow to analyse the incidence (e.g., time when the AB usage is started).

3.2. The usage of the methodology of the defined daily dosage in antibiotic consumption studies

The UCH AB consumption data were analysed by using DDD (characterises AB total consumption), DDD/100 BD and DDD/100 patients (both characterise the intensity of AB usage). The usage of cephalosporins and especially the 3rd generation cephalosporins has increased (Figure 2.6.). There was no evidence found that the highest seasonal AB consumption would be in last quarter of the year, when it could be linked with, for example, increase of lower respiratory tract infections. In 2013 the second highest AB consumption was registered in summer (DDD/100 BD (Figure 2.5.) as well as DDD/100 patients. At the same time the number of treated patients bed-days was the lowest in the 3rd quarter if to be compared with other quarters in 2013. (The 2nd lowest number of treated patients and bed-days was the 4th quarter –4976 and 28009 respectively.) Such results could not be explained by the fact that some chief nurses may build medicines stockpiles in their wards or with administrative (ward therapeutic profile) changes that took place during different quarters as of 2011 and 2012. The UCH had provided results similar to those in *Porta et al.* study (*Porta et al.*, 2012) by using 90%DU method – in both the UCH hospital "Torņakalns" and hospitals in the *Porta et al.* study 90%DU made in average 14 AB. Average usage of AB in total was less than in the *Porta et al.* study – 31 and 47 respectively. Differences were also observed in AB that accounted for 90%DU: amoxicillin all study period was among top five AB in the UCH hospital “Torņakalns” (Figure 2.7.), but the *Porta et al.* study amoxicillin was not among the five most frequently used AB.

Strength and limitations of the methods

The strength of this method is that it is possible to obtain information about the AB consumption (DDD) and the intensity of AB usage (DDD/100 BD and DDD/100 patients) in the hospital in general or in the hospital ward or clinic in particular. DDD method similarly to PPS does not require large financial resources to perform the analysis. One of limitations of this method is that it does not show the real AB consumption, because the DDD is artificially created unit of measurement and does not necessarily reflect the recommended or Prescribed Daily Dose (*Haug et al.*, 2014, *Müller et al.*, 2006). AB consumption analysis in hospital wards complicated situation where the structure of wards changed significantly during 2011-2013: some wards were merged together, some wards changed medical profiles, some wards were closed while the hospital pharmacy continued to count AB by using the same old administrative ward principle and did not take into account different medical profiles. Therefore there could be a situation that in the ward where previously patients with gastroenterology and endocrinology problems were hospitalized, after the restructuring had not only patients with gastroenterology and endocrinology problems, but also with rheumatology and nephrology problems. But the pharmacy still regarded it just as a ward number four. These administrative changes had negative influence on the quality of results and AB consumption analysis in wards had not significant value. The Thesis results focused on AB consumption analysis performed only at the Paediatric Surgery Clinic. In 2006 there were four surgery wards, but in 2013 – remained only two. In 2008-2012 abdominal surgery, gastroenterology and endocrinology patients were hospitalized in the same ward, but the hospital pharmacy did not specify, which AB was received by surgical patients.

The main problem in the context of AB consumption studies in children is that, although DDD has been one of the most common unit used in measuring AB use, the measuring of AB use in paediatrics is a problem. The reason – the WHO DDD methodology is not applicable in children due to the vast differences in body weight within this particular population. There are no established similar analyses principles for AB consumption analysis established in Latvian hospitals, and almost all consumption studies are voluntary and based on researchers enthusiasm. Nevertheless, this is not a problem only in Latvia, but also in in other countries (*Norberg et al.*, 2014). At the moment hospitals in Latvia can choose to conduct or not to conduct AB consumption studies, as well as what methodologies use. It was possible to use the DDD method in the Thesis, because one of the tasks was to analyse AB consumption trends provided by this method.

3.3. Surgical prophylaxis

AB surgical prophylaxis is important quality indicator, which indicates correctness of the AB usage at the hospital. When analysing AB use in patients with acute appendicitis and upper and lower extremities injuries it was impossible to use all EDCD (2013) proposed quality indicators, as all necessary information was not always available (e.g., time of AB administration).

