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Antibiotic Utilization in Pediatric Hospitalized Patients – A Single Center Study

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Abstract

BACKGROUND: Antibiotics are among the most commonly prescribed drugs in paediatrics. In most cases, antibiotics are started on an empirical basis, without proof of a bacterial infection, either before the start of therapy or afterwards.

AIM: The main objective of this study was to analyse the consumption of antibiotics in hospitalised paediatric patients.

MATERIAL AND METHODS: This retrospective study investigated the consumption of antimicrobials in defined daily doses (DDDs according to the Anatomical Therapeutical Chemical/DDD index) in Pulmonology, Gastroenterology and Nephrology Departments at Pediatric Clinic of the tertiary hospital. The data on the consumption of antimicrobials were collected for five years by using properly designed form. The consumption was related to days of hospital care.

RESULTS: The most utilised antibiotics group in all three departments Pulmonology, Gastroenterology and Nephrology Departments were penicillins. Cephalosporins were mostly used in Pulmonology department. Metronidazole and Chloramphenicol were used in minimal quantities in all three departments.

CONCLUSION: This study demonstrates that surveillance programs on antibiotic resistance should be established and accompanied by analyses of drug utilisation data which can aid in the creation of valid cross-national studies on antibiotic usage and resistance, to motivate improvements in prescribing and guideline-directed antibiotic prescribing.

Introduction

Drug therapy is considered to be a major component of paediatric management in health care settings like hospitals. Effective medical treatment of a paediatric patient is based upon an accurate diagnosis and optimum course of therapy, which usually involves a medication regimen.

Antibiotics are the most commonly prescribed drugs in children with the highest incidence rates in preschoolers [1].

Investigating and monitoring the consumption of antimicrobials in hospitals is necessary to encourage prudent use of these drugs. The use of broad spectrum antibacterials is a potential problem. The issue of antibiotic resistance is of global concern and considered a threat to modern health care, rendering patients at risk of ineffective treatment regimens and societies strained by increasing health care costs. Antibiotic consumption is directly related to the antibiotic resistance rates of common bacteria [2].

In European countries, antibiotics are mainly used in primary care. However, hospitals are considered to be the centre of antimicrobial resistance owing to the higher use of broad-spectrum agents in both adults and children [3].

Numerous studies have investigated the

consumption of antimicrobials in hospitalised adult patients by using DDDs, but such studies in paediatric patients are in large scale missing [3–6].

The determination of criteria for rational antimicrobial therapy is derived from the definition for rational therapy: ordination of antibiotics drug in optimal dose, in safe mode and optimal duration.

The Center for Disease Control and Prevention (CDC) 12-step program to prevent antimicrobial resistance was launched in 2000 to educate clinicians about antimicrobial resistance and provide strategies to improve clinical practice. However, the drug prescription in our centre depends on drug availability in Central Pharmacy while the drug supply is depended on donations. On the other hand, there is no official drug policy or protocol of treatments, so the doctors are not obligated to follow any official antibiotic protocols.

Detailed knowledge of actual prescribing patterns is necessary to plan relevant activities that limit excessive use of antibiotics in general as well as of particular types of antibiotics.

The aim of this study was the analysis of antibiotic consumption structure used to treat the respiratory, urinary and gastrointestinal infections in children in Pediatric Clinic of University Clinical Center of Kosovo (UCKK).

Material and Methods

Pediatric Clinic, University of Prishtina, is a tertiary hospital in Kosovo. It has active units of Pulmonology, Nephrology and Gastroenterology Departments.

All data were collected retrospectively by the clinical pharmacologist from the inpatient medication charts and the patient's medical notes of 143 hospitalised patients for five years. Properly designed form sheet was used for data collection.

Our retrospective study investigated the consumption of antimicrobials in daily defined dose (DDD) per 1000 bed days (BD) [7]. Because the study was held in paediatric settings, the modified DDD/1000 – BD was used. The modified DDD/100 – BD for children is presented in age-group categories. The appropriateness of DDD by age-group is determined as a conclusion of WHO [2].

