

MONITORING OF THE CEPHALOSPORINS CONSUMPTION IN THE TERTIARY CARE HOSPITAL

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Irrational antibiotic consumption, especially in the case when there is no appropriate indication for its usage, may be one of the most crucial global issues for public health care, leading to bacterial resistance and the increase of indirect medical expenses. According to the report of the European program for the monitoring of the antibiotic consumption, Serbia is on the fifth place among the countries which are not members of EU. The goal of this work is the evaluation of antibiotic consumption in the Clinical Centre Niš, from 2007 to 2013, with the focus on the monitoring of the cephalosporins utilization, as they are one of the most prescribed groups of antibiotics in the tertiary health care.

The utilization of antibiotics in the Clinical Center Niš in the observed period was obtained from the computerized database of the Department of Pharmacotherapy and expressed as defined daily dose (DDD) per 100 bed/days (DBD).

Our results showed that there was an increase in antibiotic use of the whole group of cephalosporins and penicillin as well as a reduction of quinolones consumption within the observed period. Our analysis showed that ceftriaxone was the most frequently prescribed cephalosporin, followed by cefuroxime.

Although antibiotic therapy and prophylaxis in our hospital are in keeping with the recommended guidelines, the obtained results may suggest that cephalosporin consumption, and especially ceftriaxone consumption is higher than in other European countries. *Acta Medica Medianae* 2015;54(2):31-36.

Key words: antibiotics consumption, cephalosporins, ceftriaxone, defined daily dose

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Introduction

Antibiotics are the most frequently used drugs among the hospitalized patients, comprising 15–30% of all prescribed drugs in hospitals. However, studies showed that in 50% of the cases the prescribed antibiotics were inadequate. Providing a rationale antibiotic pharmacotherapy in the tertiary health care includes antibiotic procurement, prescribing, dispensing and administration. All these processes should be controlled in order to promote appropriate antibiotic usage, which may be useful for an individual as well for the entire society (1). Irrational antibiotic consumption, especially in the case when there is no appropriate

indication for its usage, may be one of the most crucial global issues for public health care, leading to bacterial resistance and the increase of indirect medical expenses (2,3). This problem has been reported in all European countries, whereby Greece, France and Italy have been the leaders (4). According to the report of the European program for the monitoring of the antibiotic consumption, Serbia is on the fifth place among the countries which are not members of EU (5). Monitoring of antibiotic consumption is of crucial importance due to the increasing problem of the antibiotic resistance that has a global trend (6).

The goal of this work is the evaluation of antibiotic consumption in the Clinical Centre Niš, from 2007 to 2013, with the focus on the monitoring of the cephalosporins utilization, as they are one of the most prescribed groups of antibiotics in the tertiary health care.

Methods

Antibiotics consumption was monitored in the Clinical Centre Niš, Serbia: a 1460-bed,

tertiary care university hospital in Serbia, in the study period extending from 2007 to 2013. Results were presented for every second year since 2007. As this study did not collect any data on individual patients and surveillance was a part of quality assurance, an approval by Ethical Committee was not considered necessary. This study generally used the WHO classification system ATC and the volume unit defined daily dose (DDD). Utilization of antibiotics in the Clinical Center Niš in the observed period was obtained from the computerized database of the Department of Pharmacotherapy and expressed as DDD per 100 bed/days (DBD). Thirty-six different antibiotic drugs were used in our hospital. Following implementation of restriction policy in 2011, prescription of spare antibiotics (carbapenems, piperacillin/tazobactam, vancomycin, and linezolid) was placed under the control. These agents may only be prescribed after the clinical pharmacologist/

infectious disease specialist consultation or following an approval by the medical director.

Results

Trends of antibiotic consumption classified by pharmacological groups in DBD were showed in Figure 1. The most frequently used antibiotics were cephalosporins, followed by penicillins, aminoglycosides and quinolones. During the investigation period, the utilization of cephalosporins increased by 34%, from 17.4 DBD (2007) to 23.32 DBD (2013), where as aminoglycosides utilization was decreased by, 50.71%, from 5.58 DBD (2007) to 2.75 DBD (2013). Quinolones consumption was variable during the observation period. There was a reduction in quinolones usage by 66.02% and 48.03% from 2007 to 2009 and from 2007 to 2013. (Figure 1).

