THE ANALYSIS OF ANTIBIOTIC CONSUMPTION WITHIN THE TERTIARY HEALTHCARE INSTITUTION IN SERBIA DURING 10-YEAR PERIOD (2001-2010)

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ABSTRACT

Objective: To present conclusions related to the antibiotic drug consumption in one tertiary healthcare institution in Serbia in a 10-year period (2001-2010).

Methods: It has been analyzed the issue of antibiotics for prevention and treatment of patients hospitalized at the Military Medical Academy between 2001 and 2010. Antibiotic consumption was expressed as a number of Defined Daily Doses per 100 bed-days (DDD/100BD).

Results: Total antibiotic consumption ranged from 49.6 DDD/100BD in 2001 up to 60.4 DDD/100BD in 2005. The leading group of antibiotic was third-generation cephalosporins which accounted for 15.1 DDD/100BD of its maximum consumption in 2007. Ceftriaxone was the most frequently used.

Conclusion: Analysis of antibiotic consumption, and multidisciplinary approach, has a crucial importance for further survey of protocols compliance concerning the antibiotic consumption in one hospital.

Keywords: Antibiotics, Hospital consumption, ATC, DDD, Bacterial resistance.

The irrational use of antibiotics in hospital settings represents public health problem. The aim of the antibiotic consumption control is an improvement of the healthcare quality, decrease in the treatment costs, and reduction of microorganism resistance. The strategy for the antibiotic use should be determined, by guidelines, for prevention and treatment of infections on the basis of local epidemiological data and resistance to antibiotics [1, 2].

The rational use of antibiotics is a very complex problem requiring the cooperation of different professionals. Changes in the antibiotic usage patterns are implying changes in healthcare workers' behavior and attitude, which is extremely difficult to achieve, but possible, if strongly supported by the hospital administration [3]. The aim of this study is to highlight the antibiotic consumption at the

Military Medical Academy (MMA), a 1200-bed tertiary care teaching hospital during, a 10-year period (2001-2010).

According to the recommendation of World Health Organization (WHO), the antibiotic consumption is expressed as a number of Defined Daily Doses per 100 bed-days (DDD/100BD) [4, 5]. Monitoring of drug dispensing-related data was carried out through the computer-based support system of the MMA. *The data of the total bed-days of care in hospital, are obtained from the medical statistics in the form of annuals [6].*

The total use of antibiotics, observed over the 10-year investigation period, ranged from 49.6 DDD/100BD in 2001 up to 60.4 DDD/100BD in 2005 (table 1).

Table 1: Total consumption of systemic antibiotics at *the MMA during the 2001-2010 period* expressed as the number of DDD/100BD

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Antibiotic consumption	49.6	57.0	54.4	58.3	60.4	56.4	56.8	58.2	54.9	59.5

The most widely used groups of antibiotics, were the other beta-lactam antibiotics, including cephalosporin and Carbapenem with the maximum of 25.9 DDD/100BD in 2010, while penicillin and quinolone were the second and third of all groups antibiotics consumed (fig. 1).
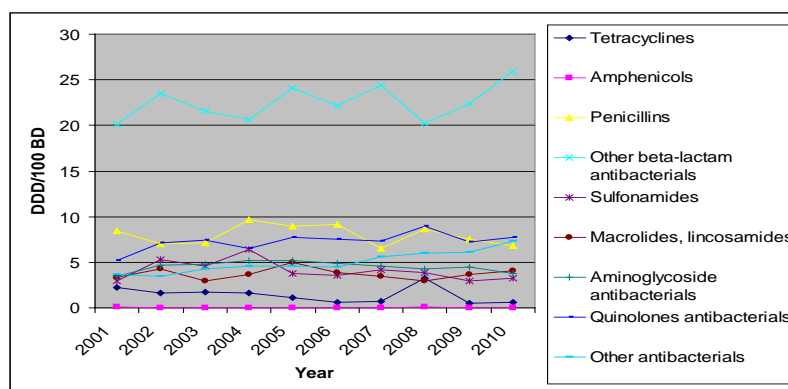

Fig. 1: The consumption of antibiotic for systemic use at the MMA during the 2001-2010 periods expressed as the number of DDD/100BD

