

ANTIBIOTSKA PROFILAKSA U ABDOMINALNOJ HIRURGIJI - USAGLAŠENOST PREPORUKA I PRAKSE

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ANTIBIOTIC PROPHYLAXIS IN ABDOMINAL SURGERY – COMPLIANCE WITH INTERNATIONAL GUIDELINES

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SAŽETAK

Uvod: Antibiotiska profilaksa (AP) u hirurgiji predstavlja značajnu meru za smanjenje incidencije nastanka infekcija operativnog mesta. Međunarodne smernice i Nacionalni vodič daju jasne preporuke za pravilno sprovođenje antibiotiske profilakse, međutim podaci u literaturi ukazuju na nedovoljno poštovanje ovih smernica u mnogim zdravstvenim ustanovama.

Cilj: Cilj naše studije je bio da se ispita stepen usaglašenosti prakse u primeni antibiotiske profilakse u abdominalnoj hirurgiji sa međunarodnim i nacionalnim smernicama.

Materijali i metode: Retrospektivnom studijom su obuhvaćeni svi bolesnici operisani na Klinici za digestivnu hirurgiju Univerzitetskog kliničkog centra Srbije (UKCS), u periodu januar – mart 2019. godine (270 pacijenata). Iz medicinske dokumentacije dobijeni su podaci koji se odnose na vrstu operacije, primenjenu antibiotisku profilaksu, vreme primene prve doze, način primene, potrebu za redoziranjem, kao i na dužinu primene profilakse i postojanje alergije na lekove. Prikupljeni podaci su analizirani metodama deskriptivne i analitičke statistike (χ^2 test).

Rezultati: Tokom perioda ispitivanja, na Klinici za digestivnu hirurgiju je operisano 270 bolesnika, od kojih je antibiotisku profilaksu primilo 227 (84,1%) bolesnika. Cefazolin, koji je preporučen za većinu operacija u digestivnoj hirurgiji, primilo je 17 (6,3%) bolesnika. Najveći broj bolesnika (64,4%) je profilaksu primilo unutar 30 minuta po započinjanju operacije. Trajanje profilakse do 24 sata od operacije sprovedeno je kod 13,1% operisanih bolesnika.

Zaključak: Usaglašenost kliničke prakse sa preporukama iz vodiča za antibiotisku profilaksu u abdominalnoj hirurgiji je bila na niskom nivou. Potpuna usaglašenost sa preporukama za primenu antibiotiske profilakse je zabeležena samo po pitanju puta primene antibiotika.

Ključne reči: antibiotiska profilaksa, abdominalna hirurgija, infekcija hirurškog mesta

ABSTRACT

Introduction. Antibiotic prophylaxis (AP) in surgery is an important measure that contributes to the prevention of surgical site infection. International and national guidelines provide clear recommendations for the proper implementation of antibiotic prophylaxis. However, many studies indicate poor compliance in many health care centers.

Aim: Our study aimed to determine the level of compliance in the application of antibiotic prophylaxis in abdominal surgery with the guidelines.

Materials and methods: The retrospective study included all patients which were operated on at the Clinic for Digestive Surgery of the University Clinical Center of Serbia (UCCS), during the period January - March 2019 (270 patients). Medical records provided information about the type of surgery, the choice of antibiotic, the time of application, the route of administration, the need for redosing, the duration of antibiotic prophylaxis administration, as well as the presence of drug allergies. The collected data were analyzed by descriptive and analytical statistics (χ^2 test).

Results: During the study period, 270 patients were operated on at the Clinic for Digestive Surgery, of whom 227 (84.1%) received antibiotic prophylaxis. Cefazolin, an antibiotic recommended for most abdominal surgeries, was administered to only 17 (6.3%) patients. The majority of patients (64.4%) received antibiotic prophylaxis within 30 minutes of the beginning of surgery. The duration of antibiotic prophylaxis of up to 24 hours after the operation was applied in 13.1% of patients.

Conclusion: Compliance with the guidelines was low, while full compliance with the recommendations for antibiotic prophylaxis was achieved only with regards to the route of antibiotic administration.