The antimicrobials included in this study were the following (according to Anatomical Therapeutic Chemical/Daily Defined Doses–ATC/DDD classification system defined by WHO 2010):

J anti-infectives for systemic use:

- *J01 antibacterials*: J01A tetracyclines, J01B amphenicols, J01C beta-lactam antibacterials, penicillins, J01D other beta-lactam antibacterials, J01E sulfonamides and trimethoprim, J01F macrolides, lincosamides and streptogramins, J01G aminoglycoside antibacterials, J01M quinolone antibacterials, J01R combinations of antibacterials, J01X other antibacterials.
- *J02 antifungals*: J02AA antibiotics, J02AC triazoles, J02AX other systemic antifungals.
- *J05 antivirals*: J05AB nucleosides and nucleotides excluding reverse transcriptase inhibitors, J05AD phosphonic acid derivatives, J05AE protease inhibitors, J05AF nucleoside and nucleotide reverse transcriptase inhibitors, J05AG non-nucleoside reverse transcriptase inhibitors, J05AH neuraminidase inhibitors, J05AR antivirals for treatment of HIV infections.

Results

The total consumption of antibiotics in Pulmonology Department (PD) was 472.82 DDD/1000 B.D, while in Gastroenterology Department (GD) was 121.95 DDD/1000 B.D and in Nephrology Department (DN), 294.22 DDD/1000 B.D.

The most utilised antibiotics group in Pulmonology Department were penicillins (271.22 DDD/1000 - BD or 57.36%. of total consumption), cephalosporins (98.46 DDD/1000-BD or 20.82%) than macrolides (72.70 DDD/1000-BD or 6.27%).

In Gastroenterology Department the most utilized groups were penicillin (53.63 DDD/1000 - BD or 43.98 % and amino glycosides (40.18 DDD/1000 - BD or 32.95 % of total consumption), while in ND the most utilized antibiotics, were penicillin (179.11 DDD/1000 – BD or 60.88 %) and cephalosporin (51.87 DDD/1000 – BD or 17.63%)

Metronidazole and Chloramphenicol were used in minimal quantities in all three departments (Tale 1).

Table 1: Structure of antibiotics expenditure (J group by ATC classification)

ATC		Drug Group	Pulmonology Department DDD/ 1000- BD	%	Gastroenterology Department DDD/ 1000 – BD	%	Nephrology Department DDD/ 1000 – BD	%
J01	J01BA01	Chloramphenicol	0.0041	0.0008	0.658436	0.54	0.92	0.31
	J01C	Penicillin	271.23	57.36	53.63	43.98	179.11	60.88
	J01DA	Cephalosporin	98.46	20.82	18.92	15.51	51.87	17.63
	J01FA	Macro lids	72.70	15.38	6.48	5.31	9.26	3..15
	J01G	Amino glycosides	29.65	6.27	40.18	32.95	14.43	4.90
	J01XD01	Metronidazole	0.77	0.16	2.08	1.71	3.55	1.21
J04		Antituberculosis	0.00	0.00	0.00	0.00	35.08	11.92
Total			472.82	100.00	121.95	100.00	259.14	100.00

Three departments used drug combination of Trimethoprim and Sulfamethoxazole (Table 2).

Trimethoprim - sulfamethoxazole was most utilised in Nephrology Department (75.926 ED/1000-BD), than in Gastroenterology Department (67.67 ED/1000-BD), while less utilised was in Pulmonology Department (Table 2).

Table 2: Expenditure on combine anti-infective drugs by departments

ATC				Drug	Pulmo-nology Depart-ment ED/ 1000- BD	Gastroentero-logy Department ED/ 1000 - BD	Nephrology Department ED/ 1000 - BD
J01	J01E	J01EE	J01EE01	Trimethoprim+ Sulfamethoxazole	45.062	67.670	75.926

In Pulmonology Department the most utilised antibiotics are Procaine penicillin (23.10% of total consumption), than Erythromycin (13.88%), Amoxicillin (13.02%) and Benzyl penicillin (10.53%). The expenditure of cephalosporin took in the second place, and most utilised antibiotics from this group were: Ceftriaxone (4.11%), and Cefuroxime (2.21%).

In Gastroenterology Department most utilised, antimicrobics were: Procaine-Penicillin (34.17%), than Gentamycin (23,46%), Ceftriaxone (9.82%), Amoxicillin-clavulanic acid (6.20%) and Erythromycin (5.31%).

