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Issuing the Antibiotics for Children with and without Prescription in Pharmacies in Republic of Macedonia

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Abstract: The use of medicines for infants and children is presenting one unique set of challenges, because children are the most vulnerable population in any society. In this study, we set out to present the characteristics and classification of antibiotics recommended for children according to WHO, EMA and EBM. Also, the aim of this study was to analyze the most prescribed pediatric antibiotics in 2013 in Republic of Macedonia compared with standard treatments. Presented data was collected according to the number of prescribed recipes of pediatric dosage forms covered by the Fund of Republic of Macedonia. The obtained results showed that the most prescribed pediatric antibiotic is amoxicillin with clavulanic acid (875mg + 125mg) in form of tablet, with 280 863 prescribed recipes which corresponds to the recommendations of EBM.

Key words: Antibiotic, WHO, recipes, children.

1. Introduction

The use of medicines for infants and children is presenting one unique set of challenges for doctors, day by day, because children are the most vulnerable population in any society [1, 2]. In contrast to adults, absorption, distribution, metabolism and excretion of drugs in infants and children can be very different [3, 4]. In Republic of Macedonia and also worldwide, the problem with AMR (antimicrobial resistance) is enormous for healthcare services and communities [5, 6]. This major problem is associated with complicated treatments, extra costs of therapy and longer hospitalization with increased mortality risks [7, 8]. Generally, antibiotics are usually prescribed in primary healthcare organizations, commonly for viral diseases such as flu, cold etc., which results with non-effective treatment and increased risk of antimicrobial resistance [9-11]. Also, irrational use can be connected with consumption of antibiotics from previous treatment courses or issued by pharmacist without prescription [12]. According to National regulation in Republic of Macedonia, antibiotics can be purchased from pharmacies only with prescription. However, different surveys showed significant abuse of antibiotics in Republic of Macedonia, related to increased OTC sale of antibiotics despite the law existence [12, 13]. Compared with other Balkan countries, one pilot study presented that citizens in Republic of Macedonia had the highest readiness for self-medication [14, 15].

The aim of this study is to present the characteristics and classification of antibiotics recommended for children, according to WHO, EMA and EBM, pediatric dosage forms registered in Republic of Macedonia and also the most prescribed antibiotics for children in 2013 in Republic of Macedonia compared with standard treatment methods.

2. Methods

2.1 Data Analysis

The first step in data analysis refers to selection and evaluation of pediatric drug formulations, classified according to route of administration and if they are included at reimbursement list of National Fund of Health insurance represented in tabular form (Table 1). Analyzed pediatric dosage formulations were obtained from the Register of medicinal products in Republic of

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Table 1 Pediatric antibiotics registered in Republic of Macedonia.

ATC code	Generic name	Dosage form	Reimbursement list
JO1CA01	Ampicillin	Injection	Yes
JO1CA01	Ampicillin	Caps/Tabl.	No
JO1CA01	Ampicillin	Suspension	No
JO1CA04	Amoxicillin	Caps/Tabl	Yes
J01CA04	Amoxicillin	Suspension	Yes
01CR01	Ampicillin + Sulbactam	Injection	Yes
J01CR02	Amoxicillin + clavulanic acid	Tablets	Yes
J01CR02	Amoxicillin + clavulanic acid	Suspension	Yes
J01CE10	Benzathine phenoxyme-thylpenicillin	Tablets	Yes
J01CE10	Benzathine phenoxy-methylpenicillin	Suspension	Yes
J01DB01	Cefalexin	Capsules	Yes
J01DB01	Cefalexin	Suspension	Yes
J01DB05	Cefadroxil	Capsules	Yes
J01DB05	Cefadroxil	Suspension	Yes
J01DC04	Cefaclor	Capsules	Yes
J01DC04	Cefaclor	Suspension	Yes
J01DH02	Meropenem	Inection	Yes
J01EE01	Sulfametxazole + trimethroprim	Tablets	Yes
J01EE01	Sulfametxozole + trimethroprim	Suspension	Yes
J01EE03	Sulfametrole + trimethoprim	Tablets	Yes
J01EE03	Sulfametrole + trimethoprim	Suspension	Yes
J01FA01	Erythromycin	Caps/Tabl	Yes
J01FA09	Clarithromycin	Tabl/Susp	Yes
J01FA09	Clarithromycin	Suspension	Yes
J01FA10	Azithromycin	Tabl/Caps	Yes
J01FA10	Azithromycin	Suspension	Yes
J01FA10	Azithromycin	Injection	Yes
J01FF01	Clindamycin	Capsules	Yes
J01FF01	Clindamycin	Injection	Yes
J01FF02	Lincomycin	Capsules	Yes
J01FF02	Lincomycin	Injection	Yes
J01GB03	Gentamicin	Injection	Yes
J01MA01	Oflaxin	Tablets	No
J01MA02	Ciprofloxacin	Tablets	Yes
J01MA02	Ciprofloxacin	Injection	Yes
J01MA12	Levofloxacin	Infusion	No
J01AA02	Doxycycline	Capsules	Yes
J01XE01	Nitrofurantoin	Solid capsules	No
J0XA01	Vancomycin	Injection	Yes

Macedonia, published on official website of Macedonian agency of medicines and medical devices.

After the classification and evaluation, the second step was data summarization. Data were collected through a number of prescribed recipes covered by the Fund in Republic of Macedonia. The study covered recipes of prescribed antibiotics intended for children aged 0-15 years in 2013 carried out in all cities in Republic of Macedonia. Recipes were obtained from Ministry of health, summarized in tabular form and compared with the recommendations of WHO, EMA and EBM (Table 2).