Keywords: antibiotic prophylaxis, abdominal surgery, surgical site infection

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UVOD

Antibiotska profilaksa (AP) u hirurgiji predstavlja efikasan metod za prevenciju i smanjenje rizika od nastanka infekcija operativnog mesta. Prema podacima Centra za kontrolu i prevenciju bolesti u Atlanti (engl. *Centers for Disease Control and Prevention - CDC*), infekcije operativnog mesta se smatraju važnim globalnim problemom [1]. Infekcije operativnog mesta su povezane sa dužim trajanjem lečenja, potrebom za dodatnim hirurškim procedurama, i većom stopom mortaliteta [2]. Međunarodne smernice i Nacionalni vodič kliničke prakse daju jasne preporuke za pravilno sprovođenje antibiotske profilakse u hirurgiji [3,4]. Međutim, podaci u literaturi ukazuju na nedovoljno poštovanje ovih smernica u mnogim zdravstvenim ustanovama [5,6]. Neracionalna i neadekvatna upotreba antibiotika predstavlja jedan od glavnih pokretača razvoja rezistencije bakterija, a može biti udružena sa pojavom brojnih neželjenih efekata antibiotika i povećanim ukupnim troškovima lečenja [1,2].

Izbor antibiotika najviše zavisi od područja na kome se izvodi hirurški zahvat, ali na osnovu najvećeg broja preporuka iz međunarodnih smernica i vodiča kliničke prakse, cefalosporini prve generacije (cefazolin) su lekovi prvog izbora u prevenciji infekcija operativnog mesta u abdominalnoj hirurgiji. Preporučuje se intravenska primena antibiotika. Za većinu antibiotika u hirurškoj antibiotskoj profilaksi, adekvatnim se smatra primena antibiotika unutar 60 minuta pre početka operacije [3]. Uvek treba razmotriti davanje još jedne doze antibiotika kod procedura koje su trajale duže od dva poluvremena eliminacije leka, kao i u slučaju gubitka više od 1.500 ml krvi. Kod pacijenata sa dokazanom alergijom na penicilin, treba izbegavati davanje beta-laktamskih antibiotika, i u tom slučaju se koristi alternativni antibiotik naveden u smernicama. Smatra se da je jedna doza antibiotika dovoljna za efikasnu antibiotsku profilaksu kod najvećeg broja hirurških zahvata, te da je treba završiti unutar 24 sata [3,4].

Cilj naše studije je bio da se ispita stepen usaglašenosti prakse u primeni antibiotske profilakse u abdominalnoj hirurgiji sa međunarodnim smernicama i preporukama Nacionalnog vodiča.

MATERIJALI I METODE

Retrospektivna studija načina primene antibiotske profilakse u abdominalnoj hirurgiji je obuhvatila 270 bolesnika operisanih na Klinici za digestivnu hirurgiju Univerzitetskog kliničkog centra Srbije (UKCS), u periodu januar - mart 2019. godine. Pacijenti podvrgnuti hitnoj operaciji, oni sa prethodno dokazanom infekcijom kod kojih je antibiotska terapija u toku, i pacijenti

INTRODUCTION

Antibiotic prophylaxis (AP) in surgery is an efficient method for preventing and reducing the risk of surgical site infection. According to the Centers for Disease Control and Prevention (CDC), surgical site infections are considered an important global problem [1]. They are connected with a longer duration of treatment, the need for additional surgical procedures, and a higher mortality rate [2]. International guidelines and the Serbian National Good Clinical Practice Guideline provide clear recommendations for the proper implementation of antibiotic prophylaxis in surgery [3,4]. However, data from literature indicate insufficient compliance with these guidelines, in many healthcare institutions [5,6]. Irrational and inadequate use of antibiotics represents one of the main drivers of bacterial resistance development and may be accompanied by the occurrence of many adverse effects of antibiotics and increased overall treatment costs [1,2].

The choice of the antibiotic mostly depends on the region of the body where the surgical procedure is performed. However, based on the majority of recommendations from international guidelines and clinical practice guides, first generation cephalosporins (cefazolin) are the medicaments of first choice in the prevention of surgical site infections in abdominal surgery. Intravenous administration of antibiotics is recommended. For most antibiotics in surgical antibiotic prophylaxis, the application of antibiotics within 60 minutes of the beginning of the surgical procedure is considered appropriate [3]. Administering one more dose of the antibiotic should always be considered in procedures lasting longer than two drug elimination half-lives, as well as in cases where there was more than 1,500 ml of blood loss. In patients with proven penicillin allergy, administration of beta-lactam antibiotics should be avoided. In such cases, the alternative antibiotic proposed in the guidelines should be administered. It is believed that a single dose of antibiotic is sufficient for effective antibiotic prophylaxis in most surgical procedures and that it should be completed within 24 hours [3,4].