Broad-spectrum penicillins, with the maximum of 6.5 DDD/100BD in 2001 were the most commonly used in the penicillin group., Third-generation cephalosporins represented the most widely used

antibiotics, which accounted for 15.1 DDD/100BD of its maximum consumption in 2007, in the group of other beta-lactam antibiotics (fig. 2).
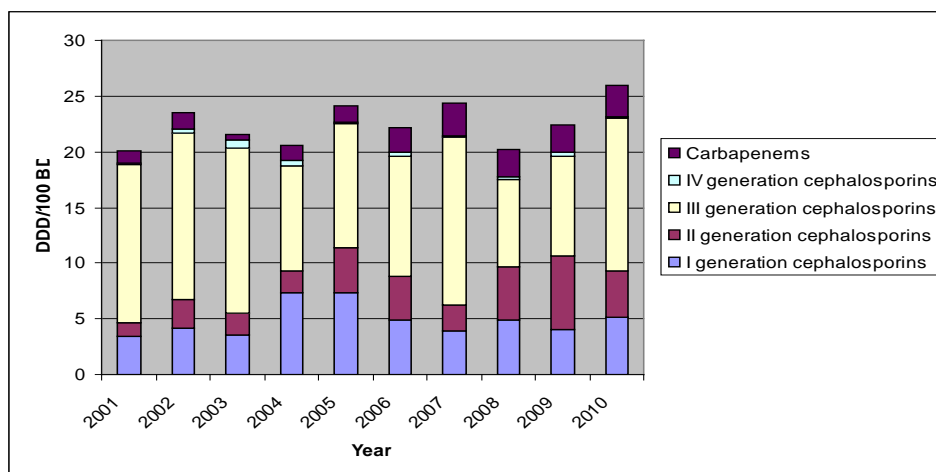

Fig. 2: The consumption of beta-lactam antibiotics at the 2001-2010 periods expressed as the number of DDD/100BD

The most widely used, within the 10-year period of investigation, was ceftriaxone. Its maximum consumption was reported in 2007 (14.4 DDD/100BD). The secondly used was ciprofloxacin. Maximum consumption was registered in 2008 (8.5 DDD/100BD). The use of the first-and second-generation

cephalosporins increased throughout the years. The use of carbapenem also increased, which reached its maximum consumption in 2007 (3.0 DDD/100BD). It was the case with glycopeptides as well, which were maximally consumed in 2007 (1.8 DDD/100BD) (fig. 2, table 2).

Table 2: The consumption of particular antibiotics and groups of antibiotic drugs at the MMA between 2001 and 2010 expressed as the number of DDD/100BD

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Piperacillin-Tazobactam	0.2	0.0	0.2	0.2	0.6	0.4	0.8	0.5	0.4	0.6
Cefazolin	0.0	0.0	0.3	2.7	2.2	1.6	0.0	2.3	1.9	1.9
Cefuroxime	0.0	0.0	0.0	0.6	1.5	1.2	1.7	3.7	6.0	3.9
Ceftriaxone	13.9	14.0	13.4	8.0	9.0	9.2	14.4	5.9	7.4	12.7
Imipenem-Cilastatin	1.0	1.4	0.5	1.2	0.9	1.4	1.6	0.5	1.1	0.7
Meropenem	0.0	0.0	0.0	0.2	0.5	0.9	1.2	2.0	1.4	1.7
Amikacin	0.1	2.3	3.4	2.7	2.8	3.3	3.9	2.9	2.7	2.4
Ciprofloxacin	2.5	4.7	6.0	2.3	3.9	6.5	6.6	8.5	6.8	7.3
Vancomycin	0.2	0.3	0.1	0.7	1.3	0.6	1.3	0.7	1.3	1.1
Teicoplanin	0.2	0.3	0.6	0.3	0.2	0.3	0.5	1.0	0.2	0.5
Glycopeptides	0.4	0.6	0.7	1.0	1.5	0.9	1.8	1.7	1.5	1.6

There are not many publications which used the numbers of DDD/100 BD as indicators, to express the antibiotic consumption. Published papers, only confirmed the correlation between the antibiotic consumption and increased antibiotic resistance, and vice versa. The increase of doses of particular antibiotic consumption leads to reduce its use, as modifying existing protocols. It is recommended to improve alternative protocols in such cases. [7]. During 2004 and 2005, the total antibiotic consumption, in 25 hospitals, in the South and East Mediterranean, ranged from 45 to 836 DDD/100BD [8], while, at the MMA, it reached the maximum of 60.4 DDD/100BD over the 10-year period (table 1).