3. Results and Discussion

In the Register of medicinal products in Republic of Macedonia, 39 dosage forms belong to antibiotics for

children from 19 INN, with determined prescribing regime and issuance. 92% of them are at reimbursement list of Fund of Health insurance. According to prescribing regime, 83% of pediatric antibiotics are prescribed in primary healthcare organizations, 5% with specialist recommendation, while 12% belong to antibiotics for parenteral administration [16].

The registered pediatric antibiotics in Republic of Macedonia, classified according to the prescribing regime are represented in Table 1.

According to registered pediatric dosage formulations, represented in Table 1, unfortunately ampicillin is not covered by the National Fund of Health

Table 2 Number of recipes of prescribed pediatric antibiotics in 2013.

Generic name and dosage form	Number of recipes
Amoxicillin caps. 250 mg	8.457
Amoxicillin susp. 250 mg/5ml	77.992
Amoxicillin + clavulanic acid tabl./fct. (250 mg + 125mg)	171
Amoxicillin + clavulanic acid tabl./fct. 500 mg	40.842
Amoxicillin + clavulanic acid susp. (125mg + 31,5mg)	14.986
Amoxicillin + clavulanic acid susp. (250 mg + 62,5mg)	8.557
Amoxicillin + clavulanic acid susp. (400 mg + 57 mg)	130.961
Amoxicillin + clavulanic acid tabl./fct. (875 mg + 125mg)	280.863
Amoxicillin caps. 500 mg	106.626
Azithromycin caps. 250 mg	7.976
Azithromycin susp.100mg/5ml	5.109
Azithromycin susp.200mg/5ml	8.564
Benzathinephenoxymethylpenicillin susp. 750.000 IU	31.664
Cefaclor caps. 500 mg	8.940
Cefaclor caps. 250 mg	1
Cefaclor susp. 250 mg/5ml	30.628
Cefaclor susp.125 mg/5ml	23.037
Cefadroxil caps. 500 mg	16.793
Cefadroxil susp. 250 mg/5ml	32.640
Cefalexin caps. 250 mg	1.902
Cefalexin caps. 500 mg	129.782
Cefalexin susp. 250 mg/5ml	58.638
Cefixime susp.100mg/5ml	13.307
Cefixime tabl. 400 mg	40.209
Cefuroxime tabl. 125 mg	6.805
Cefuroxime tabl.250 mg	24.423
Cefuroxime tabl. 500 mg	80.677
Ciprofloxacin tabl. /fct. 250 mg	1.371
Ciprofloxacin fct. 500 mg	209.603
Clarithromycin fct. 500 mg	34.706
Clarithromycin caps. /fct. 250 mg	5.193
Clarithromycin susp.125mg/5ml	11.202
Clarithromycin tabl.mod.rel. 500 mg	2.069
Erythromycin tabl. /fct. /caps. 250 mg	6.291
Erythromycin fct. 500mg	380
Sulfamethoxazole + trimethoprim susp. (200 + 40) mg	9.885
Sulfamethoxazole + trimethoprim tabl.(100 + 20) mg	3
Sulfametrole + trimethoprim susp. (200 + 40) mg	12.833
Sulfametrole + trimethoprim tabl. (100 + 20) mg	658

Insurance despite the lower incidence of side effects in comparison with amoxicillin with clavulanic acid as first treatment choice [17].

Azithromycin, clarithromycin, doxycycline and trimethoprim with sulfamethoxazole are covered by the National Fund without limitations in prescribing regime which is contrary to recommendations according to WHO and EBM [18].

Regarding the second step, the most commonly prescribed antibiotics in 2013, covered by the Fund of Republic of Macedonia intended for children aged 0-15 years, are represented in Table 2.

The obtained results from the performed research showed that the most commonly prescribed antibiotic in 2013 is amoxicillin with clavulanic acid (875mg + 125mg) in form of tablet, with 280 863 prescribed recipes. Ciprofloxacin 500mg tablet is represented with slightly fewer prescriptions 209 603, while the prescribed recipes for amoxicillin with clavulanic acid suspension are 130 961. Other antibiotics covered by the Fund, object of this study, are represented with number of prescribed recipes in range of 1200-100000 (Table 2) [19].

Most prescribed antibiotics for pediatric use represented in Table 2 from 2013 in Republic of Macedonia are according to recommendations of WHO [20]. Cephalexin and cefuroxime are most widely used cephalosporin antibiotics according to the performed survey. However, cefuroxime is not recommended by EBM [21].

In Republic of Macedonia there are guidelines for pediatric antibiotic prescribing related to EBM (Evidence-based medicine). Only 6 antibiotics (INN) from 19 registered are recommended according to these guidelines.

Non-compliance with the recommendations of reimbursement is generally due to frequent and inconsistent regulation changes. Weak control mechanisms also play major role in inappropriate use of antibiotics.

4. Conclusion

According to the obtained results, the most prescribed pediatric antibiotic in 2013 is amoxicillin with clavulanic acid (875mg + 125mg) in form of tablet, with 280 863 prescribed recipes, which corresponds to recommendations of EBM. In contrast, the second most prescribed antibiotic Ciprofloxacin is not recommended according to WHO. Despite the regulation in Republic of Macedonia, self-medication is represented with relatively high percentage due to the availability of antibiotics without prescription and the inappropriate use, general lack of knowledge about mechanism of action of antibiotics, side effects and the emergence of resistance.

The situation could be improved by revising / updating the lists of medicines in accordance with applicable regulations, clear determination of priorities for rational antibiotic use, continuous education of health professionals and also amplification of control state mechanisms.

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