THE ANALYSIS OF ANTIBIOTIC CONSUMPTION AND BACTERIAL RESISTANCE AS AN INDICATOR OF THEIR PROPER USE AT THE UROLOGY DEPARTMENT IN THE HEALTH CENTRE "STUDENICA" KRALJEVO

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ANALIZA POTROŠNJE ANTIBIOTIKA I BAKTERIJSKE REZISTENCIJE KAO INDIKATORA NJIHOVE RACIONALNE UPOTREBE NA ODELJENJU UROLOGIJE ZDRAVSTVENOG CENTRA "STUDENICA" U KRALJEVU

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ABSTRACT

The objective of the study was to analyze antibiotic consumption and determine bacterial resistance rates as an indicator of the rational utilization of this drug group at the urology department in the Health Centre "Studenica" Kraljevo.

Over a two-year period, the average antibiotic consumption was 104.55 DDD/100BD. Of the total financial assets used for medical treatment, the antibiotic group JO1 had a share of 49.52% in 2011 and 47.53% in 2012. Antibacterial drugs from a group of β-lactamic antibiotics were consumed most commonly, at 54.02% (2011) and 43.44% (2012). First-generation cephalosporins, quinolones and aminoglycosides were the most frequently used drug groups, while cephalexin was the antibiotic with the highest individual consumption. E. coli was the most frequently isolated bacterium in 2011, while in 2012, Klebsiella pneumoniae was the most frequently isolated bacterium. The total bacterial resistance both in 2011 and 2012 was above 50%. Gram-negative bacteria showed a higher resistance rate (2011, 59.3%; 2012, 58.9%) than Gram-positive bacteria (2011, 44.4%; 2012, 40.6%). Klebsiella pneumoniae was the bacterium with the highest resistance (75.3%) in 2011, while in 2012, there was a resistance increase in Pseudomonas aeruginosa (71.4%), especially to carbapenems. A correlation was determined between the consumption of individual antibiotics and bacterial strain resistance in 2011 (r=0.433, p=0.044) and in 2012 (r=0.478, p=0.024).

The high resistance rate shown in the bacterial strains, which was correlated with antibiotic consumption, as well as the great financial assets used for this group of drugs suggest the necessity for the rationalization of their utilization. Empirical therapy with Gram-negative bacteria should be based on carbapenems utilization, except with Pseudomonas aeruginosa, where piperacillin/tazobactam should be used.

Key words: *antibiotics, bacterial resistance, DDD methodology, urology departments.*

SAŽETAK

Cilj ovog istraživanja je analiza potrošnje antibiotika i utvrđivanje stepena rezistencije bakterijskih sojeva kao indikatora racionalne primene ove grupe lekova na odeljenju urologije Zdravstvenog centra "Studenica" u Kraljevu.

U toku dvogodišnjeg perioda prosečna potrošnja antibiotika iznosila je 104,55 DDD/100BD. Od ukupnih novčanih sredstava utrošenih za medikamentoznu terapiju na antibiotike grupe J01 izdvojeno je 49,52% u 2011. odnosno 47,53% y 2012. Antibakterijski lekovi iz grupe β-laktamskih antibiotika beleže najveći udeo u potrošnji sa 54,02% (2011) i 43,44% (2012). Cefalosporini prve generacije, hinolonski antibiotici i aminoglikozidi su najčešće korišćene grupe antibiotika, a cefaleksin je antibiotik sa najvećom pojedinačnom potrošnjom. E. Coli je bila najčešće izolovana bakterija u 2011, dok je u 2012. Klebsiella pneumoni bila najzastupljenija. Ukupna rezistencija bakterijskih sojeva je u 2011. i u 2012. bila veća od 50%. Gram negativne bakterije su pokazale veći stepen rezistencije (2011-59,3%, 2012- 58,9%) u odnosu na Gram pozitivne (2011-44,4%, 2012-40,6%). Klebsiella pneumoni je bakterija sa najvećom rezistencijom u 2011. (75,3%), dok se u 2012. beleži porast rezistencije Pseudomonas aeruginosa (71,4%), posebno na karbapeneme. Utvrđena je korelacija potrošnje pojedinačnih antibiotika i rezistencije bakterijskih sojeva u 2011. (r=0,433, p=0,044) i 2012. (r=0,478, p=0,024).