The aim of our study was to investigate the level of compliance of antibiotic prophylaxis application in abdominal surgery with international guidelines and the recommendations from the National Guide.

MATERIALS AND METHODS

This retrospective study of the method of antibiotic prophylaxis application in abdominal surgery included 270 patients, who were surgically treated at the Clinic for Digestive Surgery of the University Clinical Center of Serbia (UCCS), in the period January – March 2019. Patients undergoing emergency surgery, those with a previously

podvrgnuti invazivnim dijagnostičkim procedurama bili su isključeni iz ispitivanja (56 bolesnika). Podaci o primenjenoj antibiotskoj profilaksi, vrsti antibiotika, načinu primene, vremenu davanja prve doze, potrebi za redoziranjem, dužini primene antibiotika i postojanju alergije na lekove, dobijeni su iz medicinske dokumentacije (liste anestezije i terapijske liste).

Podaci su analizirani metodama deskriptivne i analitičke statistike. U zavisnosti od vrste obeležja posmatranja, podaci su prikazani kao medijana (interkvartilni opseg) ili broj (procenat). Usaglašenost dobijenih rezultata sa preporukama je ispitana u odnosu na Nacionalni vodič dobre kliničke prakse – Racionalna upotreba antibiotika i Vodič za antimikrobnu profilaksu u hirurgiji Američkog udruženja bolničkih farmaceuta (engl. *ASHP Therapeutic Guidelines on Antimicrobial Prophylaxis in Surgery; American Society of Health-System Pharmacists - AHSP*) (Tabela 1).

U kreiranju baze i obradi podataka korišćen je softver *IBM SPSS Statistics for Windows, Version 22.0* (IBM Corp., Armonk, NY).

proven infection who had already been on antibiotic therapy, as well as patients undergoing invasive diagnostic procedures were excluded from the study (56 patients). Data on applied antibiotic prophylaxis, the type of antibiotic, the mode of administration, the time of administration of the first dose, the need for redosing, the length of antibiotic application, and the presence of drug allergies, were obtained from medical records (anesthesia records and hospital medication charts).

The data were analyzed using the methods of descriptive and analytical statistics. Depending on the type of marker being observed, the data have been presented as the median (interquartile range) or number (percentage). The compliance of the obtained results with the recommendations was tested in relation to the Serbian National Good Clinical Practice Guideline for Rational Antibiotic Use and the ASHP Therapeutic Guidelines on Antimicrobial Prophylaxis in Surgery of the American Society of Health-System Pharmacists (AHSP) (Table 1).

In creating the database and in data processing, the software – IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY), was used.

Tabela 1. Preporuke za antibiotsku profilaksu u abdominalnoj hirurgiji odraslih [3, 4]

Tip procedure	Preporučeni antibiotik	Alternativa	Put primene	Redoziranje	Trajanje profilakse
Ezofagektomija	Cefazolin 2 - 3 g, i.v.; ampicilin/sulbaktam 3 g, i.v.	Klindamicin 900 mg, i.v.; vankomicin 15 mg/kg	i.v.	Kod operacija dužeg trajanja: nakon 4 h za cefazolin, nakon 2 h za ampicilin/sulbaktam; nakon 6 h za klindamicin	1 doza ili završiti unutar 24 h
Operacija sa ulaskom u lumen GIT-a	Cefazolin 2 - 3 g, i.v.; ampicilin/sulbaktam 3 g, i.v.	Klindamicin 900 mg, i.v.; vankomicin 15 mg/kg + aminoglikozid ili hinolon	i.v.	Kod operacija dužeg trajanja: nakon 4 h za cefazolin, nakon 2 h za ampicilin/sulbaktam; nakon 6 h za klindamicin	1 doza ili završiti unutar 24 h
Operacija bez ulaska u lumen GIT	Cefazolin 2 - 3 g, i.v.	Klindamicin 900 mg, i.v.; vankomicin 15 mg/kg + aminoglikozid ili hinolon	i.v.	Kod operacija dužeg trajanja: nakon 4 h za cefazolin, nakon 2 h za ampicilin/sulbaktam; nakon 6 h za klindamicin	1 doza ili završiti unutar 24 h
Elektivna laparoskopija niskog rizika	-	-	-	-	-
Elektivna laparoskopija visokog rizika	Cefazolin 2 - 3 g, i.v.; ampicilin/sulbaktam 3 g, i.v.; ceftriakson 2 g, i.v.	Klindamicin 900 mg, i.v.; vankomicin 15 mg/kg + aminoglikozid ili hinolon ili metronidazol 500 mg + aminoglikozid	i.v.	Kod operacija dužeg trajanja: nakon 4 h za cefazolin, nakon 2 h za ampicilin/sulbaktam; nakon 6 h za klindamicin *	1 doza ili završiti unutar 24 h
Operacija hernije	Cefazolin 2 - 3 g i.v.	Klindamicin 900 mg, i.v.; vankomicin 15 mg/kg	i.v.	Kod operacija dužeg trajanja: nakon 4 h za cefazolin; nakon 6 h za klindamicin	1 doza ili završiti unutar 24 h
Kolorektalna operacija	Cefazolin 2 - 3 g + metronidazol 1g ili ampicilin/sulbaktam 3 g ili ceftriakson 2 g + metronidazol 1 g, ili ertapenem 1 g	Klindamicin 900 mg + aminoglikozid ili metronidazol + aminoglikozid ili hinolon	i.v.	Kod operacija dužeg trajanja: nakon 4 h za cefazolin, nakon 2 h za ampicilin/sulbaktam; nakon 6 h za klindamicin **	1 doza ili završiti unutar 24 h