Surgical prophylaxis in PPS

In all PPS studies, conducted at the UCH, the number of patients that had AB prophylaxis was very low: from 11.8% in May 2011 to 30.0% in November 2013. Although in general the number of patients was very low, most of them received prophylaxis for more than 24 hours. Such a small number of patients does not allow to draw conclusions on the appropriateness of the surgical prophylaxis, which is based only on PPS results.

Surgical prophylaxis in patients with acute appendicitis

When comparing results obtained in 2001–2003 and 2011–2013, there are still many patients, who did not receive prophylaxis on time during the period of 2011–2013. 88.7% or 196 patients did not receive prophylaxis on time in 2001–2003 and 63.6% or 63 patients in 2011–2013. Situation with the duration of prophylaxis was even worse in patients with diagnosis acute phlegmanous or catarrhal appendicitis who received AB for longer than 24 hours in 2011–2013 if to be compared with 2001–2003. There were no records in the patients' medical charts regarding the reasons of this prolonged prophylaxis. In addition, the situation with the indication of AB administration time has also not improved in 2011–2013 if to be compared with 2001–2003. Currently the hospital's Recommendations (*Zavadska et al.*, 2013) state that patients with destructive appendicitis should have AB prophylaxis (cefotaxime). Different international guidelines suggest that AB prophylaxis is necessary before all appendectomies (both complicated and uncomplicated appendicitis) (*Andersen et al.*, 2005, *Daskalakis et al.*, 2014, *Hopkins*, 2010, *Lee et al.*, 2010, *SCHTA*, 2010, *SIGN*, 2008). According to some authors (*Vons et al.*, 2011), all patients, who have surgery, should receive AB prophylaxis, because routine diagnostic methods cannot guarantee that the patient will or will not have destructive appendicitis. Different AB are recommended in these guidelines, e.g., UpToDate database recommends that children with non-perforated appendicitis receive a single prophylactic dose of a broad spectrum antibiotic, e.g., cefoxitin, cefotetan, piperacillin/tazobactam, ceftriaxone and metronidazole or gentamicin and either clindamycin or metronidazole in patients allergic to penicillins and cephalosporins. Ceftriaxone suggestion is disputable taking into account the long half-life of this AB especially in situation where no need for further treatment is. Third generation cephalosporin (especially ceftriaxone) use can also lead to an increase in infections due to ESBL and MRSA producing organisms.

Surgical prophylaxis in patients with upper and lower extremities injuries

In 2011–2013 there were more surgeries with one prophylactic AB dose than in 2001–2003 (Table 2.7). It is a positive tendency that ceftriaxone usage in prophylaxis decreased but cefazolin usage increased in 2011–2013 (Table 2.8). (In 2001–2003 ceftriaxone was not used for prophylaxis.) It is not possible to explain these changes with methods used in this research. The qualitative research is needed to explain why surgeons have changed their prescription habits. If to be compared with the period of 2001–2003, in 2011–2013 there were more patients with open fractures or closed reduction with insertion of internal fixation who did not receive AB prophylaxis. According to literature these patients should receive prophylaxis and in most cases it is one AB dose (*Bratzler et al.*, 2013, *Darouiche et al.*, 2004, *Gosselin et al.*, 2004, *INESSS*, 2005, *SAAGAR*, 2014, *SCHTA*, 2010, *SFAR et al.*, 2011). There is no consensus among the UCH surgeons on when prophylaxis is necessary and when not. There are also no correct statistical data available in the UCH on how many paediatric patients with SSI were re-hospitalized in the UCH or other hospitals because of SSI. The authors (*Ng et al.*, 2012), who analysed surgeons' adherence to guidelines for surgical AB prophylaxis concluded that there was a wide variation of overall compliance with SAP guidelines, ranging from 0% to 71.9%. The misuses of prophylactic AB were common occurrence, particularly in the form of inappropriate choice and prolonged duration of administration.