Table 1. Antibiotic consumption in the Clinical Center Niš from 2007 to 2013

ANTIBIOTICS	2007		2009		2011		2013	
	DBD	%	DBD	%	DBD	%	DBD	%
Ampicillin	1.5	3.13	0.83	1.89	0.68	1.12	0.66	1.25
Amoxicillin/clav.	1.19	2.48	0.34	0.77	3.09	5.07	2.5	4.74
Cefuroxime	5.97	12.46	4.97	11.31	4.61	7.57	5.57	10.56
Ceftriaxone	6.09	12.71	8.66	19.70	11.21	18.40	10.78	20.44
Ceftazidime	0.42	0.88	0.42	0.96	0.91	1.49	0.69	1.31
Cefepime	0.18	0.38	0.51	1.16	0	0.00	0	0.00
Gentamicin	3.33	6.95	4.26	9.69	2.56	4.20	0.92	1.74
Amikacin	2.2	4.59	2.15	4.89	1.9	3.12	1.83	3.47
Ciprofloxacin	7.3	15.23	1.62	3.69	6.08	9.98	3.84	7.28
Cotrimoxazole	1.87	3.90	0.58	1.32	1.11	1.82	1.13	2.14
Piperacillin/tazobactam	0.25	0.52	0.52	1.18	0.47	0.77	0.32	0.61
Imipenem	0.29	0.61	0.37	0.84	0.36	0.59	0.52	0.99
Meropenem	0.62	1.29	0.76	1.73	1.15	1.89	0.57	1.08
Other	16.71	34.87	17.97	40.88	26.79	43.98	23.4	44.38
Total	47.92	100.00	43.96	100.00	60.24	100.00	52.73	100.00

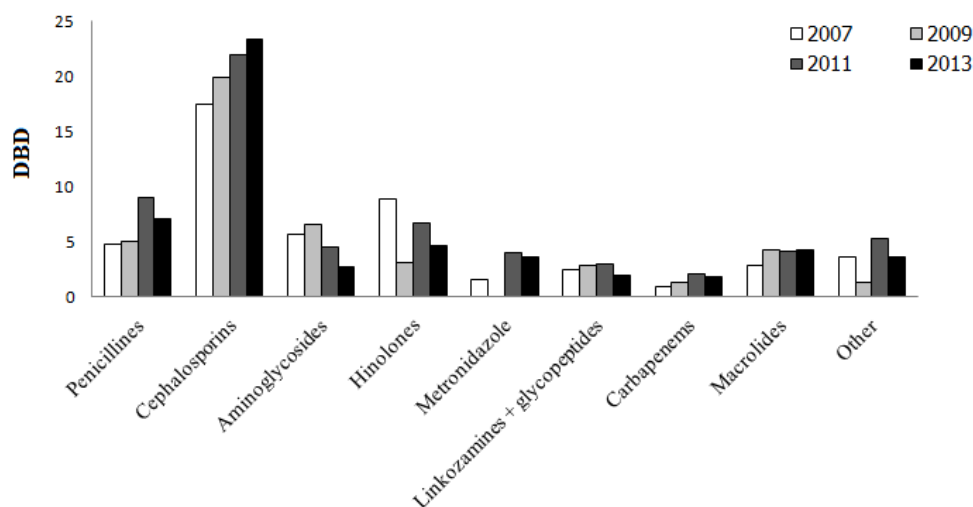


Figure 1. Trends of antibiotic consumption by pharmacological groups (in DBD) in the Clinical Center Niš from 2007 to 2013

Antibiotics consumption in the Clinical Centre Niš was shown in Table 1. During the investigation period, the total consumption of antibiotics ranged from 47.92 DBD to 52.73 DBD. The highest consumption of antibiotics was in 2011 (60.24 DBD). The most frequently used antibiotic was ceftriaxone during all observed years, but there was an increasing trend in its consumption from 12.71% of total antibiotics use in 2007 to 10.78 DBD or 20.44% of total antibiotics use in 2013. (Table 1).

Trends of cephalosporin utilization showed that the most frequently used cephalosporin was ceftriaxone, followed by cefuroxime in the observation period (Figure 2). Also, there was a trend of increased ceftriaxone consumption during 2007 to 2013. The highest consumption of ceftriaxone was in 2011, whereas there was an

increase by 77.01%, from 6.09 DBD (2007) to 10.78 DBD (2013). Furthermore, cefuroxime consumption did not fluctuate as ceftriaxone during observation period, due to the fact that there was only 6.7% reduction of cefuroxime consumption from 2007 to 2013 (5.97 DBD to 5.57 DBD).

