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APPLICATION OF THE ATC/DDD METHODOLOGY TO COMPARE ANTIBIOTIC UTILIZATION IN TWO UNIVERSITY HOSPITAL SURGICAL DEPARTMENTS

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Summary. *To analyze overall drug consumption, compare antibiotic utilization in particular, and evaluate whether sound principles of surgical prophylaxis are applied at urology clinics of two university hospitals.*
The study was carried out at the urology clinics of the Department of Surgery, University Clinical Center in Niš, and the Institute of Surgery, University Teaching Hospital in Novi Sad, Serbia. Anti-microbial consumption was calculated during a two month period as the number of Defined Daily Doses (DDDs) per 100 bed days (BD) for all antiinfectives for systemic use, i.e. group J of the Anatomical Therapeutic Chemical (ATC) classification and for classes of this group.
Antibiotics are the most frequently prescribed drug group at the Urology Clinic in Niš, amounting to 263.54 DDD/100 BD (43.05 % of total drug consumption). Co-trimoxazole (204.35 DDD/100 BD), quinolones (29.81 DDD/100 BD) and aminoglycosides (18.88 DDD/100 BD) were prescribed most. In Novi Sad, antibiotic utilization amounted to 224.85 DDD/100 BD. Similarly, co-trimoxazole was most frequently prescribed (129.03 DDD/100 BD), followed by cephalosporins (43,54 DDD/100 BD) and aminoglycosides (20.5 DDD/100 BD).
In most instances, the chosen antibiotics for surgical prophylaxis were in accordance with the international guidelines. However, overuse was noted extending to the postoperative period. We believe that indications for the anti-microbial use still need a critical evaluation and that irrational use should be discouraged.

Key words: *Antibiotic utilization, surgical prophylaxis, anatomical therapeutic chemical classification, defined daily doses*

Introduction

Drug utilization studies can provide useful information for improvement of the appropriate and effective use of pharmaceuticals in populations. Many such studies have monitored antibiotic prescribing patterns in surgical practice.

Serious morbidity and mortality are associated with postoperative wound infections. They have an enormous impact on patients' quality of life and contribute substantially to the financial cost of patient care. The use of perioperative antibiotics has become an essential component of the standard of care in virtually all surgical procedures, and has resulted in a reduced risk of postoperative infection when sound and appropriate principles of prophylaxis are applied (1).

In order to measure drug use, it is important to have both a classification system and a unit of measurement. Such a classification system is the Anatomical Therapeutic Chemical (ATC) classification. To deal with the objections against the traditional units of measurement, a technical unit of measurement called the Defined Daily Dose (DDD) to be used in drug utilization studies was developed by the WHO (2,3). The average number of DDDs per bed-day (BD) is used in hospital studies. A 'bed-day' is defined as the number of patients in hospital or each ward per day and is calculated by multiplying the number of admissions by the average length of stay. This is a useful rate of expression for comparisons made between hospitals (4,5,6). Typically, the days of admission and discharge are counted as a single bed-day (7).

Scientific literature widely documents the current overuse of antibiotics but often does not address the issue of the judicious use of antibiotics. Multiple analyses of prescribing patterns consistently reveal inappropriate prescribing of antibiotics, even when the clinician is aware of the appropriate antibiotic use.

Aim

The purpose of our study was to analyze antibiotic prescribing trends among urologists for anti-microbial prophylaxis following urologic procedures; to do a quantitative analysis of overall drug, especially antibiotic, utilization at two university hospital urology clinics; and to evaluate whether sound principles of surgical prophylaxis are applied.

Materials and Methods

The study was carried out at the urology clinics of the Department of Surgery at the University Clinical Center in Niš, and the Institute of Surgery, University Teaching Hospital in Novi Sad, Serbia.

We carried out a prospective study during a two-month period based on the data obtained from case records on surgical patients who were admitted to the above-named clinics and who received antibiotics either for prophylaxis or treatment. Also, data was obtained from the surgical departments' pharmacies which supplied the above-mentioned clinics with necessary drugs, including antibiotics. The information obtained included drug names, strengths and quantity (e.g. number of tablets) dispensed. The drugs were recorded by trade names. Each drug was then given its chemical name and a code according to the ATC classification. This classification comprises 5 levels. The first level is the anatomical group (e.g. antiinfectives for systemic use), the second is the therapeutic group (antibiotics for systemic use), the third is a therapeutic subgroup (beta lactam antibiotics), the fourth gives the chemical form (broad-spectrum penicillins), and the fifth is a chemical subgroup (e.g. ampicillin). For the purpose of our study, all five levels were used.