Visok nivo rezistencije koji pokazuju bakterijski sojevi, a koji je u korelaciji sa potrošnjom antibiotika, kao i velika novčana sredstva koja se izdvajaju za ovu grupu lekova, sugerišu na potrebu racionalizacije njihove primene. Empirijska terapija kod Gram negativnih bakterija bi trebalo da se zasniva na primeni karbapenema, osim kod Pseudomonas aeruginosa gde prednost treba dati piperacilin/tazobaktamu.

Ključne reci: *antibiotici, bakterijska rezistencija, DDD metodologija, urologija.*

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ABBREVIATIONS

ATC – Anatomical Therapeutic Chemical;
DDD – defined daily dose;
WHO – World Health Organization;
SPSS – Service Provisioning System Software;
BD – Bed-days;
ALIMS – Medicines and Medical Devices Agency of Serbia;
INN – International Nonproprietary Names.

INTRODUCTION

The antibiotic share of a hospital's consumption of all prescribed drugs goes up to 30%, which makes them one of the most frequently used groups of drugs (1, 2). This study showed that 22.9% of inpatients used at least one antibiotic. Of those patients, 5.1% had two antibiotics included in the therapyand 1.1% used three antibiotics. With 37.4% of patients, antibiotic therapy was inappropriate because it was unjustified; the choice of antibiotic was wrong or there was a utilization mistake (2). Inappropriate antibiotic utilization is one of the main reasons for microorganism resistance which, aside from increasing hospitalized treatment costs, leads to more serious consequences, such as an increase in morbidity and mortality rates (3, 4). The utilization of amoxicillin/clavulanate and quinolones was more frequently inappropriate, while the utilization of small-therapeutic-amplitude penicillins, cephalosporins, meropenem, metronidazole, and rifampicin was significantly appropriate. The inadequacy of use was connected with both the type of antibiotic and the specialist department. Urology, nephrology, otolaryngology and geriatrics were the specialist departments with risk factors for inappropriate antibiotic utilization, while paediatrics was isolated because of a significantly high rate of adequate antibiotic use (2).

Approximately 56% of the hospitalized patients at the urology department used antibiotics. According to the study, the highest percentage of patients at a urology department that used antibiotics was recorded in Turkey (approximately 70%), whereas in Hungary (49%) and Germany (47%), this number was statistically significantly lower (5), which suggests the important regional differences in the utilization of these drugs. A multicenter centre study conducted in European countries between 2003 and 2010 showed an antibiotic resistance increase in urologic patients. Imipenem was the only antibiotic whose resistance to the total bacterial spectrum was below 10% (5). *Escherichia coli*, the most frequently isolated bacterium in urologic patients, had a significant resistance rate to ampicillin, amoxicillin + clavulanic acid and fluoroquinolones (6). Monitoring and analysis of antibiotic consumption are highly important for antibiotic use rationalization in urologic patients. Due to differences in demographic characteristics, this monitoring should be conducted at regional and local levels (6).

Taking into consideration the increased bacterial strain resistance isolated in urologic patients (5), the existence of risk for inadequate antibiotic use at the urology department (2) and the necessity for local analysis of antibiotic consumption (5), the aim of this paper was to:

- analyze the individual antibiotic presence at the urology department;
- determine the presence and resistance rate expressed by bacterial strains isolated from the clinical material of inpatients at this department;
- determine the correlation between antibiotic consumption and bacterial resistance rate; and
- compare the given results with the available results of similar studies in our country and region.

