

## Antibiotic consumption monitoring at the Institute of Otorhinolaryngology and Maxillofacial Surgery – Clinical Center of Serbia in 2001–2003

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**Background.** At the Clinical Center of Serbia (CCS), which includes 21 Institutes and 6 Centers, approximately 10% of the total annual budgetary funds is spent on the drugs. During the studied period, it was estimated that 0.5% of the above amount has been spent at the Institute for Otorhinolaryngology and Maxillofacial surgery (Institute for ORL and MFS), Clinical Center of Serbia. The aim of this study was to find out if these antibiotics had been used rationally by the monitoring of antibiotics in relation to the number of inpatients, and by the 5 most frequent diagnoses. **Methods.** The authors monitored the three-year consumption of antibiotics for inpatient treated patients during the period 2001–2003. Data were obtained from the itemized quarterly report on the consumption by the Central Pharmacy of the CCS. **Results.** The results were statistically analyzed and presented in percentages and Defined Daily Doses (DDD) for each group of the antibiotics. The results were analyzed in accordance with the World Health Organization Recommendations and the Guidelines. **Conclusion.** The authors concluded that antibiotics were adequately used at the Institute for ORL and MFS-CCS. The most commonly used antibiotics for gram-positive infections were those from the penicillin and cephalosporin groups. According to the international trends and recommendations, the selected therapy was rational and the antibiotics consumption was cut down during the observed three-year period. It was a true confirmation that the recommendations for the rational antibiotics consumption had been fruitful (produced good results).

**Key words:** drug administration schedule; drug utilization review; anti-bacterial drugs; surgery, oral.

### Introduction

The Institute of Otorhinolaryngology and Maxillofacial Surgery, Clinical Center of Serbia (ORL and MFS CCS) manages diseases and injuries of the upper respiratory tract, among which the five leading diagnoses are as follows: laryngeal tumors, hypopharyngeal tumors, chronic otitis, secondary otitis and polyps. The most common bacterial floras, which are the cause of the upper respiratory tract infections in our patients, are *streptococcus*, *staphylococcus*, *enterobacter*, *pseudomonas* and *E. coli*. Considering these causative agents, the selection of drugs within the following antibiotic groups: penicillins, cephalosporins, aminoglycosides, quinolones, tetracyclines and “reserve” antibiotics, was an adequate choice for our physicians. So, the upper airway infections in our pa-

tients were most frequently caused by gram-positive bacteria, and, hence, they are our pharmacotherapeutic goal. Antibiotics were used on regular basis, postoperatively for 7 days, and preoperatively as a prophylaxis in the risk group of patients, i.e., with the history of presence of bacterial endocarditis. Intraoperatively, antibiotics were administered in a single dose in endoscopic interventions (1). Bacteria, which in this region as well as according to the available literature and our clinical experience are the common for antibiotic usage, are *streptococcus*, *staphylococcus*, *enterobacter*, *pseudomonas* and *E. coli* (2).

A large number of antibiotics is commercially available and, thus, the various approaches to their application are present causing the polypragmatism and the irrational antibiotic use. The objective of this study was to determine,

by monitoring the antibiotic consumption at the Institute of ORL and MFS CCS, whether these antibiotics had been used in accordance with the current recommendation.

### Methods

This paper is a part of the planned six-year prospective study of the antibiotic consumption monitoring at the Institute of ORL and MFS CCS, representing the results of the last three-year period (2001–2003). The epidemiological protocol specially designed for this study was used. Besides general informations, the protocol included the following data: the generic name of antibiotic, the trade mark of antibiotic, dosage, the form of drug, the unit packaging, and quantity of packagings used. The number of patients treated at the Institute of ORL and MFS CCS, the five most common diagnoses and the groups of used antibiotics were followed up. The choice of the antibiotic group, as well as the individual antibiotics within the specific group was compared with the European standard (3). In addition, the local (CCS) guidelines for antimicrobial therapy and the Sanford Guide to Antimicrobial Therapy were used (4). The used antibiotics were analyzed in regard to their consumption, presented by the schedule, percentages and Daily Defined Dosages (DDD).