In Nephrology Department most utilised antibiotics were: Procaine Penicillin (29.37%), Amoxicillin-clavulanic acid (15.87%), Amoxicillin (10.70%), Cefuroxime (6.29%) and Cefaclor (5.85%). In Department of Nephrology the antituberculosis are utilised in smaller quantities (Rifampicin 3.25%, Isoniazid and Pyrazinamide with 4.34 %) (Table 1).

In all three departments, 25 antibiotics from drug group J are used (Table 3).

Table 3: The structure of systemic anti-infective (J group) by subgroup of ATC classification

ATC				Drugs	Pulmonology Department DDD/ 1000-BD	%	Gastroenterology Department DDD/ 1000 BD	- %	Nephrology Department DDD/ 1000 BD	- %
J01	J01B	J01BA	J01BA01	Chloramphenicol	0.004	0.0008	0.66	0.54	0.92	0.31
	J01C	J01CA	J01CA01	Ampicillin	7.04	1,49	2.01	1.65	12.65	4.30
			J01CA04	Amoxicillin	61.57	13.02	0.46	0.38	31.48	10.70
		J01CE	J01CE01	Benzylpenicillin	49.79	10.53	0.00	0.00	0.00	0.00
			J01CE08	Benzathine-benzylpenicillin	0.00	0.00	0.00	0.00	1.85	0.63
			J01CE30	Procaine-Penicillin	109.26	23..10	41.67	34.17	86.42	29.37
		J01CF	J01CF02	Cloxacillin Na	24.35	5.15	1.93	1.58	0.00	0.00
		J01CR	J01CR02	Amoxicillin–clavulanic acid	19.22	4.064	7.56	6.20	46.70	15.87
	J01D	J01DA	J01DA01	Cephalexin	3.78	0.80	0.00	0.00	0.00	0.00
			J01DA04	Cephazolin	5.76	1.22	0.00	0.00	0.00	0.00
			J01DA05	Cefoxitin	0.00	0.00	0.00	0.00	1.54	0.52
			J01DA06	Cefuroxime	24.69	5.22	3.70	3.04	18.52	6.29
			J01DA08	Cefaclor	7.96	1.68	3.24	2.66	17.22	5.85
			J01DA11	Ceftazidime	10.41	2.20	0.00	0.00	1.62	0.55
			J01DA13	Ceftriaxone	45.86	9.70	11.98	9.82	12.96	4.41
	J01F	J01FA	J01FA01	Erythromycine	65.62	13.88	6.48	5.31	9.26	3.15
			J01FA10	Azithromycine	7.08	1.49	0.00	0.00	0.00	0.00
	J01G	J01GA	J01GA01	Streptomycin			1.48	1.21	0.00	0.00
		J01GB	J01GB03	Gentamycin	25.32	5.35	28.61	23.46	10.08	3.43
			J01GB06	Amikacin	4.33	0.91	10.09	8.27	4.35	1.48
	J01X	J01XD	J01XD01	Metronidazol	0.77	0.16	2.08	1.71	3.55	1.21
J04	J04A	J04AB	J04AB02	Rifampicin	0.00	0.00	0.00	0.00	9.57	3.25
		J04AC	J04AC01	Isoniazid	0.00	0.00	0.00	0.00	12.76	4.34
			J04AK01	Pyrazinamide	0.00	0.00	0.00	0.00	12.76	4.34
Total					472.82	100.00	121.95	100.00	294.22	100.00

Discussion

Antibiotic resistance is an emerging public health issue of major concern worldwide which has been associated with antibiotic consumption.

To our knowledge, few studies on antibiotic prescribing in paediatric patients have been performed until now, especially in developing countries like Kosovo [5, 8, 9].

The drug utilisation research enables the identification of eventual problems and application of right measurement with an aim for rational and modern treatment therapy.

In our study, we demonstrated a relatively stable high overall incidence rate of antibiotic use in paediatric patients. The utilisation of antibiotics is different in three departments, due to different pathologies which have been treated in those departments.

The criteria for diagnosis in Departments of Pulmonology, Gastroenterology and Nephrology, were history taking, clinical examination, biochemistry, haematology, bacteriologic analyses, pulmonary radiological examination and ultrasound examination of the gastrointestinal tract and urinary tract.

The results of drug expenditure from our research are classified as rational expenditure comparing with drug expenditure in other countries in transitional phase [8–10].