Figure 3 shows ceftriaxone and cefuroxime consumption by clinical departments in 2013. Surgical clinics were the biggest consumers of ceftriaxone, 199.64 DBD or 63.4 % of total ceftriaxone consumption. Also, surgical clinics were the biggest consumers of cefuroxime as well as ceftriaxone, 98.33 DBD or 54.5 % of total cefuroxime consumption (Figure 3). Figure 4 shows that Urgent surgery was the biggest consumer of ceftriaxone and it was followed by Cardiovascular surgery. Alternatively, cefuroxime was the most consumed drug at Neurosurgery, which is opposite

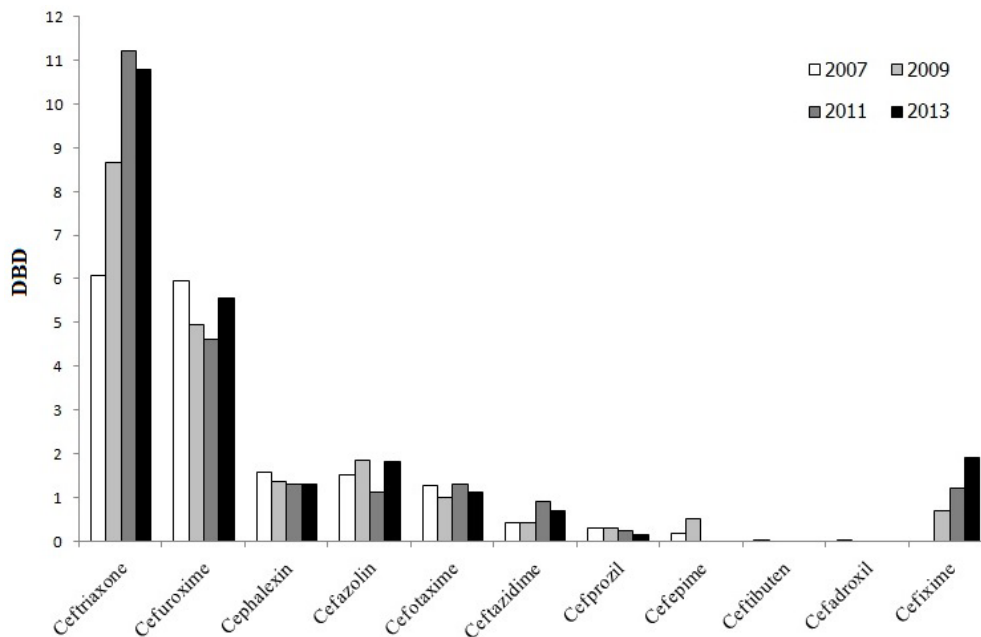


Figure 2. Trends of cephalosporins utilization (in DBD) in the Clinical Center Niš from 2007 to 2013

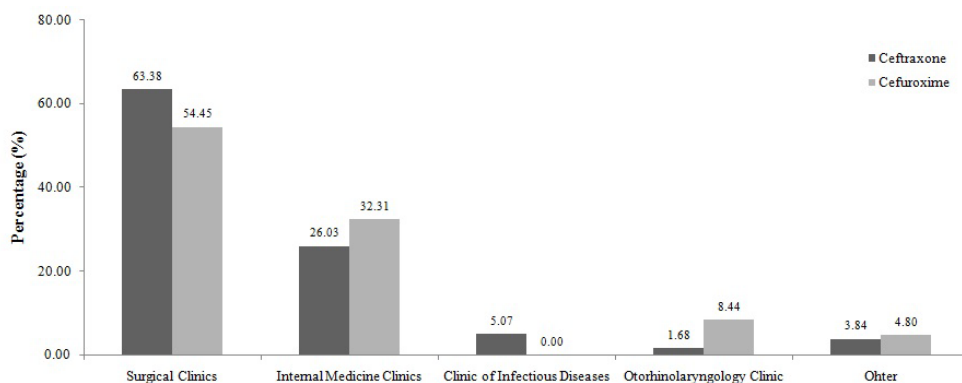


Figure 3. Comparison of ceftriaxone and cefuroxime use in different clinics of the Clinical Centre Niš (Data is expressed as a percentage of total ceftriaxone and cefuroxime consumption, which is 315 DBD and 180.6 DBD, respectively).