### Results

Five leading diagnoses followed up during a three-year period at the Institute of ORL and MFS-CCS, are in Table 1.

during the entire three-year period (Table 2). In 2002, the consumption of penicillin was by 7.67% less than in 2001, while in 2003, the consumption was by 1.22% less than in 2002. On the contrary, cephalosporins consumption was reported to be by 18.33% higher in 2002 in comparison to 2001. In 2003, cephalosporins were used only by 0.2% less than in 2002. During 2003, cefepime, a 4th generation cephalosporin, was used according to the drug susceptibility test for *pseudomonas*-associated infections. During 2001 and 2002, the groups of quinolones and aminoglycoside antibiotics alternatively took the third and fourth place: in 2001, quinolones were third in regard to the consumption, which was 16.64%, while in 2002, they took the fourth place and their consumption was reduced by 10.68%; in 2003, they were not reported among the first five groups of the used antibiotics. In 2001, aminoglycoside antibiotics took the fourth place (12.04%), then in 2002, they fell on the third place due to the increase of the consumption by 0.21%, while in 2003, their consumption at the Institute of ORL and MFS CCS increased for 1.63% in comparison with 2002, but they were still third according to the administration. The tetracycline group of antibiotics was fifth over the entire five-year period of the observation. Their consumption in clinical practice was 6.67% in 2001, then it was reduced by 0.85% in 2002, and increased by 0.81% compared to the previous year. In 2003, during the observation period, the macrolide group of antibiotics was forth for the first time (9.79%) (Figures 1–3).

The overall antibiotic consumption presented as DDD/hospital day during the observed period was on the decrease: in 2001, it was 123.07 DDD/hospital day, in 2002

**Table 1**  
**Five most prevalent diagnoses at the Institute of Otorhinolaryngology and Maxillofacial Surgery, Clinical Center of Serbia**

2001 (Total number of inpatients: 3 047)			
1	Exploratory laryngomicroscopy with sampling	306	10.04%
2	Tympanoplasty	200	6.56%
3	Laryngectomy	160	5.25%
4	Neck dissection	150	4.92%
5	Nasal polyps ablation	122	4.00%
2002 (Total number of inpatients: 3 092)			
1	Exploratory laryngomicroscopy with sampling	835	27.00%
2	Laryngectomy	250	8.08%
3	Tympanoplasty	219	7.08%
4	Maxillary sinus trepanation	168	5.43%
5	Vocal cord polyps extirpation	150	4.85%
2003 (Total number of inpatients: 2 971)			
1	Tympanopasty	244	8.11%
2	Laryngectomy	235	7.91%
3	Vocal cord polyps extirpation	154	5.18%
4	Nasal polyps ablation	150	5.05%
5	Maxillary sinus trepanation	145	4.88%

The results suggested that penicillins and cephalosporins had ranked first in regard to the antibiotic consumption

– 82.52 DDD/ hospital day, and in 2003, a total number of DDD/hospital day was 57.51.

Table 2

Antibiotic consumption – first 5 groups at the Institute of ORL and MFS-CCS from 2001–2003

