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M.V. Khaitovych, O.A. Temirova, K. Yu. Kyrilchuk[1], V.A. Sova[1], D.V. Turchak
Bogomolets National Medical University, Kyiv
[1]National Children's Specialized Hospital "OKHMATDYT", Kyiv

USING THE AWaRe CLASSIFICATION FOR ASSESSING COMPLIANCE WITH OUTPATIENT ANTIMICROBIAL THERAPY OF CHILDREN

e-mail: lfitsner@gmail.com

In ambulatory care for children, excessive use of antibiotics is a common phenomenon, which indicates the importance of introducing antimicrobial drug administration programs into ambulatory practice. The purpose of the study was to establish the appropriateness of the choice of antimicrobial drugs in the outpatient treatment of children according to the AWaRe classification. A retrospective analysis of the antimicrobial therapy regimens of 30 consecutive children in outpatient settings was performed. It was found that 2nd (cefuroxime) and 3rd generation (cefpodoxime and cefixime) cephalosporin drugs were mainly prescribed (56.7 %), quite often (3 children each) aminopenicillins, sulfonamides, and nitrofurans were prescribed, 1 patient each received macrolide azithromycin, fluoroquinolone ofloxacin, tetracycline antibiotic doxycycline, lincosamide clindamycin. The presence of bacterial infection justified all prescriptions of antimicrobial drugs and was according to current clinical guidelines. Among the prescribed antimicrobial drugs, 19 (cephalosporins, fluoroquinolones, macrolides) belonged to the Watch group, and the others to the Access group. Therefore, in 63.3 % of cases, children in outpatient settings were prescribed drugs of the Watch group. This can contribute to the spread of antimicrobial resistance and indicates the requirement for outpatient administration of antimicrobial drugs.

Key words: child, outpatients, anti-bacterial agents, drug resistance, bacterial, antimicrobial stewardship

М.В. Хайтович, О.А. Темірова, К.Ю. Кирильчук, В.А. Сова, Д.В. Турчак

ВИКОРИСТАННЯ КЛАСИФІКАЦІЇ AWaRe ДЛЯ ОЦІНКИ ВІДПОВІДНОСТІ АМБУЛАТОРНОЇ АНТИМІКРОБНОЇ ТЕРАПІЇ ДІТЕЙ

В умовах амбулаторної допомоги дітям поширеним явищем є надмірне використання антибіотиків, що вказує на важливість впровадження в амбулаторну практику програм адміністрування антимікробних препаратів. Метою дослідження було встановити відповідність вибору антимікробних препаратів при амбулаторному лікуванні дітей класифікації AWaRe. Проведено ретроспективний аналіз схем антимікробної терапії 30 послідовних дітей в амбулаторних умовах. Встановлено, що переважно (56,7 %) призначались препарати цефалоспоринового ряду 2-ї (цефуроксим) та 3-ї генерації (цефподоксим та цефіксим); досить часто (по 3 дітей) – амінопеніциліни, сульфаніламіди та нітрофурани, по 1 пацієнту отримували макролід азитроміцин, фторхінолон офлоксацин, тетрациклiновий антибіотик доксициклін, лінкозамід кліндаміцин. Всі призначення антимікробних препаратів були обґрунтовані наявністю бактеріальної інфекції та відповідали чинним клінічним настановам. Серед призначених антимікробних препаратів 19 (цефалоспорини, фторхінолони, макроліди) належали до групи спостереження (Watch), решта – до групи доступу (Access). Отже, у 63,3 % випадках дітям в амбулаторних умовах призначались препарати групи спостереження, що може сприяти поширенню антимікробної резистентності і вказує на необхідність здійснення амбулаторного адміністрування антимікробних препаратів.

Ключові слова: дитина, амбулаторні пацієнти, антимікробні лікарські засоби, антимікробна резистентність, адміністрування антимікробних препаратів

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It has been demonstrated that excessive use of antibiotics is a common phenomenon in outpatient care for children [6]. For instance, in the USA, the majority (59.1 %) of antibiotic costs are related to outpatient treatment [12]. Approximately 80–90 % of all antibiotics are used in outpatient settings [2]. At the same time, a third of antibiotic prescriptions in outpatient settings are unnecessary. It was established that out of 506 antibiotic prescriptions, only 353 were acceptable on an outpatient basis [4]. All of this indicates the importance of implementing antimicrobial stewardship programs (ASP) in outpatient practice [6].