* Redoziranje nije potrebno za većinu operacija za ceftriakson, metronidazol, vankomicin, aminoglikozid i hinolone.

** Ertapenem nije potrebno redozirati.

Table 1. Recommendations for antibiotic prophylaxis in abdominal surgery in adults [3, 4]

Type of procedure	Recommended antibiotic(s)	Alternative antibiotic(s)	Route of administration	Redosing	Duration of prophylaxis
Esophagectomy	Cefazolin 2 - 3 g, IV; ampicillin/sulbactam 3 g, IV	Clindamycin 900 mg, IV; vancomycin 15 mg/kg, IV	IV	In prolonged surgery: after 4 hours for cefazoline; after 2 hours for ampicillin/sulbactam; after 6 hours for clindamycin	1 dose or to be completed within 24 hours
Surgery with GIT involvement	Cefazolin 2 - 3 g, IV; ampicillin/sulbactam 3 g, IV	Clindamycin 900 mg, IV; vancomycin 15 mg/kg + aminoglycoside or a quinolone	IV	In prolonged surgery: after 4 hours for cefazoline; after 2 hours for ampicillin/sulbactam; after 6 hours for clindamycin	1 dose or to be completed within 24 hours
Surgery without GIT involvement	Cefazolin 2 - 3 g, IV	Clindamycin 900 mg, IV; vancomycin 15 mg/kg + aminoglycoside or a quinolone	IV	In prolonged surgery: after 4 hours for cefazoline; after 2 hours for ampicillin/sulbactam; after 6 hours for clindamycin	1 dose or to be completed within 24 hours
Low-risk elective laparoscopic cholecystectomy	-	-	-	-	-
High-risk elective laparoscopic cholecystectomy	Cefazolin 2 - 3 g, IV; ampicillin/sulbactam 3 g, IV; ceftriaxone 2 g, IV	Clindamycin 900 mg, IV; vancomycin 15 mg/kg + aminoglycoside or a quinolone or metronidazole 500 mg + aminoglycoside	IV	In prolonged surgery: after 4 hours for cefazoline, after 2 hours for ampicillin/sulbactam; after 6 hours for clindamycin*	1 dose or to be completed within 24 hours
Hernia repair	Cefazolin 2 - 3 g, IV	Clindamycin 900 mg, IV; vancomycin 15 mg/kg, IV	IV	In prolonged surgery: after 4 hours for cefazoline; after 6 hours for clindamycin	1 dose or to be completed within 24 hours
Colorectal surgery	Cefazolin 2 - 3 g + metronidazole 1 g or ampicillin/sulbactam 3 g or ceftriaxone 2 g + metronidazole 1 g or ertapenem 1 g	Clindamycin 900 mg + aminoglycoside or metronidazole + aminoglycoside or quinolone	IV	In prolonged surgery: after 4 hours for cefazoline; after 2 hours for ampicillin/sulbactam; after 6 hours for clindamycin**	1 dose or to be completed within 24 hours

* Redosing not required for a majority of the surgical procedures for ceftriaxone, metronidazole, vancomycin, aminoglycoside, and quinolones