MATERIAL AND METHODS

This study was based on data collected in the Health Centre "Studenica" that provides primary health care at the Health Centre Kraljevo and secondary health care in the General Hospital Kraljevo. The General Hospital has 580 beds and provides secondary health care for approximately 250,000 patients.

In accordance with the Anatomical Therapeutic Chemical (ATC) Classification System, the analysis was conducted on the antibiotic groups for systemic use, J01, used between January 2011 and December 2012 at the urology department. The data concerning total patient number and average hospitalization length at the urology department were obtained from the planning and analysis department. The central pharmacy provided the data concerning antibiotic consumption at the urology department, while bacteriological analysis results of samples were obtained from The Institute of Public Health.

All antibiotics were classified according to the ATC Classification System and their generic names; their total consumption was calculated and presented in units of measurement (mg and ij) which were then presented in DDD per 100 bed-days (BD), using the ATC/DDD methodology of the World Health Organization (WHO) (8).

The sensitivity of all of the bacterial strains isolated from the clinical material of hospitalized patients was estimated by the disc-diffusion method on Mueller-Hinton Agar.

During the study, data on individual patients were not collected. Thus, it was determined that approval by the Ethical Committee was not necessary.

The collected data were statistically analyzed. The descriptive statistical data were expressed as a percentage or as the arithmetic mean with the standard deviation. The data distribution normality was checked by the Kolmogorov-

Table 1: The systemic use of different pharmacotherapeutic groups of antibiotics in the department of urology.

ATC*	Pharmacotherapeutic group of antibiotics	2011		2012	
		DDD/100BD#	%	DDD/100BD#	%
J01C	Penicillins	3.18	3.09	2.90	2.73
J01DB	Cephalosporins 1st generation	28.58	27.81	24.41	22.95
J01DC	Cephalosporins 2nd generation	15.21	14.80	7.10	6.68
J01DD	Cephalosporins 3rd generation	6.74	6.56	10.78	10.13
J01DE	Cephalosporins 4th generation	0.00	0.00	0.00	0.00
J01DH	Carbapenems	1.80	1.75	1.01	0.95
J01E	Sulfonamides	1.81	1.76	11.23	10.56
J01F	Macrolides	1.78	1.73	0.87	0.82
J01G	Aminoglycosides	18.33	17.84	21.66	20.37
J01M	Quinolones	19.44	18.92	19.17	18.03
J01XA	Glycopeptides	0.06	0.06	0.12	0.11
J01A	Tetracyclines	0.07	0.07	0.47	0.44
J01XD	Imidazole derivatives	5.67	5.52	6.63	6.23
J01B	Amphenicol	0.09	0.09	0.00	0.00
In total		102.76	100	106.35	100

* Anatomical Therapeutic Chemical; # Defined daily dose/100 bed-days.

Smirnov and Shapiro-Wilk tests. Student's t-test i.e., and its non-parametric alternative, Mann-Whitney U test, were used for determining statistically significant differences between the values of two continuous variables. The comparison between categorical variables was conducted using the Chi-square test. The relationship between antibiotic consumption and bacterial resistance was determined using Pearson's correlation. A value of $p<0.05$ was considered statistically significant. All statistical analyses were performed with the computer programme SPSS, version 18.

RESULTS

The urology department of the General Hospital Kraljevo has 22 beds. In 2011, there were 1484 hospitalized patients with an average hospitalization length of 4.83 days; therefore, the number of achieved bed-days was 7167 (BD). In 2012, there were 6326 bed-days. The number of hospitalized patients for this year was 1451, and the average hospitalization length was 4.36 days.

Of the total financial assets used for medical treatment in this department in 2011, antibiotics had a share of 49.52%, while in 2012 that share was 47.53%.

