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OUTPATIENT USE OF SYSTEMIC ANTIBIOTICS IN POLAND: 2004-2008

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ABSTRACT

OBJECTIVES. The goal of this study was to evaluate the quantity and pattern of outpatient antibiotic use in Poland between 2004 and 2008 and to determine the trends in prescribing practice. To investigate the oral and parenteral outpatient antibiotic use in Poland.
MATERIAL AND METHODS. Data concerning outpatient use of systemic antibiotics between 2004 and 2008 were obtained from Polish National Health Fund databases expressed as the number of defined daily doses (DDD) per 1000 inhabitants per day (DID) according to the international Anatomical Therapeutic Chemical ATC classification system of the World Health Organization (WHO, version 2009).
RESULTS. Total outpatient antibiotic use in Poland varied from the lowest 17.88DID in 2004 to the highest 21.39DID in 2007. Penicillins (J01C) represented the most frequently prescribed antibiotics constituting more than 50% of the total outpatient antibiotic use. The other most popular groups of antibiotics were tetracyclines (J01A), macrolides (J01F). On the fourth and fifth position were cephalosporins (J01D) and quinolones (J01M), respectively. The parenteral antibiotic use did not exceed 1% of the total outpatient antibiotics prescribed with cefuroxime being the most frequently prescribed drug.
CONCLUSIONS. Total outpatient use of antibiotics in Poland in 2004-2008 was comparable to the median European level. The consumption of all antibiotics slightly increased from 2004 to 2007, and decreased in 2008. The most often prescribed antibiotics were penicillins, mainly amoxicillin and amoxicillin with enzyme inhibitor. During the study period the use of the older (narrow-spectrum) antibiotics decreased in favour of the newer (broad-spectrum) antibiotics. The results suggest the discrepancy between national recommendations and choice of antibiotics by physicians.

Key words: *drug consumption, ambulatory care, defined daily dose*

INTRODUCTION AND OBJECTIVE

Antibiotic resistance has become an important public health issue (1). Antibacterial drug use is increasingly recognized as the main driver of this resistance (2). In Poland, as in other countries, drug resistance in bacterial pathogens is on the increase (3, 4). This process is, to a large extent, linked to the excessive, often unnecessary consumption of antibiotics (5). In recent years several activities have been launched in Poland aiming at more rational antibiotic prescribing. Since 2004 National Programme of Antibiotic Protection has been operating (6). Within this programme guidelines for antibiotic prescribing in hospital and out of hospital setting have been prepared and published on line (7). Since 2008 European Antibiotic Awareness Day has been celebrated with information about unnecessary antibiotic use directed not only towards health professionals but also towards general public (8).

Drug consumption research is necessary to improve the use of medications. Without precise knowledge of what is being used, it is not possible to reliably define the problems and set priorities in improving prescribing (9). Excessive inappropriate use of antibiotics can result in both medical and economic loss. For this reason, various surveillance programmes have been developed for evaluation of appropriate use of antibiotics (10, 11).

This paper presents data of outpatient antibiotic use in Poland between 2004 and 2008 and aims to determine the trends in prescribing practice.

MATERIAL AND METHODS

Data. In Poland, antibiotics are available only with a prescription issued by a physician and are dispensed by pharmacies. Every antibiotic sale operation was collected by Polish National Health Fund databases. Therefore data concerning outpatient use of systemic antibiotics between 2004 and 2008 were obtained from Polish National Health Fund databases. The year 2004 was the first year when full data on antibiotic sales were available. The consumption of antimicrobial agents was expressed as the number of defined daily doses (DDD) per 1000 inhabitants per day (DID) according to the international Anatomical Therapeutic Chemical ATC classification system of the World Health Organization (WHO, version 2009) (12), and as percentage of total drug consumption (%DDD). Demographic data concerning number of inhabitants in different regions were obtained from the Poland Central Statistical Office (Główny Urząd Statystyczny,GUS) (13).