Even though total drug consumption was calculated, a special attention was given to antibiotic utilization. Anti-microbial consumption was determined in terms of defined daily doses (DDDs) per 100 bed days (BD) for all antiinfectives for systemic use, i.e. group J of the ATC classification and for classes and subclasses of this group. This method allows drug utilization to be analyzed irrespective of the period the study is carried over.

DDDs were calculated according to the 2004 ATC classification, while data on BDs were obtained from the surgical department's administrative services.

The statistical analysis was performed using a Student's t-test for comparison of means and a Chi2 test to examine the association of qualitative variables.

Results and Discussion

Recent studies have shown large differences in the use of antibacterial agents among European countries (8). These differences warrant a closer analysis of antibiotic usage so as to identify the reasons for their overuse and find out measures that might rationalize this utilization (9). One could wonder how far drug consumption may vary across country or practice settings. Therefore, this study set out to analyze the consumption of medicines at two university hospital urology clinics in two Serbian cities with a special accent on antibiotic utilization.

The total drug consumption at the Urology Clinic in Niš amounts to 612.19 DDD/100 BD, where antiinfectives for systemic use (group J) constitute the most utilized group with 263.54 DDD/100 BD or 43.05% of overall drug utilization (Table 1), followed by drugs for blood and blood-forming organs (203.52 DDD/100 BD or 33.24%), central nervous system drugs (42.14 DDD/100 BD or 6.88%) and drugs for the alimentary tract and metabolism (38.86 DDD/100 BD or 6.35%).

Table 1. Total drug consumption according to the ATC classification at the Urology Clinic in Niš for the period 22.11.2004.- 31.12.2004.

ATC classification level	Main Group	DDD/ 100 BD	%
A	Alimentary tract and metabolism	38.86	6.35
B	Blood and blood forming organs	203.52	33.24
C	Cardiovascular system	23.20	3.79
D	Dermatologicals	0.38	0.06
H	Systemic hormonal preparations	14.31	2.34
J	Antiinfectives for systemic use	263.54	43.05
M	Musculo-skeletal system	19.59	3.20
N	Nervous system	42.14	6.88
R	Respiratory system	1.22	0.20
V	Various	5.43	0.89
Total		612.19	100.00

Bed Days (BD)=1840

In Novi Sad, the total drug utilization at the Urology Clinic amounts to 727.03 DDD/100 BD. The most utilized group were drugs for blood and blood-forming organs (318.34 DDD/100 BD or 43.79% of total drug consumption). Antiinfectives for systemic use were at second place (224.85 DDD/100 BD or 30.93%), followed by drugs for the alimentary tract and metabolism (72.01 DDD/100 BD or 9.9%), central nervous system drugs (51.58 DDD/100 BD or 7.09%), while utilization of other drug groups was negligible (Table 2).

Table 2. Total drug consumption according to the ATC classification at the Urology Clinic in Novi Sad for the period 08.10.04. - 17.11.04

ATC classification	Main Group	DDD/ 100 BD	%
A	Alimentary tract and metabolism	72.01	9.90
B	Blood and blood forming organs	318.34	43.79
C	Cardiovascular system	30.35	4.17
D	Dermatologicals	0.68	0.09
H	Systemic hormonal preparations	0.50	0.07
J	Antiinfectives for systemic use	224.85	30.93
M	Musculo-skeletal system	24.86	3.42
N	Nervous system	51.58	7.09
R	Respiratory system	3.86	0.53
Total		727.03	100.00

BD=1333

There was no statistically significant difference in total drug utilization between the urology clinics in Niš and Novi Sad ($p<0.05$). There was no significant difference in antibiotic utilization, either (Fig. 1).

Antiinfectives for systemic use were the most utilized drug group at the Urology Clinic in Niš, while they took second place in Novi Sad accounting for one-third

of the overall drug consumption. A qualitative and quantitative analysis of this utilization is shown in Tables 3-4, while Fig. 2 displays the most commonly prescribed antibiotics by our urologists.

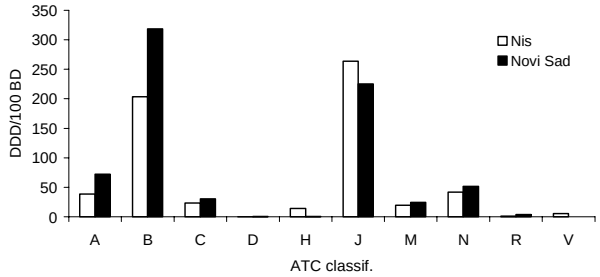

Fig. 1. Total drug consumption according to the ATC classification at the urology clinics in Niš and Novi Sad expressed in DDD/100 BD