Lack of awareness of existing guidelines, influence of initial training, personal preference and influence from colleagues were among the factors, which hindered the surgeons' adherence to guidelines. There is a need for educating the UCH surgeons on the correct AB prophylaxis. The UCH Paediatric Surgery Clinic has the same AB prophylaxis problems as those described in the respective literature (*Amadeo et al.*, 2010, *Kesler et al.*, 1982, *Rangel et al.*, 2011, *Voit et al.*, 2005) (Figure 3.1.).

Prolonged surgical prophylaxis

Prophylaxis started to early or too late

Unnecessary use of high risk AB (e.g., ceftriaxone)

Avoiding AB prophylaxis when necessary

Figure 3.1. **Surgical prophylaxis problems in the UCH Paediatric Surgery Clinic**

3.4. Patients with acute appendicitis treatment

In 2011–2013 the percentage of patients with phlegmanous or catarrhal appendicitis, who received AB for more than 24 hours was higher than in 2001–2003 – 80,2% (150 patients) and 66.3% (183 patients) respectively. In the systematic review completed in 2008 the authors concluded that children with uncomplicated (acute or gangrenous), but not perforated, appendicitis can be treated with prophylactic AB for approximately 24 hours or less (*Nadler et al.*, 2008). The authors also concluded that although the triple AB therapy has been the main standard in paediatric patients, monotherapy with broad-spectrum AB could be equally effective, and quite possibly it could be more cost–effective. Also the evidence supports the use of the guidelines in the paediatric population similar to those suggested for the adult population when managing acute appendicitis. It is not possible to ignore the fact that some information, which could justify the prolonged use of AB, was missing from the UCH patients' medical charts as the data were collected retrospectively. However, despite this potential confounder, there was a high number of patients with uncomplicated appendicitis, who have received prolonged AB therapy.

3.5. Patients with mesadenitis treatment

In 2011–2013 there were more patients whose diagnosis was confirmed by the USG than in 2001–2003. It could be explained by the development of the USG technic, as well as more frequent USG use in situations when mesadenitis was suspected. In 2001–2003 there were more cases when the patients' medication charts held no records on reasoning for AB administration than it was during the period of 2011–2013 (74.0% and 30.6%), confirming the results obtained from analysis of cases of acute appendicitis and injuries of upper and lower extremities – not always the physicians had the grounded arguments for the AB use. In addition, there are still gaps in the patients' medical charts. Although acute mesadenitis treatment does not always require AB treatment (*East Cheshire NHS Trust*, 2013, *Mao clinic*, 2013), there was a higher proportion of patients who received AB in 2011–2013 – 39.8% (72 patients) than in 2001–2003 – 26.6% (106 patients). Since the data were collected retrospectively, it was not possible to explain this higher proportion of patients on AB in 2011–2013.

Historical control group

Historical control group used in the analysis of patients with acute appendicitis, mesadenitis and injuries of upper and lower extremities has the following advantages: saving of time and resources required to carry out the research because of the same control group of patients with the same diagnoses treated at the UCH. There are also some limitations: a special sensitivity to the selection bias, e.g., changes in diagnostic criteria over the time (e.g., in the mesadenitis diagnostic) and the possibly incomplete information recorded in the patients' medical records (e.g., the high number of patients with injuries of upper and lower extremities in 2001–2003, whose medical records had no information on the time of AB administration).

3.6. Resources of the medicines information

Paediatric information on AB dosage and indications is often incomplete or even contradictory, e.g., *Pamecil* (2008) SPC has the following information on paediatric dosage: "children younger than 2 years must use ¼ the adult dose, children aged 2–10 years must use ½ the adult dose. The dose can be calculated more accurately according to body mass, 25 mg to 50 mg/kg body weight per day". Dose 25-50 mg/kg/day is 2–4 times lower than it is established in the SPC of another pharmaceutical company (*Pan–ampicillin*, 2010) or in BNFC (2013) (Table 3.1.).

Table 3.1.