Group	%	DDD/hospital day
2001		
1 Penicillins: Amoxicillin, Ampicin	34.99	43.06
2 Cephalosporins: Ceftriaxone, Cephalexin, Cefotaxime, Cefuroxime, Ceftazidime	19.55	24.06
3 Quinolones: Ciprofloxacin	16.64	20.48
4 Aminoglycosides: Gentamicin	12.04	14.82
5 Tetracyclines: Doxycycline	6.67	8.20
6 Others	10.11	
2002		
1 Cephalosporins: Cephalexin, Ceftriaxone, Cefotaxime, Ceftazidime	37.88	31.26
2 Penicillins: Amoxicillin + clavulanic acid, Ampicillin	27.32	22.55
3 Aminoglycosides: Amikacin, Gentamicin	12.25	10.11
4 Quinolones: Ciprofloxacin, Ofloxacin	5.96	4.92
5 Tetracyclines: Doxycycline	5.82	4.80
6 Others	10.77	
2003		
1 Cephalosporins: Cephalexin, Ceftriaxone, Cefotaxime, Ceftazidime	37.68	21.67
2 Penicillins: Amoxicillin, Ampicillin, Amoxicillin + clavulanic acid	26.10	15.01
3 Aminoglycosides: Amikacin, Gentamicin	13.88	7.98
4 Macrolides: Clindamycin, Erythromycin, Lincomycin	9.79	5.63
5 Tetracyclines: Doxycycline	6.63	3.80
6 Others	5.92	

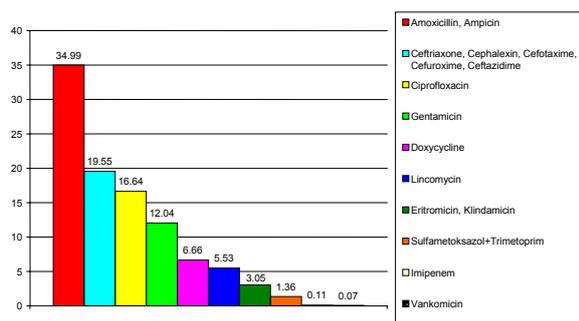


Fig. 1 – Antibiotic consumption at the Institute of ORL and MFS CCS in 2001

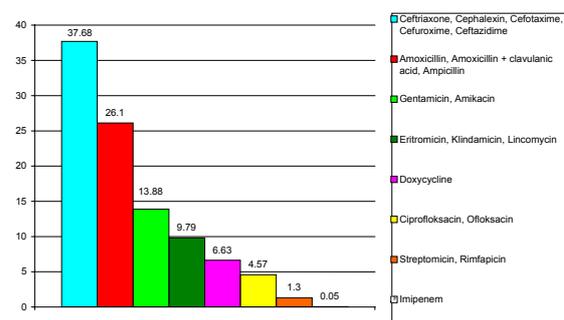


Fig. 3 – Antibiotic consumption at the Institute of ORL and MFS CCS in 2003

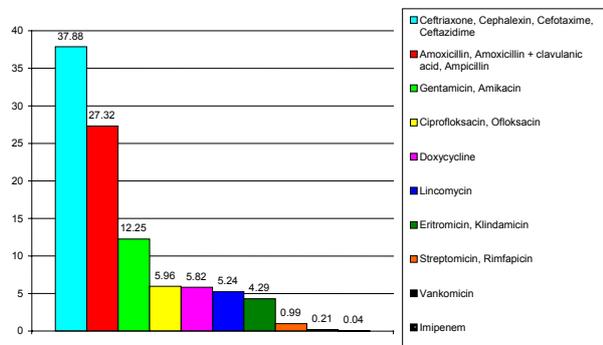


Fig. 2 – Antibiotic consumption at the Institute of ORL and MFS CCS in 2002

Discussion

The basic principles of rational antibiotic treatment, with multiple modifications, included several factors (5): clinical findings, bacteriological test results, causative agents of infection, the choice of antibiotics, antibiotic combinations, the dosage regimens, the way of application, the duration of the therapy, the modification of the initial therapy as well as the patient’s condition. There was the big difference between the characteristics of antibiotic prescription in the primary health care, and their usage in the hospital setting, particularly in clinical centers (6). These principles were the baseline for making the working schemes – algorithms; their goal was the effectiveness of treatment, with the delayed development of bacterial resis-

tance and the reduction of the costs. Data on antimicrobial drug consumption were important, because they indicated the extent of their probable irrational application.