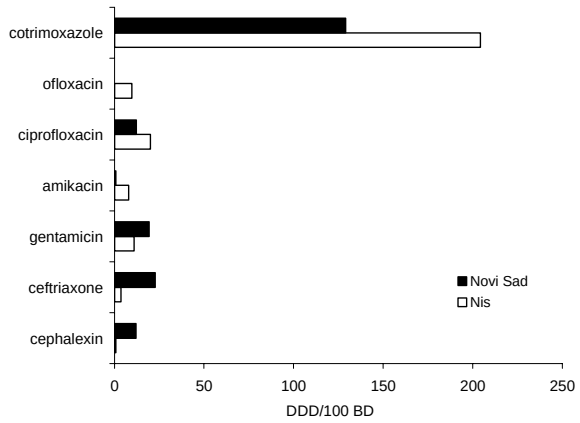

Fig. 2. The most commonly used antibiotics following urologic procedures in Niš and Novi Sad expressed in DDD/100 BD

Table 3. Consumption of drugs in group J (antiinfectives for systemic use) at the Urology Clinic in Niš for the period 22.11.2004.- 31.12.2004

J		DDD/100 BD	%
J01DA	cephalosporins	7.85	2.98
J01DH	carbapenems	0.42	0.16
J01EE	cotrimoxazole	204.35	77.54
J01FA	macrolides	0.42	0.16
J01FF	linkozamines	0.88	0.33
J01G	aminoglycosides	18.88	7.16
J01MA	quinolones	29.81	11.31
J01XD	imidazoles	0.89	0.34
J05	antivirals	0.07	0.03
Total		263.54	100.00

Cotrimoxazole was the most utilized antiinfective for systemic use at both clinics (subclass J01EE) with 204.35 DDD/100 BD or 77.54 % of total antibiotic consumption in Niš and 129.03 DDD/100 BD (57.39% of total anti-microbial utilization) in Novi Sad. This practice should be commended since it is in accordance with the guidelines based on the evidence obtained from clinical trials and cohort studies. According to the recommendations given by the American Society of Health-System Pharmacists (ASHP) and the guidelines from the Hospital Infection Control Practices Advisory Committee (HICPAC), if oral anti-microbials are used, a single dose of trimethoprim with sulfamethoxazole or lomefloxacin is recommended two hours before carrying out urology procedures (10).

Table 4. Consumption of drugs in group J (antiinfectives for systemic use) at the Urology Clinic in Novi Sad for the period 08.10.04. - 17.11.04.

J		DDD/100 BD	%
J01A	tetracyclines	5.25	2.34
J01CA	broad spectrum penicillins	6.53	2.91
J01CE	Beta-lactamase-sensitive penicillins	0.08	0.03
J01DA	cephalosporins	43.54	19.37
J01DH	carbapenems	1.86	0.83
J01EE	cotrimoxazole	129.03	57.39
J01FF	linkozamines	0.26	0.12
J01G	aminoglycosides	20.50	9.12
J01MA	quinolones	12.17	5.41
J01XD	imidazoles	4.80	2.14
	other	0.80	0.36
Total		224.85	100

Quinolones were at second place in Niš with 29.81 DDD/100 BD or 11.31%. Amongst the quinolones, ciprofloxacine was the most frequently prescribed drug (20.03 DDD/100 BD or 7.6%), while ofloxacin was prescribed half as much (9.78 DDD/100 BD or 3.71%). It is recommended that patients without demonstrated sterile urine, who have preoperative catheters in place, who are undergoing a transrectal prostatic biopsy, or who are undergoing surgeries involving prosthetic material receive antibiotics to prevent contamination with enteric gram-negative bacilli and enterococci. The choice of prophylaxis is ciprofloxacin. In cases of prostatectomy where the predominant infecting microorganisms are coliforms, ciprofloxacin or gentamicin are the recommended agents (10).

In Novi Sad, cephalosporines were at second place with 43.54 DDD/100 BD or 19.37%. Amongst the cephalosporins, ceftriaxone, a third-generation cephalosporin, was most frequently administered (22.66 DDD/100 BD). Ceftriaxone obviously has some theoretical advantages for prophylaxis over first and second generation cephalosporins, including stability against degradation by b-lactamase, broader spectrum coverage against gram-negative organisms, and extended serum half-life allowing once-daily administration (11,12). The second place among the cephalosporins belonged to cephalexin (11.93 DDD/100 BD), a first generation cephalosporin, followed by cefotaxime (7.08 DDD/100 BD). Other authors recommend cefazolin intravenously as acceptable prophylaxis in urologic surgery (13).

The third place, in both clinics, belonged to the aminoglycosides (Niš:18.88 DDD/100 BD or 7.16%; Novi Sad: 20.5 DDD/100 BD or 9.12%). Gentamicin was prescribed more frequently (Niš:10.94 DDD/100 BD; Novi Sad:19.34 DDD/100 BD) than amikacin (Niš:7.93 DDD/100 BD; Novi Sad:0.64 DDD/100 BD).