Examples of ampicillin doses in different resources of medicines information

Information resource	Age and/or weight	Route of administration	Usage
BNFC (2013)	1 month–18 years	IV, IM	25 mg/kg (max 500 mg) every 6 h (dose double in severe infection)
Lexi (*Takemoto*, 2011)	< 12 years	IV, IM	100–200 mg/kg/day, dividing every 6 h
	> 12 years	IV, IM	500 mg–3 g every 6 h; max dose 14 g/day
Micromedex 2.0	< 40 kg	IV, IM	50 mg/kg/day, dividing every 6–8 h
	≥ 40 kg	IV, IM	500 mg every 6–8 h
Pan-Ampicillin (2010)	children		½ of the adult dose 250 mg every 4–6 h or:
	children and infants	IM	50 mg/kg/day
	children and infants (and neonates)	IV	100–300 mg/kg/day
Pamecil (2008)	≤ 17 years	IV	25–50 mg/kg/day Max IV dose: 400 mg/kg/day Max total dose per day: 10–12 g/day

The dosing principle of ¼ and ½ of the adult dose is similar to the old penicillin V dosing principle described in *Ahmed et al.* (2011): "big child = half an adult, small child = half a big child, baby = half a small child". AB doses in BNFC are mostly based on age bands, although weight bands or weight based calculations (mg/kg) are provided for some indications. Lexi (*Takemoto*, 2011) dosages are mostly based on some age bands and weight (e.g., < 40 kg or > 40 kg). *Pamecil* SPC has a single dose calculation principle for all ages, but *Pan–Ampicillin* SPC – two groups: newborns and infants and children, but nothing is said about adolescents. Similar problems are present in other AB (e.g., ceftriaxone) SPC and formularies. The BNFC has a specific dose 50 mg/kg administered once a day (children under the age of 12 years), Lexi has a dose range 50–75 mg/kg administered once a day or divided dose for twice a day. There are differences in ages from which ceftriaxone could be used (older than 7 days (*Takemoto*, 2011) or 15 days (*Ceftriaxone-BCPP*, 2015), from 1 month (*Rocephin*, 2015)), timing of administration (once or twice a day), when to start using for surgical prophylaxis (e.g., 12 years).

Almost none of medicines data bases, that are widely used in other European hospitals (Meylers Side Effects of Drugs, Micromedex 2.0, Stockley's Drug Interactions), could be used in Latvian hospitals, as these hospitals do not have the respective subscriptions. The use of formularies, such as BNFC and Lexi, depends on whether the individual specialist can afford buying these books.

3.7. Antibiotic prescription problems at the UCH Paediatric Surgery Clinic

Incorrectly prescribed doses are among the most common medical errors (*Stultz et al.*, 2015, *Wong et al.*, 2004). The results of the study at the UCH Paediatric Surgery Clinic show that AB doses were prescribed incorrectly more often to patients under the age of 12 years. Usually doses are calculated in accordance with the body mass in this patient group, and thus it is more likely to make a calculation error than in children older than 12 years of age, e.g., cefazolin dose to children under the age of 12 years is 25–100 mg/kg/day, but starting from 12 years – 250–500 mg every 8 hours (*Takemoto*, 2011). Electronic prescriptions may help to reduce prescribing errors (*Wong et al.*, 2009). Evaluation of prescribed AB doses was complicated by the fact that medicines charts for all patients were in the paper forms and only PICU and NICU had the electronic order forms. In addition, at least a part of nurses transfers information about AB doses from patients medication charts to separate paper forms, thus possibly increasing the number of wrong doses. Another problem is overweight patient, as there are no many studies available about medicines dosages regarding this patient group (both children and adults) and only few SPC establish what AB dose should be prescribed in this case. In the UCH study medicines (gentamicin) dose recalculation was performed in one overweight patient. There are two gentamicin solutions for injections registered in Latvia, but only one (*Gentamicin Sopharma*, 2014) has information what doses should be prescribed to overweight patients.