The Medicines and Medical Devices Agency of Serbia published the data on the drug consumption throughout the years of 2004-2006. The highest rate of antibiotic consumption in hospitals was observed in 2005 (119.19 DDD/100BD) while the lowest rate of their use was reported in 2006 (57 DDD/100BD). The extended-spectrum penicillins, along with aminoglycosides and cephalosporins of the third generation, were among the leading

drugs used [9]. MMA in comparison with the other hospitals, in Serbia, use antibiotics much rationally. According to the European Surveillance of Antibiotic Consumption (ESAC), the penicillin consumption ranged from 17.9% in Finland to 56.9% in France; cephalosporins were the least frequently used in Ireland 8.4% and the most widely used in Bulgaria 44.5%, while the rate of quinolones use was from 6.9% in Norway to 21.8% in Hungary, in 2008. The rate of penicillin use at the MMA, in 2008 totaled 14.8%, while cephalosporins and quinolones, were used at the rates of 30.4% and 15.3% respectively, in relation to the total antibiotic consumption [10]. The penicillins were less frequently used at the MMA, while cephalosporins and quinolones were used within the ranges reported from the European hospitals [10-12].

The most widely used antibiotic, in MMA, was ceftriaxone. The first significant drop in the consumption was observed in 2004 (8 DDD/100BD), when the use was reduced by 42.1% in relation to the average consumption rate, in the last three years. The second significant drop, in the ceftriaxone consumption, occurred in 2008

(5.9 DDD/100BD), when its use decreased by 45.5% (table 2). These reductions in consumptions were the result of efforts of a multidisciplinary team in order to rationalize the use of antibiotics in MMA. However, over 2009 and 2010, its consumption started to rise, steadily again, because of the problems in supplying hospitals with antibiotics and other drugs.

During the same period, a rise in the ciprofloxacin consumption has been noted (table 2). Increased quinolones consumption, may also be attributed to the healthcare-related diarrheas caused by *Clostridium difficile* (CDAD). The wide use of quinolones and cephalosporins was an important risk factor for epidemic CDAD in Denmark and Canada [13, 14]. In 2010, CDAD incidence rate at the MMA was 3.3 on 10.000 hospital days [15].

A prospective cohort study of risk factors for SSI In 2006 in patients of MMA, demonstrated that SSIs were the most usually caused by *Staphylococcus aureus* (27.8%). The 64% isolates were methicillin-*resistant*. Second causation was *Enterococcus spp.* (16.2%) without registered vancomycin resistance, along with *Klebsiella spp.* (13.9%) with 90% of the third-generation cephalosporins-resistant isolates [16]. Between 2006 and 2010 the SSI rate decreased from 6.3% to 3.2% [17]. Furthermore, the use of carbapenems over 2006-2010 period was stable (2.2-3 DDD/100BD). However, it was twice higher when compared to the period from 2001-2005. It was also concluded that the glycopeptides consumption was twice higher, in relation to the previous period in the last six years. (fig. 2, table 2). Nevertheless, consumption of carbapenems and glycopeptides, in particular, European hospitals and MMA in the early consumption period, was similar [10, 12]. It is important to stress out, that in 2006 the *Enterococcus spp* isolated from SSIs was not resistant to vancomycin, while in 2010 was vancomycin-resistant in 25% of nosocomial infections (NI) registered in MMA [16, 18].

The increase in consumption, of the third-generation cephalosporins, quinolones, carbapenems, and glycopeptides, may be correlated with the high rate of multi-resistance causative agents of NI registered within the framework of the Third National Prevalence Study of NI. More precisely, besides the increased *Enterococcus spp.* vancomycin bacterial resistance, it has been noted the *Acinetobacter spp.* resistance, to the third-generation cephalosporins and carbapenems as well as the high resistance of bacteria *Pseudomonas spp.* on the third-generation cephalosporins (100%) and carbapenems (66.7%) [16, 18]. Within the 10-year period the most widely used antibiotic, at the MMA, was ceftriaxone. There was a rise in the consumption of quinolones, carbapenems, and glycopeptides, which may be correlated to the high antimicrobial resistance of bacteria causative agents of NI in MMA. Analysis of antibiotic consumption and multidisciplinary approach has a crucial importance for further survey of protocols compliance, concerning the antibiotic consumption in one hospital.

CONFLICT OF INTERESTS

Declared none

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