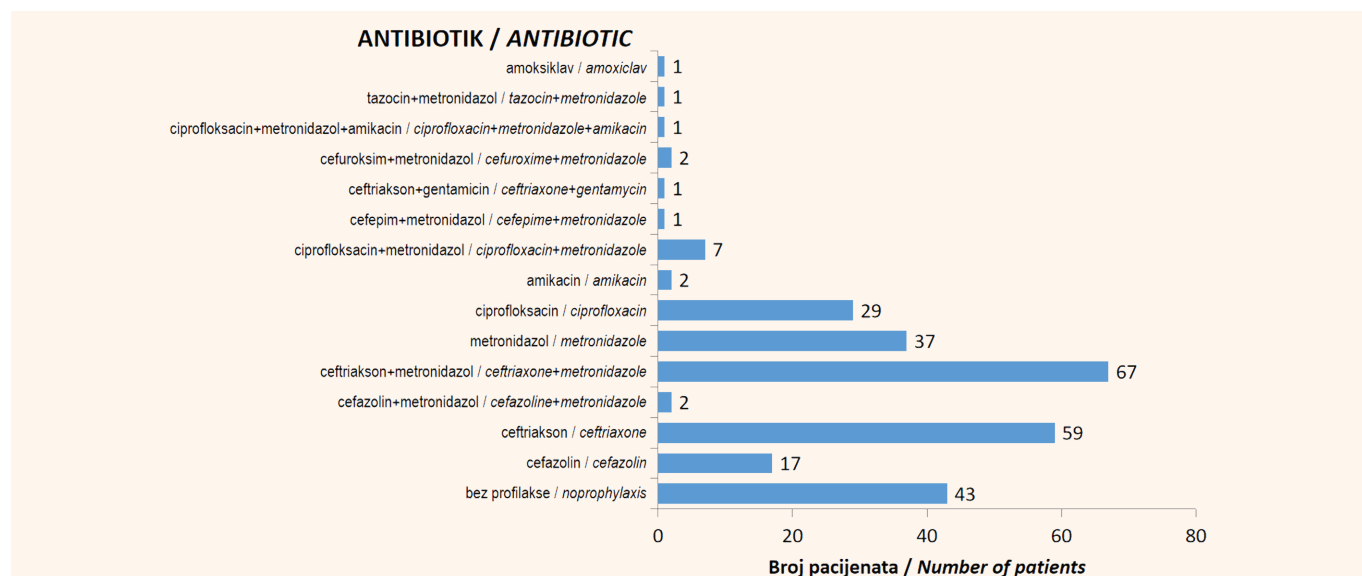
** Redosing not required for ertapenem

REZULTATI

U toku perioda ispitivanja, na Klinici za digestivnu hirurgiju je operisano 270 bolesnika, čije su operacije grupisane u 13 grupa, a koje su bile prosečnog trajanja od 100 (60 – 160) minuta. Antibiotiku profilaksu je primilo 227 (84,1%) bolesnika. Vrsta primenjene antibiotiske profilakse (lekovi i njihove kombinacije) prikazani su u **Grafikonu 1**. Cefazolin, antibiotik preporučen za većinu operacija u digestivnoj hirurgiji, primilo je 17 (6,3%) bolesnika. Svi bolesnici su antibiotiku profilaksu primili intravenskim putem. Od bolesnika koji su primili profilaksu, 24 (8,9%) pacijenta je primilo antibiotik više od jedan sat pre operacije, 8 (3%) bolesnika ju je primilo unutar 60 minuta pre početka operacije, 19 (7%) pacijenata je primilo antibiotiku profilaksu nakon više od 30 minuta od početka operacije, dok je većina, 174 (64,4%) bolesnika, antibiotik primila unutar 30 minuta po započinjanju operacije. Potreba za redoziranjem antibiotika zbog trajanja operacije ili masivnog krvarenja postojala je kod 27 (10%) bolesnika. Među njima, antibiotik je redoziran kod 5 (18,5%) bolesnika. Primena antibiotika u profilaktičke svrhe završena je unutar 24 sata kod 30 (13,1%) bolesnika. Podatak o alergiji