3.8. Antibiotic off–label use

Study results at the UCH Paediatric Surgery Clinic confirmed the data provided by other studies (*Cuzzolin et al.*, 2006, *Doherty et al.*, 2010, *Hsu et al.*, 2009) about AB off–label use. The off-label use of ampicillin, gentamicin, metronidazole, cefazolin, cefuroxime and ceftriaxone was analysed in patients with acute appendicitis. None of these AB, except for ceftriaxone, had a brand name medicine registered at the Latvian Medicines State Agency. There were no united AB dosages approved by the European Heads of Mediciens Agencies website (*HMA*, 2014), except for gentamicin and metronidazole. Nevertheless, there was no information indicating that gentamicin could be used for surgical prophylaxis (*Gentamicin*, 2010). Metronidazole had indication for surgical prophylaxis (*Metronidazole*, 2010). BNFC and Lexi also had no information indicating that gentamicin could be used for surgical prophylaxis. *Cefazolin-BCPP* (2014) SPC establishes that cefazolin could be used for surgical prophylaxis in adults. *Pan–cefazolin* (2010) SPC did not specify, which patients' age groups could use it for prophylaxis, but the dose of 2 grams would be too high for children. Similar situation was with the *Reflin* (2014) SPC – patients age groups were not specified, but the dose 1 gram would be too high for most children under the age of 12 years. *Axetine* (2011) (cefuroxime) SPC also did not provide any information on whether or not the AB could be used in children. Nevertheless, the suggested dose 1.5 grams could be too high for most of children under the age of 12 years and with body weight < 40 kg. Cefuroxime had indication for surgical prophylaxis both with BNFC and Lexi. Neither *Pamecil* nor *Pan–Ampicillin* SPCs, as well as BNFC and Lexi, had established that ampicillin would be used for surgical prophylaxis. The *Gentamicin Krka* (2011) SPC states that "it could be used in postoperative infection prophylaxis after abdominal surgery especially if the urinary tract or intestines were involved". *Gentamicin Sopharma* (2014) SPC had nothing on surgical prophylaxis. The use of metronidazole in surgical prophylaxis was included in both *Metronidazole B. Braun* and *Metronidazole Fresenius* (2014) SPCs.

AB off–label use (indications for AB use) at the UCH Paediatric Surgery Clinic was more common in 2011–2013, except for patients with acute appendicitis, who had more off-label prescriptions in 2001–2003 (90.6% and 79.9% prescriptions respectively). All patients (with acute appendicitis, mesadenitis and injuries of upper and lower extremities) had more off–label dose prescriptions in 2011–2013. Patients with injuries of upper and lower extremities had also more off-label indication prescriptions in 2011–2013 than in 2001–2003 (28.2% and 21.2% prescriptions respectively). It was not possible to evaluate the appropriateness of ampicillin and gentamicin prescriptions according to the mesadenitis indication, because there was no complete information available on what origin (e.g., viral, bacterial) it was. Paediatric Surgery Clinic study results show that situation with AB off–label use has not improved in 2011–2013 if to be compared with 2001-2003. Methods used in this research do not allow to explain the reasons why the situation remained without any improvement. There is no a requirement in Latvia for the physicians and pharmacists to inform patients about drug off–label use. At present all pharmacists and physicians are free to choose whether to inform patients or not about off–label use. Such information could be vital as patients have rights to know about it. In order to provide such information specialists probably would need to have more time for consultations, as well as receive additional training in order to be able to provide such information.

CONCLUSSIONS

1. At the UCH the total AB consumption expressed in DDD, as well as for DDD/100 patients, has decreased. Nevertheless, AB consumption for DDD/100 GD has increased. Spectrum of the most commonly used AB also has changed, as the use of AB from penicillin group has decreased, but the use of high risk AB (e.g., the 3rd generation cephalosporins and especially ceftriaxone) has increased. This situation may contribute to the development of AB resistance.
2. If to compare the period of 2011–2013 with 2001–2003, then it was established that there is still high number of incorrect prophylaxis. Also, AB were used for a longer period of time contrary to the timescale suggested by the international guidelines (in patients with acute appendicitis). In addition, there is still large number of surgeries, where patients did not receive AB prophylaxis although it was recommended (both patients with acute appendicitis and injuries of upper and lower extremities).
3. AB doses were administered incorrectly mostly for patients under the age of that 12 years. Also there was a high number of cases when there was no records of the reason why AB was used – mostly with patients having acute appendicitis and mesadenitis.
4. AB off–label use (regardless of particular indication and age, dose and frequency) was observed in patients with acute appendicitis, mesadenitis and injuries of upper and lower extremities, as well as in patients under the age of 12 years and starting from 12 years of age.