During this two-year period, the average antibiotic consumption was 104.55 DDD/100BD. The increase of total antibiotic consumption from 102.76 DDD/100BD in 2011 to 106.35 DDD/100BD in 2012 was not statistically significant ($p=0.645$, $U=81.000$). Antibacterial drugs for systemic use that belonged to the β-lactamic group were consumed most frequently at: 54.02% (2011) and 43.44% (2012). The decreased consumption of β-lactamic antibiotics by slightly more than 10% was not statistically significant ($p=0.781$, $t=0.288$). The consumption of first-generation cephalosporins was the highest when compared to other drug groups. The second most frequently consumed antibiotic was quinolones in 2011, and aminoglycosides in 2012 (Table 1).

During the monitored period at the urology department, 24 generically different antibiotics were used. During

Table 2: Ranking of the antibiotics composing 90% of the total DDDs prescribed in the department of urology.

ATC*	INN¥	2011		2012	
		DDD/100BD#	%	DDD/100BD#	%
J01DB01	Cephalexin	25.34	24.66	18.59	17.48
J01MA02	Ciprofloxacin	12.95	12.60	14.74	13.86
J01GB06	Amikacin	9.91	9.64	13.20	12.41
J01EE01	Co-trimoxazole	/	/	11.23	10.56
J01DD04	Ceftriaxone	6.25	6.08	10.43	9.81
J01GB03	Gentamicin	8.42	8.19	8.46	7.95
J01DC02	Cefuroxime	15.21	14.80	7.10	6.68
J01XD01, P01AB01	Metronidazole	5.67	5.52	6.63	6.23
J01MB04	Pipemidic acid	6.49	6.32	4.43	4.17
In total		90.24	87.82	90.38	89.15

* Anatomical Therapeutic Chemical; # Defined daily dose/100 bed-days; ¥ International Nonproprietary Names.

Table 3: Resistance of all of the isolates to individual antibiotics in the department of urology.

Antibiotics	Resistance N (%)	
	2011	2012
Amikacin	105 (57.1)	63 (57.8)
Amoxicillin	6 (31.6)	5 (29.5)
Amoxicillin/clavulanate	81 (54.7)	39 (40.2)
Ampicillin	142 (78.9)	73 (70.2)
Cefaclor	4 (40.0)	2 (20.0)
Cefalexin	9 (64.3)	17 (53.1)
Cefepime	2 (100)	4 (80.0)
Cefixime	101 (67.3)	58 (64.4)
Cefotaxime	105 (66.9)	57 (65.5)
Ceftazidime	18 (46.2)	20 (66.7)
Cefrixsone	7 (70.0)	13 (76.5)
Ciprofloxacin	169 (81.6)	108 (85.0)
Erythromycin	0 (0.0)£	0 (0.0)£
Fusidic acid	1 (100)	/
Gentamicin	140 (71.4)	79 (66.4)
Chloramphenicol	1 (50.0)	1 (33.3)
Imipenem	20 (10.7)	16 (14.7)
Meropenem	17 (9.1)	17 (15.3)
Clindamycin	0 (0.0)£	/
Nalidixic acid	/	0 (0.0)£
Norfloxacin	170 (75.9)	105 (77.2)
Ofloxacin	108 (68.4)	52 (71.2)
Penicillin G	8 (30.8)	9 (33.3)
Pipemidic acid	/	18 (75.0)
Piperacillin	127 (73.8)	69 (70.4)
Piperacillin/tazobactam	12 (22.6)	12 (35.3)
Tetracycline	16 (69.6)	13 (76.5)
Co-trimoxazole	8 (57.1)	18 (60.0)
Vancomycin	0 (0.0)	0 (0.0)
Ertapenem	0 (0.0	/
In total	1377 (57.8)	868 (56.6)

£ One to two probes

both years, the same antibiotics comprised 90% of the total antibacterial drugs for systemic use, except cotrimoxazole, which was not included in 2011. Cephalexin was the antibiotic with the highest individual consumption (Table 2).

The total bacterial resistance was higher than 50% both in 2011 and in 2012. Table 3 shows the resistance for each individual antibiotic.