RESULTS

Within the study period, at the Clinic for Digestive Surgery, 270 patients were surgically treated; their operations were grouped into 13 groups; the average duration of the operations was 100 (60 – 160) minutes. In total, 227 (84.1%) patients received antibiotic prophylaxis. The type of administered antibiotic prophylaxis (the drugs and their combinations) are presented in **Graph 1**. Cefazolin, the antibiotic recommended for most surgical procedures in digestive surgery, was administered to 17 (6.3%) patients. All of the patients received AP intravenously. Of the patients who received AP, 24 (8.9%) patients were given the antibiotic more than an hour prior to surgery, 8 (3%) patients got their AP in the space of 60 minutes prior to the beginning of the operation, 19 (7%) patients received AP more than 30 minutes after the start of the surgical procedure, while most of the patients, i.e., 174 (64.4%) of them, were given the antibiotic within 30 minutes of the beginning of the operation. The need for antibiotic redosing due to the duration of the surgical procedure or because of massive bleeding arose in 27 (10%) patients. Amongst them, the antibiotic was redosed



Grafikon 1. Distribucija vrsta antibiotika primenjenih za antimikrobnu profilaksu

Figure 1. Distribution of drugs administered for antibiotic prophylaxis

Tabela 2. Usaglašenost prakse u primeni antibiotiske profilakse sa smernicama, prema vrsti hirurgije

Vrsta operacije	Trajanje operacije (min); medijana [IKO**]	Antibiotik dat; n/N* (%)	Vrsta antibiotika; n/N (%)	Put primene; n/N (%)	Vreme davanja leka; n/N (%)	Lek redoziran ukoliko je potrebno; n/N(%)	Trajanje profilakse; n/N (%)
Hernioplastika	85 [70 – 110]	36/52 (69.2%)	2/52 (3.8%)	36/36 (100.0%)	2/52 (3.8%)	-	6/36 (16.6%)
Laparoskopska holecistektomija	80 [70 – 110]	41/47 (87.2%)	10/47 (21.3%)	41/41 (100.0%)	2/47 (4.3%)	-	1/41 (2.4%)
Ezofagektomija	460 [430 – 535]	4/4 (100.0%)	0/4 (0.0%)	4/4 (100.0%)	0/4 (0.0%)	2/4 (50.0%)	0/4 (0.0%)
Laparoskopska antirefluks operacija	145 [120 – 160]	6/8 (75.0%)	0/9 (0.0%)	6/6 (100.0%)	0/8 (0.0%)	-	1/6 (16.6%)
Gastrektomija	240 [190 – 320]	11/12 (91.7%)	2/12 (16.7%)	11/11 (100.0%)	0/12 (0.0%)	0/5 (0.0%)	1/11 (9.1%)
Hepatobilijarna hirurgija	180 [120 – 345]	23/24 (95.8%)	1/24 (4.2%)	24/24 (100.0%)	1/24 (4.2%)	0/10 (4.2%)	0/23 (0.0%)
Resekcija pankreasa	220 [140 – 410]	6/7 (85.7%)	1/7 (14.3%)	6/6 (100.0%)	1/7 (14.3%)	2/3 (28.6%)	1/6 (16.6%)
Kolorektalna hirurgija	120 [80 – 180]	47/53 (88.7%)	35/53 (66.0%)	47/47 (100.0%)	2/53 (3.8%)	0/2 (3.8%)	18/47 (38.3%)
Proktološka intervencija	30 [30 – 45]	23/26 (88.5%)	0/23 (0.0%)	23/23 (100.0%)	0/26 (0.0%)	-	0/23 (0.0%)
Operacija tankog creva	120 [50 – 165]	4/5 (80.0%)	0/4 (0.0%)	4/4 (100.0%)	0/5 (0.0%)	-	1/4 (25.0%)
Multiorganska resekcija	220 [120 – 360]	3/3 (100.0%)	2/3 (66.6%)	3/3 (100.0%)	0/3 (0.0%)	1/1 (100.0%)	0/3 (0.0%)
Splenektomija	160 [160 – 160]	3/3 (100.0%)	1/3 (33.3%)	3/3 (100.0%)	0/3 (0.0%)	-	0/3 (0.0%)
Ostale operacije	85 [50 – 120]	21/26 (80.8%)	7/26 (26.9%)	21/21 (100.0%)	0/21 (0.0%)	0/2 (0.0%)	0/21 (0.0%)
Ukupno	100 [60 – 160]	227/270 (84.1%)	61/270 (22.6%)	227/227 (100.0%)	8/270 (3.0%)	5/27 (18.5%)	30/227 (13.1%)