In 2017, the WHO Expert Committee on Selection and Use of Essential Medicines proposed, and in 2021, updated, the classification of antibiotics AWaRe, which divides them into three groups considering the impact of different antibiotics and classes of antibiotics on antimicrobial resistance, as well as the importance of their appropriate use. The use of this classification of antibacterial agents is an important intervention in the preauthorization and restriction of the use of antimicrobial drugs. According to the standard of medical care "Rational use of antibacterial and antifungal drugs for therapeutic and preventive purposes" [1], in healthcare institutions that provide specialized (inpatient) medical care, the preauthorization procedure is mandatory when using drugs from the Reserve group, and in in the case of

prescription of drugs of the Watch group, the prospective pharmaceutical audit should be carried out. For primary care facilities providing outpatient medical care, it is recommended to select antibacterial agents according to approved guidelines, seemingly relieving the physician from the necessity of using the AWaRe classification. At the same time, the percentage of prescriptions of drugs of the Access group characterizes the rationality of the use of antibacterial drugs in healthcare institutions that provide primary (ambulatory) medical care. According to the standard, doctors should give priority to the appointment of antibacterial drugs of the Access group, as antibiotics with a lower potential for the spread of antimicrobial resistance, are less expensive, and with a narrow spectrum of action [1].

The purpose of the study was to establish the appropriateness of the choice of antimicrobial drugs in the outpatient treatment of children according to the AWaRe classification.

Materials and methods. A retrospective analysis of antimicrobial therapy regimens was done on 30 consecutive children who were prescribed treatment by physicians at the consulting and diagnostic outpatient clinic of the National Specialized Children's hospital "Ohmatdyt" in August-September 2022. Among those examined, there were 22 girls and 8 boys. In terms of age, 3 children (2 girls, 1 boy) were younger than 1 year, 17 children (14 girls, 3 boys) were aged 1–6 years, 7 children (4 girls, 3 boys) were aged 7–11 years, and 3 children (2 girls, 1 boy) were aged 12–14 years. Nearly half of the children (14) were diagnosed with a urinary tract infection (acute pyelonephritis, exacerbation of chronic pyelonephritis), 5 children had Lyme disease (migratory erythema), 1 child had recurrent furunculosis, 1 child had pharyngotonsillitis, 3 children had acute sinusitis, and 6 children had acute otitis media.

Statistical processing of the obtained data was carried out using the programs "Microsoft Office Excel 2016", "IBM SPSS Statistics Base version 22.0".

Results of the study and their discussion. According to the data presented in Table 1, 2nd (cefuroxime) and 3rd generation (cefpodoxime and cefixime) cephalosporin drugs were prescribed more often (17 children); quite often (3 children each) were prescribed aminopenicillins, sulfonamides, and nitrofurans; 1 patient each received macrolide azithromycin, fluoroquinolone ofloxacin, tetracycline antibiotic doxycycline, lincosamide clindamycin. All prescriptions of antimicrobial drugs were justified by the presence of bacterial infection and were in accordance with existing clinical guidelines.

Table 1

Antibacterial agents that were prescribed for children

Drug	Pharmacological group	Group according to classification AWaRe	Number of children	
Amoxicillin	Aminopenicillins	A	1	3.3
Amoxicillin/ clavulanate	Inhibitor-protected aminopenicillins	A	2	6.7
Cefuroxime	Cephalosporins of the 2nd generation	B	8	26.7
Cefpodoxime	Cephalosporins of the 3rd generation	B	4	13.3
Cefixime	Cephalosporins of the 2nd generation	B	5	16.7
Azithromycin	Macrolide	B	1	3.3
Doxycycline	Tetracyclines	A	1	3.3
Ofloxacin	Fluoroquinolones	B	1	3.3
Clindamycin	Lincosamides	A	1	3.3
Co-trimoxazole	Sulfanilamides	A	3	10.0
Nifuratel	Nitrofurans	A	2	6.7
Furazidin	Nitrofurans	A	1	3.3
Total			30	100.0

Among the prescribed antimicrobial drugs, 19 (cephalosporins, fluoroquinolones, macrolides) belonged to the Watch group, while the remainder belonged to the Access group.

According to the data given in Table 2, 2 children with Lyme disease were prescribed Access group drugs: amoxicillin/clavulanate (1-year-old boy) and doxycycline (11-year-old girl); 3 children aged 5–9 years –drug of the Watch group cefuroxime.