Our study showed that this antibiotic therapy was applied according to the drug susceptibility test results, in compliance with the WHO recommendations and the applied guidelines for antimicrobial therapy. Within the structure of antibiotics prescribed in 2001, the predominant ones were as follows: penicillins, cephalosporins, quinolones, aminoglycosides, and tetracyclines. Lincomycin (5.53%, 6.81 DDD), erythromycin and clindamycin (3.05%, 3.75 DDD), sulfamethoxazole + trimethoprim (1.36%, 1.67 DDD), imipenem (0.11%, 0.13 DDD) and vancomycin (0.07%, 0.09 DDD) were used rarely. In 2001, i.e., within 365 days, 44 920 DDD of antibiotics were spent on 3 047 inpatients, which was around 14 DDD/patient/year. In addition, in 2001, the number of DDD/day was 123.07 per 140 hospital beds. If one takes into account that there were patients who received combination of two or three antibiotics, that nosocomial infections and septic conditions were treated by antibiotics, and that there were patients from the smaller hospitals referred to the Institute of ORL and MFS CCS for further treatment, then it may be concluded that the consumption of antibiotics was adequate. One must be aware of the fact that 2001 was the first year after the hard ten-year period when our physicians were in a position to opt for various antibiotics. Gram-positive infections of the upper respiratory tract are generally treated at the Institute of ORL&MFS, and therefore, the physicians could make the adequate choice of the aforementioned antibiotics according to the Sanford guide to antimicrobial therapy and the local CCS Guides. Due to the pathology of diseases and the head and neck injuries, the characteristic of antibiotic to pass through the blood-brain barrier is crucial. Moreover, the penicillin and cephalosporin groups of antibiotics, closely tied for first place with a consumption during the past years, have the fast-acting pharmacokinetic characteristics which was very important for the treatment of our patients (7).

Within the structure of antibiotic consumption in 2002, the predominant ones were: cephalosporins, penicillins, aminoglycosides, quinolones and tetracyclines. Lincomycin (5.24%, 4.32 DDD), clindamycin and erythromycin (4.29%, 3.54 DDD), streptomycin and rifampicin (0.99%, 0.82 DDD), imipenem (0.04%, 0.03 DDD) and vancomycin (0.21%, 0.17 DDD) were used rarely. During 2002, at our institute, a total of 30120 DDD were therapeutically applied, which was 9.74 DDD per inpatient. It clearly indicated that the possibility of choice reduced the antibiotic consumption i.e., that one was able to choose an adequate antibiotic to obtain the fastest cure. It led to the rationalization of antibiopharmacotherapy. The specialists in clinical pharmacology, in compliance with recommendations of the Good Clinical Practice and WHO (8), also contributed to the implementation of the rational pharmacotherapeutical standpoints at the CCS Institute of ORL and MFS.

Of the antibiotics consumed in 2003, the most commonly used were as follows: cephalosporins, penicillins, aminoglycosides, macrolides and tetracyclines. In 2003, cefepime, a 4th generation cephalosporin, was used for the first time for the treatment of the upper respiratory tract infections caused by pseudomonas, according to the drug susceptibility test, i.e., in case of the infection of surgical site wound. The application of quinolones (ciprofloxacin, ofloxacin) – 4.57% 2.63 DDD, antituberculous (streptomycin, rifampicin) – 1.30% 0.75 DDD, and other antibiotics (imipenem) – 0.05% 0.04 DDD was rather rare. Within the group “others”, antibiotics from the so-called “reserve” group were included (9). During 2003, at our institute, a total of 20 991 DDD were therapeutically applied, which was 7.07 DDD/inpatient (Table 3).