RECOMMENDATIONS

1. To conduct regular AB consumption studies both at the UCH and other Latvian hospitals, which have paediatric wards, in order to obtain information on AB consumption tendencies. It could help to improve AB usage in hospitalized children.
2. Along with AB consumption studies, to conduct regular HAI studies and analysis.
3. To introduce electronic patient records in order to obtain more precise information on actual situation with AB use and consumption.
4. To introduce SSI monitoring system in order to be informed on the actual number of patients with SSI.
5. To encourage AB use, which would be based on the evidence acquired from surgical prophylaxis and treatment.
6. To improve the situation with information to be included in patients' medical records, thus ensuring that these records contain clearly stated reasons for AB use.
7. To provide regular training for health-care professionals regarding the correct use of AB.
8. To define official reference documents on medicine dosage at the hospital.

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PUBLICATIONS AND THESIS

PUBLICATIONS

Doctoral thesis is based on following international publications:

1. **Sviestina I**, Aston J, Lorrot M, Mozgis Dz. A comparison of antibiotic use in three specialist paediatric hospitals in France, Latvia and the UK. Eur J Hosp Pharm. 2015;22:132–137.
2. **Sviestina I**, Mozgis Dz. Evaluation of the antibiotic use for surgical prophylaxis in paediatric acute appendicitis. J Young Pharm. 2015;7(1):7–11.
3. **Sviestina I**, Mozgis Dz. Antimicrobial usage among hospitalized children in Latvia: a neonatal and pediatric antimicrobial point prevalence survey. Medicina (Kaunas). 2014:175–181.
4. Versporten A, Sharland M, Bielicki J, Drapier N, Vankerckhoven V, Goossens H and the ARPEC project group members: [..] **Sviestina I** [..]. The Antibiotic Resistance and Prescribing in European Children (ARPEC) Project: A Neonatal and Paediatric Antimicrobial web-based Point Prevalence Survey in 73 Hospitals worldwide. Pediatr Infect Dis J. 2013 Jun;32(6):e242–253.
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6. **Sviestina I.** Trends in Antibiotic Use at the University Children's Hospital in Latvia During 2005–2009. Medicina (Kaunas). 2011;47(Suppl 2):91–96.

Doctoral thesis is based on following local publications

1. Rasnača K., Grope I., **Sviestiņa I.**, Pavāre J., Rasnačs O., Gardovska D. Punkta prevalences pētījums par antibakteriālo līdzekļu lietošanu Bērnu Klīniskajā Universitātes slimnīcā Latvijā. RSU Zinātniskie raksti 2011. 2. sējums. 2012. 20.–25.lpp. ISBN: 9789984793092.

THESIS

Results are reported in the following international conferences:

1. **Sviestina I**, Mozgis Dz. Antibiotic Consumption at the University Childrens' Hospital in 2006–2014. FIP congress, Düsseldorf, Germany, 29.09.–3.10.15. Poster and thesis.
2. **Sviestina I.** Correct use of antibiotics. 3rd Baltic Pediatric congress, Riga, Latvia, 19.–21.08.15. Oral presentation.
3. **Sviestina I**, Mozgis Dz. The impact of hospital antibiotic guidelines on surgical prophylaxis in paediatric patients suffering upper and lower extremity injuries. EAHP congress, Hamburg, Germany, 25.–27.03.15. Poster and thesis (*Eur J Hosp Pharm* 2015;22:A28–A29).
4. **Sviestina I** Mozgis Dz. Evaluation of the antibiotic use for surgical prophylaxis in paediatric acute non-perforated appendicitis. ESCP congress, Copenhagen, Denmark, 22–24.10.14. Poster and thesis (Available: http://www.bdp-congress.dk/ESCP2014/img/ESCP_Copenhagen_2014_Abstractbook_141007.pdf, P. 101).
5. **Sviestina I**, Mozgis Dz. The use of antibiotics for surgical prophylaxis in hospitalized children at the University Children's Hospital. FIP congress, Bangkok, Thailand, 31.08.–4.09.14. Poster and thesis (Available: http://www.fip.org/abstracts?page=abstracts&action=generatePdf&item=10860).