Table 2

Number of Access and Watch group drugs prescribed for children

Nosology	Number of drugs			
	Access group		Watch group	
	Abs.	%	Abs.	%
Diseases of the urinary system	6	42.8	8	57.7
Diseases of the ENT organs	3	30.0	7	70.0
Lyme disease	2	40.0	3	60.0
Skin disease	0	0	1	100.0
In total	11	36.7	19	63.3

Children with urinary infections were prescribed Access group drugs such as sulfonamides and nitrofurans (a total of 6 children with acute pyelonephritis or exacerbation of chronic pyelonephritis), while the rest received Watch group: 6 children were prescribed 3rd generation cephalosporins (4 children received cefixime, 2 children received cefpodoxime), 1 child received the 2nd generation cephalosporin cefuroxime, and 1 child received the fluoroquinolone ofloxacin. Positive results from bacteriological studies were obtained in 3 children with urinary infections (*E. coli* was isolated in 2 children, and Kl. pneumoniae in 1 child), and the spectrum of their sensitivity was considered when selecting antimicrobial agents.

For the treatment of 3 children with ENT pathology, Access group drugs such as clindamycin, amoxicillin, and amoxicillin/clavulanate were prescribed. Meanwhile, 7 children received Watch group drugs: cefuroxime (4 children), cefpodoxime (2 children), and azithromycin (1 child).

A child with recurrent furunculosis received the 3rd generation cephalosporin cefixime.

It has been demonstrated that frequent use of antimicrobial agents in children has led to a significant increase in multidrug-resistant bacterial infections among them. ASP programs in this case are necessary for individualizing dosages, reducing the risk of side effects, and mitigating the development of antibiotic resistance[9]. According to the results of our study, all children received antibacterial therapy according to indications and current guidelines. However, in most cases (63.3 %) a Watch antibiotic was prescribed according to the AWaRe classification, which is also associated with a greater risk of the spread of antimicrobial resistance.

As shown by the results of research in leading medical centers, the implementation of outpatient ASP programs has resulted in a reduction in antibiotic prescriptions for acute bronchitis from 64.6 % to 36.8 %. The most significant success was achieved through targeted education of prescribing doctors [5].

To enhance antimicrobial therapy in outpatient settings, the following important steps are considered necessary: support from the institution's leadership; establishment of an ASP team; engagement of prescribing physicians in ASP implementation activities; determination of access to antibiotic prescribing data; formation of communication skills regarding antibiotic use in clinical practice; implementation of educational programs on rational antibiotic therapy; monitoring of antibiotic prescribing data; implementation of a rational antibiotic therapy development plan [6]. In modern ASP guidelines, four key principles are emphasized: adherence to clinical guidelines; actions for policy and practice; monitoring and reporting; education and experience [11]. Implementation of these four basic elements will help achieve the goal of effective antibiotic use – maximizing the benefit of antibiotic treatment while minimizing harm to individuals and society.

The main obstacles to implementing ASP in outpatient practice are patient demands, time constraints for decision-making, diagnostic uncertainty, and accountability under administrative pressure [14].

It's important to educate patients as they may not be aware of the potential harm caused by antibiotics and may not understand the risks and benefits associated with antibiotic use [7, 8]. A doctor who prescribes antibiotics may prescribe antibiotics with too broad a spectrum of action when he is not sure which pathogen caused the disease and to avoid further complications. Additionally, clinician compensation is tied in part to patient satisfaction scores, and many clinicians who are trying to build and grow their practice depend on positive reviews from patients online and on social media. 74 % of doctors reported intense pressure from patients to prescribe antibiotics even when there was no need for them. This led to overprescribing of antibiotics, which increased patient satisfaction [10]. Therefore, the implementation of ASP is necessary also because reporting on adherence to guidelines has been shown to improve their compliance rates in primary care settings [10].

An analysis of the feasibility of prescribing antimicrobial drugs compared to colleagues is used to improve the outpatient use of antibiotics. This method was used to evaluate the activity of 18 outpatient facilities, in which 170 doctors worked. The program focused on antibiotic selection for acute respiratory tract infections with established guidelines (acute sinusitis, streptococcal pharyngitis, and pneumonia), for which narrow-spectrum antibiotics were recommended. As a result, the use of broad-spectrum antibiotics in all 18 hospitals decreased by 12.5 % [13].

Outpatient ASP in the USA was established in 7% of healthcare institutions. It has been shown that its effectiveness increases if local guidelines of institutions are implemented, targeted activities of the pharmacist are carried out, and ambulatory antibiograms, rapid tests for respiratory viruses or beta-hemolytic streptococcus of group A are used [3].

Conclusion

A retrospective analysis revealed that the selection of antimicrobial agents for outpatient treatment of children mostly adhered to current clinical guidelines. Children were mostly prescribed second and third-generation cephalosporins. Even though the antimicrobial therapy of children in outpatient settings was justified, the use of drugs in the Watch group prevailed, which may contribute to the spread of antimicrobial resistance. This indicates the need for outpatient administration of antimicrobial drugs.

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