ATC/DDD classification system. Defined daily dose (DDD) is a technical unit of measurement of drug consumption defined by World Health Organization as the assumed average maintenance dose per day for the drug when used for its main indication in adults (12, 14). DDD was developed as a technical unit of measurement with the purpose of enabling epidemiological comparison of drug consumption that were independent of differences in price or package size. Drug consumption data presented in DDDs provide rough estimates of consumption (9). The Anatomical Therapeutic Chemical (ATC) classification system which was developed to categorize drug substances, divides drugs into 14 main groups according to the organ or system on which they act (the first level). Subgroups to the 14 main groups refer to specific therapeutic, pharmacological, and chemical characteristics (the second, third and fourth level, respectively). The fifth level refers to the drug substances. Each level is given an ATC code. Most antibiotics are classified as antibacterials for systemic use at the second level, and have J01 ATC code (9, 12, 14).

RESULTS

Total outpatient antibiotic use in Poland varied from the lowest of 17.88DID in 2004 to the highest of 21.39DID in 2007. Table I shows the total antimicrobials consumption in Poland and in voivodships from 2004 to 2008 (there are 16 voivodships in Poland - administrative areas equivalent to regions or provinces). The consumption of all antimicrobials slightly increased from 2004 to 2007, and decreased in 2008. Almost, in all voivodships the trends of outpatient antimicrobial consumption were similar to the total outpatient antibiotic use in Poland, with the exception of opolskie voivodship, where the increase of outpatient antibiotic consumption in 2006 (24,94 DID) occurred and then decrease in 2007 (19,61 DID) and 2008 (19,41 DID) followed.

The outpatient antibiotic use was broken down into eight major antibiotic groups according to the ATC classification: penicillins (J01C), cephalosporins and other beta-lactams (J01D), macrolides, lincosamides and streptogramins (J01F), tetracyclines (J01A), quinolones (J01M), sulphonamides and trimethoprim (J01E), aminoglycosides (J01G) and the other antibiotics including amphenicols (J01B), combinations (J01R) and other antibacterials (J01X). In Table II, antibiotic consumption patterns were compared for the relative frequency of different antibiotic classes.

Table I. Total outpatient antibiotic use in Poland and in individual voivodships from 2004 to 2008 expressed in DDDs per 1000 inhabitants per day.

Voivodships	2004	2005	2006	2007	2008
Dolnośląskie	16.89	18.74	18.02	20.59	19.69
Kujawsko-Pomorskie	17.69	19.14	18.45	20.69	18.96
Lubelskie	17.66	20.09	19.28	21.60	20.63
Lubuskie	19.28	20.99	20.09	21.66	20.55
Łódzkie	15.99	21.49	21.27	23.62	22.15
Małopolskie	19.59	20.99	20.36	22.99	22.14
Mazowieckie	16.93	18.27	17.69	19.19	18.76
Opolskie	17.90	19.28	24.94	19.61	19.41
Podkarpackie	19.23	21.16	20.50	22.53	22.23
Podlaskie	17.73	20.63	20.16	21.35	20.63
Pomorskie	17.92	19.15	19.33	21.05	21.25
Śląskie	17.79	20.89	18.64	20.97	21.36
Świętokrzyskie	15.84	22.46	21.16	24.18	22.52
Warmińsko-Mazurskie	18.12	19.35	18.84	20.79	19.19
Wielkopolskie	18.74	20.06	19.67	20.51	20.40
Zachodnio-Pomorskie	18.76	20.88	19.83	20.85	19.74
Total	17.88	20.22	19.89	21.39	20.6

Table II. The outpatient antibiotic use in Poland from 2004 to 2008 broken down into eight major antibiotic groups according to the ATC classification: penicillins (J01C), cephalosporins and other beta-lactams (J01D), macrolides, lincosamides and streptogramins (MLS, J01F), tetracyclines (J01A), quinolones (J01M), sulphonamides and trimethoprim (J01E), aminoglycosides (J01G) and the other antibiotics including ampfenicols (J01B), combinations (J01R) and other antibacterials (J01X) expressed in DDDs per 1000 inhabitants per day.