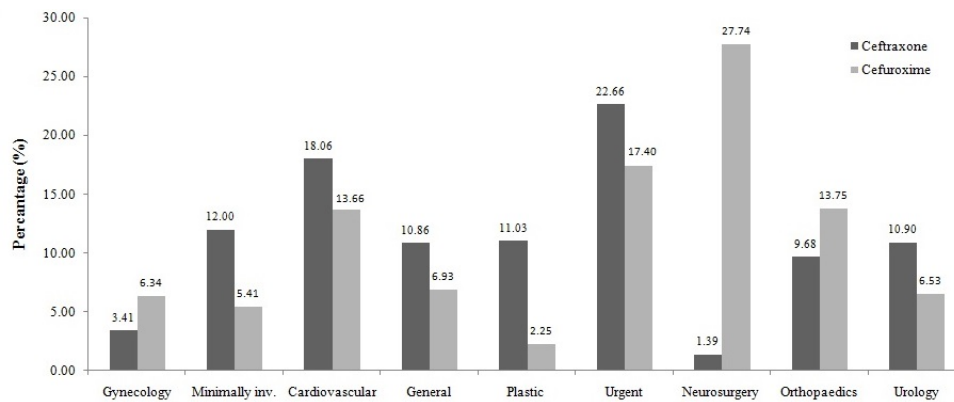


Figure 4. Comparison of ceftriaxone and cefuroxime use in different surgical departments of the Clinical Centre Niš (Data is expressed as a percentage of total ceftriaxone and cefuroxime consumption in surgical departments which is 199.64 DBD and 98.33 DBD, respectively).

to ceftriaxone consumption, which was spent the least at the same clinic (Figure 4).

Discussion

Antibiotics have significantly contributed to the reduction of the likelihood of dying from infectious diseases worldwide. However, previous studies have suggested that almost one third of drug prescriptions are questionable. We monitored antibiotic consumption in the six-year period from 2007 to 2013, in the Clinical Centre Niš, tertiary health care university hospital in Serbia. Our results showed that there was an increase in antibiotic use of the whole group of cephalosporins and penicillin as well as a reduction of quinolones consumption within the observed period (Figure 1). Furthermore, in the results for individual antibiotics, there was a trend of increased ceftriaxone and amoxicillin clavulanic acid use, whereas there was the decreasing trend of ciprofloxacin consumption during the investigation period (Table 1). The research conducted at the Freiburg University, which is a teaching hospital and tertiary care referral center, showed an overall decline of cephalosporins consumption (all generations taken together) between the two monitored periods of time, 2008–2011 and 2012–2013. After the first monitoring period, restriction policy was implemented. Especially, there was a decrease in the third generation of cephalosporins, but also an increase of the first and second generation. According to our results, there was an increase in penicillines and decrease in fluoroquinolones consumption (7). Alternatively, the research conducted in Spanish hospitals showed that fluoroquinolones usage was increased between 1999 and 2010, but there was no change of the consumption of the third generation of cephalosporins for the same period (8). Ashiru-Oredope et al. conducted the study on antimicrobial consumption between 2004 – 2009 in English hospitals. During this period, there was a 40% decline in the use of fluoro-quinolones, a 50% decline in the second generation cephalosporin usage, a 22%

decline in the third generation cephalosporin usage, but a 50% increase in carbapenem usage, a 3-fold increase in piperacillin/tazobactam usage and a 50% increase in co-amoxiclav usage (9). Differences in antibiotic use across geographical areas may be explained by demographic, cultural, and economic factors as well as supply-side factors such as the density of doctors and their prescribing policy system (10). Also, cross-country variations in antibiotic consumption in the community can be explained by a variety of factors such as incidence of infections, but it can hardly explain variations in the use of antibiotics (11).

Our analysis showed that ceftriaxone was the most frequently prescribed cephalosporin, followed by cefuroxime (Figure 2). Furthermore, ceftriaxone as well as cefuroxime consumption were the highest in Surgery Clinics, followed by Internal Medicine Clinic (Figure 3). Results from Sofia, Bulgaria showed an increase in the third generation of cephalosporins in surgical clinics between 2006 and 2009. These results are in accordance with our study, but they showed no change in penicillin as well as an increase in fluorohinolones consumption. Also, it is shown that the total antibiotic usage for the same period in the Surgery clinic fluctuated from 47.9 to 61.9 DBD, but the most commonly used antibiotics were the cephalosporins of the first generation, followed by imidazoles, which is opposite to our study (12).