Other classes of antiinfectives were prescribed less frequently, such as cephalosporines in Niš (7.85 DDD/100 BD or 2.98%), imidazoles, linkozamines, carbapenems, macrolides and antivirals.

Many studies demonstrate that considering the low risk of serious infection after urologic surgery, anti-microbial prophylaxis should be considered only in patents at high risk of postoperative bacteriuria (patients who require prolonged catheterization and those with a positive urine culture) or in hospitals with high infection rates. Low-risk patients do not seem to benefit from the use of perioperative anti-microbials (10, 14).

We are pleased to notice that our urologists' prescribing habits are in accordance with the above stated guidelines, however, we must criticize the prolongation of antibiotic administration in the postoperative period, which contributed to high drug utilization and, consequently, added to the rising cost of patient care. To illustrate this, if we take a look at quinolone use, these drugs constituted 6% of the total antibiotic administration in the University Hospital in Nijmegen, the Netherlands (3). When this is compared to the 11.31% at the Urology Clinic in Niš, this warrants measures to rationalize the prescription of these drugs.

The overuse of antibiotics at the two clinics can also be attributed to prolonged administration extending the 24-hour period in cases where treatment was not indicated, i.e. continuation of anti-microbial prophylaxis postoperatively is not recommended (10).

Conclusion

Since guidelines, formulary or an antibiotic policy did not exist at the urology clinics of the departments of surgery, the surgeons' prescribing habit was the main factor that directly influenced prescribing, while the overall antibiotic utilization was influenced by the availability of an agent through purchasing, dispensing, procurements, pricing, etc.

Even though in most cases the antibiotic choice was in accordance with the guidelines of leading medical centers and the results of various studies, there was still unwarranted overuse of prophylactic agents with increased costs to the hospital. Various methods should be developed to help curb undesirable antibiotic prescription. This can be accomplished by the development of guidelines for anti-microbial prophylaxis followed by lectures to medical and nursing staff. Also, a useful measure could be the introduction of an antibiotic policy due to rising costs and inappropriate use of anti-microbial drugs.

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ANALIZA UPOTREBE ANTIMIKROBNIH LEKOVA PRIMENOM ATC/DDD METODOLOGIJE NA DVE UNIVERZITETSKE HIRURŠKE KLINIKE

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Kratak sadržaj: *Farmakoterapijska praksa se formira pod uticajem faktora koji deluju na stvaranje propisivačkih navika pojedinih lekara. Poznavanje farmakoterapijske tradicije na nekom području omogućava sprovodjenje edukativnih programa racionalne farmakoterapije.*
Cilj našeg rada je bio da analiziramo i uporedimo upotrebu lekova, posebno antibiotika, na klinikama za urologiju u Nišu i Novom Sadu kako bi procenili da li su sprovedeni principi hirurške profilakse bili u sladu sa medjunarodnim smernicama.
U ovom radu ispitivanje je izvršeno na odeljenjima za urologiju hirurških klinika u Nišu i Novom Sadu. U analizi upotrebe antiinfektivnih lekova za sistemsku primenu, i svih lekova uopšte, korišćena je jedinica mere definisana dnevna doza (DDD) na 100 bolesničkih dana (BD). Lekovi su razvrstani po Anatomsko-Terapijsko-Hemijskoj (ATC) klasifikaciji.
Antibiotici (grupa J po ATC klasifikaciji) su predstavljali najzastupljeniju grupu u ukupnoj upotrebi u Nišu sa 263,54 DDD/100 BD (43,05% od ukupne upotrebe). Kotrimoksazol (204,35 DDD), hinoloni (29,81 DDD) i aminoglikozidi (18,88 DDD) su bili najviše propisivane grupe antibiotika. U Novom Sadu, upotreba antiinfektivnih lekova iznosila je 224,85 DDD/100 BD. Slično situaciji u Nišu, i ovde je kotrimoksazol najčešće propisivan (129,03 DDD), zatim cefalosporini (43,54 DDD) i aminoglikozidi (20,5 DDD).
U najvećem broju slučajeva izbor antibiotika za hiruršku profilaksu bio je u skladu sa medjunarodnim smernicama. Medjutim, primećena je prekomerna upotreba antibiotika s obzirom na ordiniranje istih u postoperativnom periodu bez jasnih dokaza o infekciji. Smatramo da treba postaviti jasne indikacije za primenu antibiotika u hirurškoj profilaksi kako bi se u daljem toku izbegla svaka neracionalna upotreba.

Ključne reči: *Anatomsko-Terapijsko-Hemijska klasifikacija, definisane dnevne doze, hirurška profilaksa, antibiotici*