	Penicillins (J01 C)	Cephalosporins and other beta-lactams (J01 D)	Tetracyclines (J01 A)	MLS (J01 F)	Quinolones (J01 M)	Sulfonamides and trimethoprim (J01 E)	Aminoglycosides (J01 G)	Other J01 classes
2004	9.40 52.6%	1.58 8.8%	2.87 16.1%	2.29 12.8%	0.98 5.5%	0.58 3.2%	0.01 0.1%	0.17 0.9%
2005	10.68 52.8%	1.70 8.4%	3.00 14.9%	3.02 14.9%	1.11 5.5%	0.59 2.9%	0.03 0.1%	0.09 0.5%
2006	10.25 51.5%	1.93 9.7%	2.72 13.7%	3.15 15.8%	1.2 6.3%5	0.53 2.7%	0.05 0.2%	0.01 0.1%
2007	10.73 50.2%	2.32 10.9%	2.78 13.0%	3.85 18.0%	1.12 5.2%	0.52 2.4%	0.05 0.2%	0.02 0.1%
2008	10.35 50.2%	2.45 11.9%	2.52 12.2%	3.56 17.3%	1.18 5.7%	0.47 2.3%	0.04 0.2%	0.02 0.1%

Penicillins (J01C) represented the most frequently prescribed antibiotics constituting more than 50% of the total outpatient antibiotic use. The other most popular groups of antibiotics were tetracyclines (J01A), macrolides, lincosamides and streptogramins (J01F). On the fourth and fifth position were cephalosporins (J01D) and quinolones (J01M), respectively. There has been a substantial change in the pattern of use antibiotics between 2004 and 2008. The percentage share of penicillins (J01C), tetracyclines (J01A), sulfonamides and trimethoprim (J01E) decreased, while the percentage share of cephalosporins (J01D), macrolides, lincosamides and streptogramins (J01F) increased. The general level of use of quinolones (J01M) was stable over the study period (Fig. 1.).

Penicillins (J01C) represented the most frequently prescribed antibiotics in Poland, ranging from 9,40DID in 2004 to 10,73DID in 2007. Penicillin percentage share of total antimicrobial use decreased from 52,6% in 2004 to 50,2% in 2008. Outpatient use of four main subgroups of penicillins: broad-spectrum penicillins (BSP, J01CA), narrow-spectrum penicillins (NSP, J01CE), penicillinase-resistant penicillin (PRP, J01CF), and combinations of penicillin with beta-lactamase inhibitors (COP, J01CR) was further analysed. The subclasses of penicillins (J01C) most frequently prescibed were broad-spectrum penicillins (BSP, J01CA) and combinations of penicillin with beta-lactamase inhibitors (COP, J01 CR). The use of BSP decreased from 6,51DID in 2004 to 5,71DID in 2008, and the COP consumption of increased from 2,72DID to 4,45DID. The use of narrow-spectrum penicillins (NSP, J01CE) and penicillinase-resistant penicillin (PRP, J01CF) remained on a very low level over time, 0,16DID and 0,01DID, respectively. The two most frequently used substances were amoxicillin (J01 CA 04) and amoxi-