In the study conducted in Romania, the total antibiotic consumption in hospital was 72.6 DBD, by medical specialties the indicator's values were 61.2 DBD in the department of internal medicine specialties, 62.8 DBD in the department of surgical specialties and 126 DBD in the medical/surgical intensive care unit, respectively. Almost 70% of the total defined daily doses included five antimicrobial agents: co-amoxiclav, cefuroxime, cefoperazone + sulbactam, ciprofloxacin and metronidazole. Top three groups of antibiotics were penicillin plus beta-lactamase inhibitors, 2nd generation cephalosporins and

fluorochinolons, respectively, which is opposite to our study results, where the most prescribed group was the third generation of cephalosporins (13).

Antimicrobial therapy and prophylaxis are the standard of care for surgical patients. However, the choice of antibiotics and its duration of administration remains a matter of personal choice. With the widespread presence of multi-drug resistant pathogens and limited availability of therapeutic choices, it is important to restrict the usage of broad spectrum antimicrobials, especially their prolonged courses as perioperative prophylaxis (14).

Ceftriaxone is an appropriate drug for the treatment of meningitis, endocarditis, and nonresistant bone infections and due to its broad spectrum effects, it is effective against the most positive and negative gram bacteria. Besides, this drug can also be used for prophylaxis before surgery (15). Also, many of these studies have recommended the use of cefuroxime for prophylaxis due to its high bioavailability tissue and serum after a single dose administration and is also efficacious for preventing perioperative infections (16, 17).

Healthcare policy makers are worried that, despite efforts to limit excessive use of antibiotics, consumption as well as resistance might have an increasing trend. Spending large sums of money on costly and potentially harmful antibiotics of last

defense will not protect hospitals from being confronted with epidemics of resistant germs, bad reputation, excessive expenditures and avoidable loss of human lives (18).

Conclusion

Adequate and accurate evaluation of antibiotic consumption in hospitals is an efficient approach, which can be used in analyzing a rationale pharmacotherapy of antibiotic usage. Our findings suggest that there may be a difference in antibiotic consumption between European countries especially in the sense of cephalosporins usage. Although antibiotic therapy and prophylaxis in our hospital follow the recommended guidelines, the obtained results may suggest that cephalosporin consumption, and especially ceftriaxone consumption is higher than in other European countries. A rational and strict antibiotic policy is, thus, of great importance for the optimal use of these agents.

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Conflict of interest statement

None declared.

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PRAĆENJE POTROŠNJE CEFALOSPORINA NA NIVOU TERCIJARNE ZDRAVSTVENE ZAŠTITE

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Neracionalna upotreba antibiotika, naročito u slučajevima kada je neodgovarajuća indikacija za primenu, može biti jedan od značajnih globalnih problema javnog zdravlja, uzrok bakterijske rezistencije i povećanih medicinskih troškova. U skladu sa izveštajem Evropskog programa za praćenje potrošnje antibiotika, Srbija se nalazi na petom mestu u odnosu na zemlje koje nisu članice EU. Cilj rada bio je analiza potrošnje antibiotika u Kliničkom centru Niš u periodu od 2007. do 2013. godine, sa posebnim osvrtom na praćenje upotrebe cefalosporina, najčešće propisivane grupe antibiotika u tercijarnoj zdravstvenoj zaštiti.

Praćenje potrošnje antibiotika u Kliničkom centru Niš, u posmatranom periodu, vršeno je na osnovu baze podataka Centra za farmakoterapiju i izraženo je kao broj Definisanih dnevnih doza na 100 bolesničkih dana.

Rezultati sprovedenog istraživanja pokazuju povećanje potrošnje cefalosporina i penicilina uz smanjenje upotrebe hinolona u toku posmatranog perioda. Osim toga, ceftriakson je bio najčešće propisivan antibiotik iz grupe cefalosporina, dok je cefuroksim zauzeo drugo mesto.

Navike u propisivanju antibiotika i profilaksa u Kliničkom centru Niš bili su u skladu sa važećim preporukama, ali dobijeni rezultati ukazuju na povećanu potrošnju cefalosporina, naročito ceftriaksona, u odnosu na druge evropske zemlje. *Acta Medica Mediana* 2015;54(2):31-36.

Ključne reči: *upotreba antibiotika, cefalosporini, ceftriaksona, definisana dnevna doza*