In 2011, 218 isolates (urine, 98.6%) from the urology department were analyzed. Twenty different species of bacteria were isolated; two bacteria were isolated from each of 13 isolates. *Escherichia coli* was the most frequently isolated bacterium. In 2012, 141 isolates (urine, 98.7%) were processed. Two bacteria were isolated from each of 9 isolates. *Klebsiella pneumoniae* was the most frequently isolated from 14 different isolated species of bacteria.

Gram-negative bacteria showed a higher resistance (2011, 59.3%; 2012, 58.9%) rate than Gram-positive bacteria (2011, 44.4%; 2012, 40.6%). The lowest level of Gram-negative bacterial resistance was to carbapenems, whereas Gram-positive bacteria were sensitive to glycopeptide antibiotics. Table 4 shows the resistance of the most frequently isolated bacteria.

There was a correlation between the consumption of individual antibiotics and bacterial strain resistance in 2011 ($r=0.433$, $p=0.044$) and in 2012 ($r=0.478$, $p=0.024$). There was no statistically significant correlation between antibiotic consumption during 2011 and bacterial resistance in 2012 ($r=0.367$, $p=0.093$).

DISCUSSION

One of the main objectives of the study was to determine which antibiotics were used most commonly at the urology department and whether their consumption correlated significantly with bacterial strain resistance rates.

The consumption of all antibiotics for systemic use was analyzed up to level five of the ATC/DDD classification, and then, a comparison was performed. All antibiotics used at the urology department and included in the study belonged to group J01, except metronidazole for oral use, as it belongs to group P (antiparasitic products). The average antibiotic consumption during the two-year period was 104.55 DDD/100BD, which was significantly lower than consumption at the urology departments of the Surgical Clinics in Niš and Novi Sad. The results of a two month study in 2004 showed that the consumption of group J anti-infective drugs at the urology department was 263.54 DDD/100BD in Niš and 224.85 DDD/100BD in Novi Sad (9). Lower antibiotic utilization at the urology department in Kraljevo compared with antibiotic utilization in Niš and Novi Sad was evident, even though our study included only J01 antibiotics because they were consumed the most frequently consumed antibiotic from group J (10). The average consumption of antibiotics for systemic use at the Surgical Clinic of Clinical Hospital Centre – Priština in Gračanica from 2007 to 2008 was 124.22 DDD/100BD (11), which was closer to the results of our study than to the study conducted in Niš and Novi Sad (9). According to our data, cephalosporins, quinolones and aminoglycosides had the highest utilization. In Niš and Novi Sad, cotrimoxazole had the highest consumption, followed by quinolones and aminoglycosides in Niš and cephalosporins and aminoglycosides in Novi Sad (9). The study of the Medicines and Medical Devices Agency of Serbia (ALIMS) showed that from 2004 to 2006 in health institutions in Serbia, penicillin with an extended spectrum (J01CA) was consumed

Table 4: Resistance within the most frequently isolated bacteria.