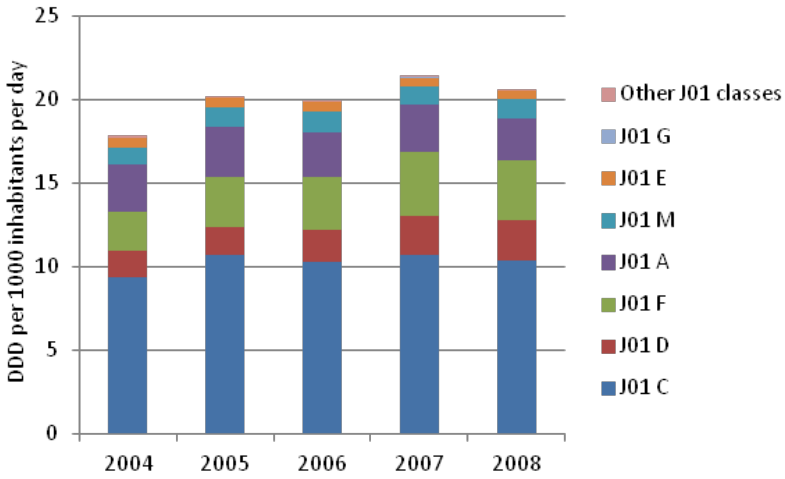

Fig. 1 Trends of outpatient antibiotic use in Poland from 2004 to 2008 broken down into eight major antibiotic groups according to the ATC classification: penicillins (J01C), cephalosporins and other beta-lactams (J01D), macrolides, lincosamides and streptogramins (J01F), tetracyclines (J01A), quinolones (J01M), sulphonamides and trimethoprim (01E), aminoglycosides (J01G) and the other antibiotics including ampfenicols (J01B), combinations (J01R) and other antibacterials (J01X) expressed in DDDs per 1000 inhabitants per day.

cillin and enzyme inhibitor (J01CR02). During the study period (2004-2008), amoxicillin (J01 CA 04) use decreased from 36%DDD (6,50 DID) to 28%DDD (5,71DID), whereas the level of amoxicillin and enzyme inhibitor (J01CR02) use increased from 15%DDD (2,72 DID) to 22%DDD (4,45 DID). The consumption of phenoxymethylpenicillin (J01 CE02) remained on a very low level 0,03-0,17DID (0,2-1%DDD). Three antibiotics (amoxicillin, amoxicillin clavulanate and phenoxymethylpenicillin) represented almost 100% of the total outpatient penicillin use in Poland.

The outpatient use of cephalosporins and other beta-lactams (J01D) was continuously increasing in Poland in years 2004-2008 from 1,58 DID (8,8%DDD) to 2,45 DID (11,9%DDD). The cephalosporins contributed for almost the entire total use within this class. Four cephalosporins represented almost 100% of total outpatient cephalosporin use in Poland. Cefuroxime (J01DC02, second-generation) was the most frequently prescribed substances in this group, and its consumption increased from 0,91 DID (5%DDD) in 2004 to 2,12 DID (10%DDD) in 2008. The other three cephalosporins were: cefadroxil (J01DB05, first-generation) - consumption decreased during study period from 0,33DID (1,9%DDD) to 0,13DID (0,6%DDD), cefaclor (J01DC04, second-generation) - consumption decreased from 0,29 DID (1,6%DDD) in 2004 to 0,18 DID (0,9%DDD) in 2008 and cefalexin (J01DC01, first-generation) - consumption decreased from 0,05 DID (0,3%DDD) in 2004 to 0,04 DID (0,2%DDD) in 2008.

The outpatient use of tetracyclines (J01A) was continuously decreasing from 16,1%DDD (2,87 DID) to 12,2%DDD (2,52 DID). The level of tetracyclines use during the study period shifted from the second position to the third position with regard to places in total outpatient antimicrobial use in Poland. Doxycycline (J01AA02) was the most frequent used antibiotic and accounted for almost the total use within this class.

The outpatient consumption of macrolides, lincosamides and streptogramins (MLS, J01F) increased from 12,8%DDD (2,29 DID) in 2004 to 18,0%DDD (3,85 DID) in 2007 and decreased in 2008 to 17,3%DDD (3,56DID). The level of consumption of MLS during the study period shifted from third position to the second position with regard to places in total outpatient antimicrobial use. The most used sub-group were the macrolides (J01 FA). Outpatient use of two major subgroups of macrolides was further analysed: the older generation (spiramycin, erythromycin) and the newer (roxithromycin, clarithromycin, azithromycin). These five substances represented almost 100% of the total outpatient macrolides use in Poland. The most frequently used substances were clarithromycin (J01FA09) and azithromycin (J01FA10). During the study period the use of clarithromycin (J01FA09) increased from 5%DDD (0,90DID) in 2004 to 8,5%DDD (1,82DID) in 2007 with decrease in 2008 to 7,4%DDD (1,53DID), and azithromycin (J01 FA10) use increased from 1,7%DDD (0,31DID) in 2004 to 4,2%DDD (0,87DID) in 2008. The use of macrolides other then clarithromycin or azithromycin was low, i.e. spiramycin (J01FA02) use ranged from 0,27DID to 0,31DID, erythromycin (J01FA01) from 0,03DID to 0,02DID and roxithromycin (J01FA06) 0,25-0,35DID. The most frequently used representative of lincosamides was clindamycin (J01FF01). Streptogramins were not used at all.