Table 3

**Antibiotic consumption at the Institute of Otorhinolaryngology and Maxillofacial Surgery, Clinical Center of Serbia**

Year	DDD/year	No of patients	DDD/patient
2001	44 920	3 047	14.00
2002	30 120	3 092	9.74
2003	20 991	2 971	7.07

Interestingly, the decrease of the number of DDD/day during a three-year observation period was 123.07 : 82.52 : 57.51 respectively, probably due to the appropriate supply and, hence, to an adequate choice of antibiotics as to the well as observation of the instructions for the rational usage of antibiotics.

The activity of the Center for Clinical Pharmacology, Clinical Center of Serbia (CCP CCS), includes the preparation of the priority antibiotic list exclusively based on the up-to-date principles of pharmacotherapy regardless of their position on the negative-or positive-drug list. As a measure for pharmacotherapeutic rationalization, CCP CCS uses the practical population pharmacokinetic approach based on the collection and processing of a rather small number of data on antibiotic concentrations in our patients. Such monitoring of antibiotic concentrations is the safest measure for dosage, adequacy control, and the base for the prevention of bacterial resistance (10).

This work is a part of a six-year study, which goes on, and upon its completion, the comparative results of antibiotic consumption of similar studies will be published.

### Conclusion

The results of our study showed that the consumption of antibiotics at the Institute of ORL and MFS CCS, in the period 2001 to 2003, was rational, due to the adequate choice of antibiotics based on the isolated or expected causative agent, the localization and the severity of infection and pharmacokinetic drug characteristics. We believed that it was the result of making a “true” choice of antibiotics, stable domestic drug market in that period, and also of

the implementation of current international recommendations on antimicrobial therapy. Certainly, much credit was given to CCP CCS for the rational antibiotic consumption in

our Institute of ORL and MFS CCS, which was an additional recognition of the role of these centers in the application of the rational pharmacotherapy (11).

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#### Apstrakt

Kastratović DA, Đukić VB, Majstorović BM, Komrska JJ, Gajić MM, Marković SZ. *Vojnosanit Pregl* 2005; 62(7-8): 551–555.

#### PRAĆENJE POTROŠNJE ANTIBIOTIKA U INSTITUTU ZA OTORINOLARINGOLOGIJU I MAKSILOFACIJALNU HIRURGIJU KLINIČKOG CENTRA SRBIJE U PERIODU OD 2001. DO 2003. GODINE

**Uvod.** U Kliničkom centru Srbije (KCS), koji u svom sastavu ima 21 institut i 6 centara, u okviru budžeta se na lekove godišnje odvoji 10%. U proseku, u toku praćenog perioda, Institut za otorinolarinologiju i maksilofacijalnu hirurgiju (Institut za ORL MFH) troši 0,5% od ovih 10%. Cilj ovoga rada je da se praćenjem potrošnje antibiotika u odnosu na broj hospitalno lečenih bolesnika i najčešćih pet dijagnoza ustanovi da li se oni racionalno koriste. **Metode.** Praćena je potrošnja antibiotika kod bolnički lečenih bolesnika u periodu od 2001. do 2003. godine. Za bazu ovih podataka korišćeni su podaci iz izveštaja Centralne apoteke KCS o utrošku antibiotika svakog tromesečja. Rezultati su statistički obrađeni i prikazani procentualno i u dnevno definisanim dozama (DDD) po grupama antibiotika. **Rezultati.** Na osnovu analize sprovedene u skladu sa preporukama Svetske zdravstvene organizacije (SZO), zaključeno je da su u našem Institutu antibiotici korišćeni adekvatno. Za gram pozitivne infekcije najčešće korišćeni antibiotici bili su iz grupe penicilina i cefalosporina. **Zaključak.** U skladu sa međunarodnim tokovima i preporukama izabrana terapija je bila racionalna, a potrošnja antibiotika smanjena u toku tri prikazane godine, što pokazuje da su preporuke za racionalizaciju potrošnje antibiotika dale rezultate.

**Ključne reči:** lekovi, propisivanje; lekovi, korišćenje, izveštaji; antibiotici; hirurgija, maksilofacijalna.