Antibiotics	Resistance N (%)							
	Escherichia coli		Klebsiella pneumoniae		Proteus mirabilis		Pseudomonas aeruginosa	
	2011	2012	2011	2012	2011	2012	2011	2012
Amikacin	9 (28.1)	2 (12.5)	24 (64.9)	16 (43.2)	14 (53.8)	16 (72.7)	27 (71.1)	25 (86.2)
Amoxicillin	/	0 (0.0)[£]	/	/	/	/	/	/
Amoxicillin/clavulanate	5 (20.8)	1 (5.9)	23 (63.9)	17 (45.9)	18 (72.0)	17 (70.8)	4 (100)	1 (100)
Ampicillin	27 (69.2)	15 (68.2)	39 (100)	29 (93.5)	26 (86.7)	18 (81.8)	3 (100)	2 (100)
Cefalexin	1 (50.0)	2 (28.6)	/	7 (100)	0 (0.0)[£]	3 (75.0)	/	/
Cefepime	/	/	/	0 (0.0)[£]	/	/		2 (100)
Cefaclor	/	1 (100)	/	/	/	/		/
Cefixime	6 (16.2)	4 (17.4)	36 (94.7)	32 (84.2)	20 (69.0)	19 (76.0)	4 (100)	1 (100)
Cefotaxime	6 (15.8)	2 (10.0)	37 (94.9)	29 (90.6)	18 (64.3)	17 (73.9)	4 (100)	1 (33.3)
Cefriaxone	0 (0.0)[£]	1 (33.3)	1 (100)	5 (100)	0 (0.0)[£]	1 (33.3)	/	/
Ceftazidime	/	/	/	/	/	/	15 (45.5)	17 (63.0)
Ciprofloxacin	14 (42.4)	9 (52.9)	38 (100)	33 (89.2)	20 (76.9)	19 (86.4)	35 (94.6)	30 (100)
Fusidic acid	1 (100)	/	/	/	/	/	/	/
Gentamicin	15 (35.7)	4 (17.4)	32 (84.2)	26 (74.3)	16 (57.1)	16 (64.0)	32 (91.4)	27 (96.4)
Chloramphenicol	/	/	/	/	/	1 (100)	1 (100)	/
Imipenem	0 (0.0)	0 (0.0)	2 (5.3)	0 (0)	3 (11.5)	0 (0)	11 (28.2)	15 (50.0)
Meropenem	0 (0.0)	0 (0.0)	2 (5.3)	0 (0)	0 (0.0)	0 (0)	11 (28.9)	14 (48.3)
Ofloxacin	12 (30.0)	8 (44.4)	37 (94.9)	27 (96.4)	19 (70.4)	15 (75.0)	5 (83.3)	1 (100)
Norfloxacin	14 (33.3)	10 (41.7)	38 (97.4)	34 (89.5)	20 (69.0)	18 (75.0)	35 (94.6)	28 (100)
Nalidixic acid	/	0 (0.0)[£]	/	/	/	/	/	/
Piperacillin	13 (59.1)	5 (38.5)	35 (97.2)	26 (92.9)	20 (83.3)	16 (80.0)	23 (63.9)	18 (60.0)
Penicillin G	/	0 (0.0)[£]	/	/	/	/	/	/
Pipemidic acid	/	4 (57.1)	/	10 (83.3)	/	4 (80.0)	/	/
Piperacillin/tazobactam	0 (0.0)	/	1 (50.0)	/	1 (50.0)	/	8 (23.5)	10 (35.7)
Tetracycline	0 (0.0)[£]	1 (25.0)	/	0 (0.0)	/	0 (0.0)[£]	/	/
Co-trimoxazole	1 (50.0)	2 (25.0)	/	8 (80.0)	2 (66.7)	5 (83.3)	/	/
Ertapenem	0 (0.0)[£]	/	/	/	/	/	/	/
Vancomycin	/	0 (0.0)[£]		/		/		/
In total	124 (29.2)	71 (27.4)	345 (75.3)	299 (65.7)	197 (59.5)	185 (63.1)	218 (62.5)	192 (71.4)
Frequently isolated bacteria N (%)	43 (18.6)	25 (16.7)	39 (16.9)	38 (25.3)	31 (13.4)	26 (17.3)	37 (16.0)	30 (17.3)

[£] One to two probes

most frequently, followed by aminoglycosides and cephalosporins of the third and first generation (10). However, at the urology department of the Health Centre "Studenica" during 2011 and 2012, penicillin (J01C) consumption was only approximately 3% of total antibiotic consumption (Table 1). High consumption of this antibiotic group, as opposed to others from J01, was not recorded at the urology departments in Niš or Novi Sad (9).