The use of quinolones (J01M) was stable over the study period, and varied only slightly from 5,2%DDD (1,12 DID) in 2007 to 6,3%DDD (1,25 DID) in 2006. Fluoroquinolones (J01MA) represented almost the entire consumption within this class. The most frequently prescribed substances were ciprofloxacin (J01MA02) and norfloxacin (J01 MA06). Ciprofloxacin (second-generation quinolones) constituting more than 50% of the total outpatient quinolones use, i.e. 55,1% (0,54DID) in 2004, 57,6% (0,68DID) in 2008. Norfloxacin (first-generation quinolones) was the second most used chemotherapeutic within this class. Its consumption constituted 40,8% (0,40DID) of the total outpatient quinolones use in 2004 and 39,8% (0,47DID) in 2008. Ofloxacin (J01MA01, second-generation quinolones) was the third chemotherapeutic prescribed within this group in Poland, which accounted for about 0,03-0,05DID. Those three antibacterials represented almost 100% of the total outpatient quinolones use in Poland.

The outpatient consumption of sulphonamides and trimethoprim (J01E) slightly decreased from 3,2%DDD (0,58 DID) in 2004 to 2,3%DDD (0,47 DID) in 2008 . Almost, all the use was of combination of sulfamethoxazole and trimethoprim (J01EE01).

The use of aminoglycosides (J01G) was very low, and constituted about 0,1-0,2%DDD (0,01-0,05DID).

The outpatient use of other J01 classes including amphenicols (J01B), combinations (J01R) and other antibacterials (J01X) was on a low level, varied from 0,9%DDD (0,17DID) in 2004 to 0,1%DDD (0,02DID) in 2008. The most frequently used sub-class were other antibacterials (J01X).

The parenteral antibiotic use in Poland did not exceed 1% of the total outpatient antibiotics prescribed during the study period (2004-2008) with cefuroxime being the most frequently prescribed drug (J01DC02). It constituted 72,2% of total outpatient parenteral use in 2008.

DISCUSSION

This study is one of only few evaluations of total antibiotic consumption to be carried out in Poland.

This outcome is slightly different then data collected by European Surveillance of Antimicrobial Consumption (ESAC) (15). This is an international network of surveillance system with the aim of collecting data on antimicrobial use in Europe. Poland has been included in the ESAC project from the beginning, since 2001 (16). For ESAC project, sales data in Poland was provided by the National Institute for Public Health, for ambulatory care as well as hospital care. Data was derived from 200 out of 400 wholesalers (covering about 60% of the market) and was extrapolated for coverage of the complete population (16). In this surveillance, data concerning outpatient use of systemic antibiotics between 2004 and 2008 were obtained from Polish National Health Fund databases, which spread throughout the country. It could be a reason of the divergence between results of the investigations. Additionally regional consumption of antibiotics could be determined.

In Europe huge variation between outpatient antibiotic uses in different countries has been reported. The level of antibiotic consumption ranged in 2004 from 9,03DID in Switzerland to 33,01DID in Greece, and in 2008 from 9,96 DID in Russian Federation and 10,95 DID in Latvia to 45,21 DID in Greece and 32,78 DID in Cyprus (15). The median European level of outpatient antibiotic use was 17,92DID in 2004 and 20,41 DID in 2008 (15), and our study confirms that, the use of antimicrobials in Poland was on the median European level.