Krasniqi et al. in one similar survey presented that in Orthopedic Clinic of UCCK, the total consumption of antimicrobials in 2001 were 79.36 DDDs100 bed days within a small decline in total consumption of antimicrobials of 3.5% in 2006 (76.86 DDDs/100 bed days). In two time periods, the most utilised drug groups were: other ß-lactam antibiotics, aminoglycosides and ß-lactam antibiotic-penicillin's. This finding shows the higher consumption of antibiotic in the Clinic of Orthopedics compared to our study at the Clinic of Pediatrics [16].

Expenditure of penicillin in Department of Nephrology is a sign of rational treatment because penicillin is first line treatment of β-hemolytic streptococci renal infections.

Palcevski et al. [9] presented that the total consumption of antibiotic in Rijeka, Croatia was three times more than in Smolensk, Russia (28.96 vs. 8.3 DD/100 - BD). In Rijeka were administered 35 different antibiotics (the most utilised were: cefuroxime), while in Smolensk 22 antimicrobials (the most utilised amoxicillin).

In Department of Nephrology, in our centre, expenditure was 1.4 times more than in the University of Rijeka.

In Department of Pulmonology of Pediatric Clinic, the most utilised antibiotic was Procaine penicillin. Sestina et al. [10] showed that in hospitalised paediatric patients in Birmingham the most frequently used antibiotic was co-amoxiclav while in Riga ampicillin and amoxicillin were most commonly used. This difference in practice is interesting as in most cases these narrow-spectrum agents provide sufficient cover for the majority of pathogens associated with community acquired pneumonia.

Vaz et al. [11] also showed that the majority of antibiotics dispensed for respiratory tract infections for children included penicillins, cephalosporins, and second-generation macrolides.

The high non-rational expenditure of some antibiotics, especially penicillins in Department of Gastroenterology, create conditions for destroying of bowel normal bacterial flora and domination of pathogen bacteria with the possibility of development of bacterial resistance. To decrease costs, as well as to reduce the possibility of increasing antimicrobial resistance among circulating strains, clinicians should choose the narrowest antibiotic regimen that adequately covers the predicted organisms for each case.

Several studies have investigated the role of probiotics for the prevention of community- and nosocomial-acquired diarrhoea, antibiotic-associated diarrhoea and travellers' diarrhoea [12, 13], but a discussion on those topics goes beyond the scope of this article.

The high use of cephalosporins in our centre is similar to findings in other studies where cephalosporins in general (and ceftriaxone in particular) were among the most frequently used antibiotics [8–10]. Non-restricted use of third-generation cephalosporins could lead to an increase in resistant *Escherichia coli* and *Klebsiella pneumonia*.

The clinical manifestation of any infection, initially justify the antibiotics administration, but after 48-72 hours in a case, that microbiological analyses shows negative results is necessary to stop the antibiotics administration.

Because of the shortage in the budget, in public hospitals in Kosovo, the antibiotic supply also depends on donations, so there are no national recommendations promoting good antimicrobial stewardship. Actions to promote the prudent use of antibiotics remain with the individual hospitals.

Although some data suggest that restrictive methods (formulary restrictions with policing by clinical pharmacists) are more effective than educational interventions, there is a need for both [3, 14, 15].

Although the DDD method has also been used in paediatric studies, the lack of standardised international paediatric DDD could be considered as a limitation of the study. Nevertheless, to overcome this, we used the modified DDD/1000 – BD for children.

In conclusion, the antibiotic use in three departments of Clinic of Pediatrics is high compared to other European Countries. In three departments, the penicillin's are a most utilised antibiotic subgroup and this show rationality according to the structure of used antimicrobials. The total consumption of antibiotics significantly differs in three departments of Pediatric Clinic. The consumption of cefalosporins and aminoglycosides is relatively high, and this main concern is reflecting the non-rationality of antibiotic prescription due to the impact of cephalosporins in the development of bacterial resistance and problematic safety profile of aminoglycosides especially in children.

This study demonstrates that surveillance programs on antibiotic resistance should be established and accompanied by analyses of drug utilisation data which can aid in the creation of valid cross-national studies on antibiotic usage and resistance, to motivate improvements in prescribing and guideline-directed antibiotic prescribing.

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