In 2011 as well as 2012, cephalexin was the antibiotic consumed most frequently (Table 2). This antibiotic, according to the study by the ALIMS, was included in the ten most frequently used antibiotics in health institutions from 2004 to 2006, but it was not among the first three for its consumption (10). Based on the three-year study conducted in the Clinical Centre Niš, ceftriaxone had the highest consumption in 2003 and 2007, whereas in 2005, ampicillin and ciprofloxacin preceded it. Cephalexin was not among the ten most frequently used antibiotics for its consumption at the Clinical Centre Niš (12). At the Surgical Clinic of the Clinical Hospital Centre – Priština in Gračanica, cephalexin was the third most frequently consumed antibiotic in 2007, after cefuroxime and ceftriaxone, whereas in 2008, both cotrimoxazole and gentamicin had were consumed more than cephalexin (11).

According to our study, the average bacterial resistance both in 2011 and 2012 was above 50% (Table 3). A high resistance rate (70.3%) was also shown in a study that followed the prevalence and resistance rate of urinary tract infection agents in patients treated in the Clinical Centre Kragujevac from 2009 to 2011 (13). As expected, the resistance rate was positively correlated with antibiotic consumption. If we ignored antibiotics that had only one to

two tests, the lowest resistance rate was for carbapenems and glycopeptide antibiotics, i.e., vancomycin. In Table 3, it can be observed that in 2011 there was lower resistance to meropenem and imipenem in 2012. However, both antibiotics had a tendency to increase resistance. The results showing a low resistance rate to vancomycin (Table 3) should be observed with caution because there were few tests of bacterial sensitivity for this antibiotic, and these tests were not conducted on the most frequently isolated bacteria (Table 4). The results of a multicentre study conducted in Europe showed that the resistance rate to all tested antibiotics, except imipenem, was above 10% (6).

Our results showed that, of the four most frequently isolated bacteria, *Escherichia coli* had the lowest resistance rate in the monitored period. This bacterium showed the highest sensitivity to carbapenems and piperacillin/tazobactam, which is in congruence with other studies (12-14). If the number of tests was taken into consideration, *Escherichia coli* developed the highest resistance to ampicillin (69.2%, 2011; 68.2%, 2012) (Table 4). According to a study conducted in a tertiary care hospital in Spain, *Escherichia coli* resistance to ampicillin was 48.1% (7), whereas according to results from Iran, the resistance to the same antibiotic was 63.2% (14). *Escherichia coli* showed higher resistance to ampicillin in the Clinical Centre Kragujevac (13) than in the results of our study. The *Escherichia coli* resistance rate to ampicillin in the Clinical Centre Niš decreased in 2007 (57.61%) as opposed to 2003 (73.08%), but it still remained the antibiotic to which this bacterium showed the highest resistance (12).

In 2011, of all the most frequently isolated bacteria, *Klebsiella pneumoniae* showed the highest resistance, especially to quinolones and amikacin (Table 4). In a ten-year study, this bacterium showed a statistically significant increase in resistance to ceftadizime, ciprofloxacin and cotrimoxazole, whereas the sensitivity to carbapenems remained at a very high level (15), which was supported in our study.

In 2012, there was a resistance increase in *Pseudomonas aeruginosa*. The resistance increase of this bacterium to carbapenems presented a unique problem, which was also seen observed in other studies (13, 16, 17). In our study, *Pseudomonas aeruginosa* had the highest sensitivity to piperacillin/tazobactam, which was in accordance with other studies (18).

CONCLUSION

According to the results of this study, antibiotic consumption (DDD/100BD) at the urology department of the Health Centre "Studenica" was lower than in other areas of the country (9). However, the high resistance rate that the bacterial strains showed, which was in correlation with antibiotic consumption, as well as the great financial assets used for this group of drugs, suggests the necessity for rationalization of their utilization. Gram-negative bacteria were more frequently isolated and had a higher resistance rate than Gram-positive bacteria. Empirical therapy with Gram-negative bacteria should be based on carbapenem utilization, except with *Pseudomonas aeruginosa*, where piperacillin/tazobactam should be used. When choosing antibiotics, empirically or based on the results of an antibiogram, one should consider both pharmacokinetic and pharmacodynamic drug characteristics, individual patient characteristics, and the possibility of interactions with other drugs (19).

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