Majority of antibiotics in out of hospital setting are prescribed in primary care (general practice). In the UK, 80% of all antibiotic prescriptions are from primary health-care (17, 18), with majority of patients presenting with respiratory tract infections, and these condition are commonly treated with antibiotics (17, 19, 20). It is well-known that there is wide overuse of antibiotics in patients with these infections across Europe, with considerable differences between countries (21). In Poland antibiotics are prescribed in approximately 60-82% of cases of acute infections of the upper respiratory tract (22-24). Many countries have established guidelines to clarify the indications for use of antibiotics and thereby reduce their consumption. In Poland, since 1997 the national recommendation regarding outpatient respiratory tract infections treatment have been available and recent updated versions have been distributed in paper and electronic version (7). The National Program of Protection of Antibiotics provides funding for public and professional education, national surveillance of antibiotic use, the prevalence of antibiotic-resistant bacteria, and the disease they cause. This study is the first evaluation of antibiotic consumption for all country to be carried out in Poland (6).

The results of the investigation indicate that total out of hospital antibiotic consumption in Poland in years 2004-2008 remained stable and on the median European level. The study also suggests the discrepancy between national recommendations and choice of antibiotics by physicians. The recommended first-line antibiotic for typical acute bacterial pharyngitis and tonsillitis in Poland is narrow-spectrum penicillin (phenoxymethylpenicillin, benzylpenicillin) (25), but very low use of these antibiotics was demonstrated in this study. The first-line antibiotic for acute otitis media, acute sinusitis, community-acquired pneumonia in adults and in children between 4 months and 5 years is amoxicillin. Despite those recommendations the level of amoxicillin use decreased in Poland, whereas the level of amoxicillin clavulanate, cefuroxime , clarithromycin and azithromycin use increased. Earlier reports from Poland indicated that, in a typical scenario of streptococcal tonsillitis, the most popular antibiotic was amoxicillin with clavulanic acid (25, 26). In another study, antibiotics were used as empirical first-line therapy in almost 80% of cases of acute upper respiratory tract infections. Amoxicillin, amoxicillin with clavulanic acid, macrolide and doxycycline were most commonly prescribed (24).

Quality assurance programmes and public campaigns have been developed and launched across Europe to improve use of antibiotics in primary care (27, 28). One of initiatives by National Program of Protection of Antibiotics in Poland was pilot study in the opolskie voivodship (2007-2008). This involved training of primary care doctors in judicious antibiotic use, combined with provision of feedback on antibiotic prescribing to the individual physicians, distribution of free rapid strep-tests and public campaigns. The effect of this program was decrease of number of antibiotic prescriptions by about 10-15% (6). This effect was confirmed in this study. In all voivodships of Poland the trends of outpatient antimicrobial consumption were similar to the total outpatient antibiotic use in Poland, with the exception of opolskie voivodship. There the increase of outpatient antibiotic consumption in 2006 and substantial decrease as a result of educational campaigns in 2007 and in 2008 were demonstrated.

CONCLUSIONS

Total outpatient use of antibiotics in Poland in 2004-2008 was on the median European level. The most often prescribed antibiotics were the penicillins, mainly amoxicillin and amoxicillin with enzyme inhibitor. During the study period the use of the older (narrow-spectrum) antibiotics decreased in favour of the newer (broad-spectrum) antibiotics. The results of the study suggest the discrepancy between national recommendations and choice of antibiotics by physicians. Some of the recommendations have been reflected by

changes in antibiotic consumption (like decreased use of trimetophrim-sulfametoxazol and doxycycline both rendered to be unsuitable for empirical therapy of respiratory tract infections due to high level of Streptococcus pneumoniae resistance). Other expert recommendations, like preferred choice of narrow-spectrum penicillin for sore throat and more restricted use of macrolides and cephalosporins in respiratory tract infections, have not been followed.

Probably the most important public health with regard to antibacterials prescribing issue is stabilizing (or preferably decrease) in total antibiotic consumption. In this aspect the total antibiotic consumption increased in 2005 and then remained stable. In 2008 the last year of the study slight decrease was observed. It is not possible to conclude whether it is the beginning of longer tendency reflecting the effect of educational campaigns in Poland targeting both health professionals and lay people.

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Transparency declaration
No conflict of interest to declare.

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