6. **Sviestina I**, Aston J, Lorrot M, Goossens H, Sharland M, Versporten A, Mozgis Dz. Antibiotic prescribing for medical prophylaxis – a comparison of practice in the UK, France and Latvija. ESPID congress, Dublin, Ireland, 6–10.05.14. Poster and thesis (Pieejams: http://espid2015.kenes.com/PublishingImages/scientific-information/espid-abstracts/ESPID%202014%20abstracts.pdf).
7. **Sviestina I**, Aston J, Lorrot M, Prot-Labarthe S, Angoulvant F, Doit C, Mozgis Dz. Comparison of Antibiotic Prescribing for Paediatric Lower Respiratory Tract Infection in Three Paediatric Hospitals in the UK, France and Latvia. EAHP congress, Barcelona, Spain, 26–28.03.14. Poster and thesis. (Eur J Hosp Pharm 2014:21(Suppl 1):A1–224)
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12. **Sviestina I**, Mozgis Dz. Antibiotic usage in hospitalised children treatment: retrospective observational study in the infectious diseases unit at the Children University Hospital. EAHP congress, Milan, Italy, 21–23.03.12. Poster and thesis. (*Eur J Hosp Pharm* 2012;19:2 261).
13. **Sviestina I.** Antibiotic consumption studies in the Latvian State Children's University Hospital. BARN workshop, Vilnius, Lithuania, 30.11.–1.12.11. Oral presentation.
14. **Sviestiņa I.** Antibiotic Prescribing Tendencies in the Children Clinical University Hospital "Tornakalns". FIP congress, Istanbul, Turkey, 3.–8.09.09. Poster and thesis. (Thesis book (2009)).
15. **Sviestina I.** The main tendencies in the use of antibiotics in the Children hospital (2005–2008). ACCP and ESCP congress, Orlando, USA, 24–28.04.09. Poster and thesis. (Thesis book (2009)).
16. **Sviestina I**, Pujate E. Use of Antibiotics in the Children Hospital "Gailezers" in Riga, Latvia (2005–2007). 68. FIP congress, Basel, Switzerland, 29.08.–4.09.08. Poster, oral presentation and thesis. (Thesis book (2008)).

Results are reported in the following local conferences:

1. **Sviestiņa I**, Mozgis Dz. Antibiotiku patēriņa analīze Bērnu klīniskajā universitātes slimnīcā laikposmā no 2006. līdz 2013. gadam. RSU Scientific conference, Riga, Latvia, 26.03.15. Poster and thesis (Available: http://www.rsu.lv/images/stories/zk2015/antibiotiku_paterina_analize.pdf).
2. Mozgis Dz., **Sviestiņa I.**, Baltiņš M. Dr. med. Pauls Klemms un viņa redzējums vairāku ķirurģisko slimību gadījumā laikā ap 19. un 20. gs. miju. University of Latvia 73rd conference, Riga, Latvia, 25.01.15. Oral presentation.

3. **Sviestiņa I.** Antibakteriālo līdzekļu patēriņa salīdzinoša analīze bērniem stacionārā biežāko ķirurģisko slimību gadījumos. Pharmacists' Society of Latvia conference, Riga, Latvia, 22.11.14. Oral presentation.
4. **Sviestina I**, Aston J, Mozgis Dz. Analysis of Antimicrobial Prescribing at Two Specialist Paediatric Centres in the UK and Latvia. RSU Scientific conference, Riga, Latvia, 10–11.04.14. Poster and thesis (Available: 14-020_Tezes_2014_A4_CS6.indd 194 http://www.rsu.lv/images/stories/zk2014/Analysis_of_Antimicrobial_Prescribing.pdf).
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6. **Sviestiņa I**, Mozgis Dz. Antibiotiku prevalences pētījumi bērniem Latvijas stacionāros 2011.–2012. – Latvian Physicians' 7th congress, Riga, Latvia, 19-21.09.13. Poster and thesis (Available: http://www.arstukongress.lv/?&s=1361881321&fu=read&id=5).