Izvor preporuka: reference 3 i 4

n – Broj bolesnika koji je profilaksu dobio u skladu sa preporukama; N – Broj bolesnika koji je dobio profilaksu; IQR – Interkvartilni opseg;

Table 2. Compliance of clinical practice of antibiotic prophylaxis with recommendations according to the type of abdominal surgery

Type of the operation	Operation length (min); Median [IQR]	Antibiotic administered; n/N (%)	Type of antibiotic; n/N (%)	Route of administration; n/N (%)	Timing of drug administration; n/N (%)	Drug re-dosed if necessary; n/N (%)	Duration of prophylaxis; n/N (%)
Hernioplasty	85 [70 – 110]	36/52 (69.2%)	2/52 (3.8%)	36/36 (100.0%)	2/52 (3.8%)	-	6/36 (16.6%)
Laparoscopic cholecystectomy	80 [70 – 110]	41/47 (87.2%)	10/47 (21.3%)	41/41 (100.0%)	2/47 (4.3%)	-	1/41 (2.4%)
Esophagectomy	460 [430 – 535]	4/4 (100.0%)	0/4 (0.0%)	4/4 (100.0%)	0/4 (0.0%)	2/4 (50.0%)	0/4 (0.0%)
Antireflux surgery	145 [120 – 160]	6/8 (75.0%)	0/9 (0.0%)	6/6 (100.0%)	0/8 (0.0%)	-	1/6 (16.6%)
Gastrectomy	240 [190 – 320]	11/12 (91.7%)	2/12 (16.7%)	11/11 (100.0%)	0/12 (0.0%)	0/5 (0.0%)	1/11 (9.1%)
Hepatobiliary surgery	180 [120 – 345]	23/24 (95.8%)	1/24 (4.2%)	24/24 (100.0%)	1/24 (4.2%)	0/10 (4.2%)	0/23 (0.0%)
Pancreas resection	220 [140 – 410]	6/7 (85.7%)	1/7 (14.3%)	6/6 (100.0%)	1/7 (14.3%)	2/3 (28.6%)	1/6 (16.6%)
Colorectal surgery	120 [80 – 180]	47/53 (88.7%)	35/53 (66.0%)	47/47 (100.0%)	2/53 (3.8%)	0/2 (3.8%)	18/47 (38.3%)
Proctological procedures	30 [30 – 45]	23/26 (88.5%)	0/23 (0.0%)	23/23 (100.0%)	0/26 (0.0%)	-	0/23 (0.0%)
Small intestine surgery	120 [50 – 165]	4/5 (80.0%)	0/4 (0.0%)	4/4 (100.0%)	0/5 (0.0%)	-	1/4 (25.0%)
Multiorgan resection	220 [120 – 360]	3/3 (100.0%)	2/3 (66.6%)	3/3 (100.0%)	0/3 (0.0%)	1/1 (100.0%)	0/3 (0.0%)
Splenectomy	160 [160 – 160]	3/3 (100.0%)	1/3 (33.3%)	3/3 (100.0%)	0/3 (0.0%)	-	0/3 (0.0%)
Other surgical procedures	85 [50 – 120]	21/26 (80.8%)	7/26 (26.9%)	21/21 (100.0%)	0/21 (0.0%)	0/2 (0.0%)	0/21 (0.0%)
Total	100 [60 – 160]	227/270 (84.1%)	61/270 (22.6%)	227/227 (100.0%)	8/270 (3.0%)	5/27 (18.5%)	30/227 (13.1%)

Source of recommendations: references 3 and 4

n – Number of patients in whom prophylaxis was administered according to guidelines; N – Number of patients who were given prophylaxis; IQR – Interquartile range

na penicilin dalo je 20 (7,4%) bolesnika, od kojih je 6 (30%) pacijenata primilo beta-laktamski antibiotik kao profilaksu. Bolesnici bez prijavljene alergije na penicilin su statistički značajno češće dobijali cefalosporine kao profilaksu (145 (58%) naspram 6 (30%); $\chi^2 = 5,89$; $p = 0,019$). Usaglašenost prakse u primeni antibiotske profilakse sa smernicama, prema vrstama hirurgije, prikazana je u **Tabeli 2**. Način primene antibiotske profilakse je prikazan u **Tabeli 3**.

DISKUSIJA

Rezultati ove studije ukazuju na veoma nisku usaglašenost kliničke prakse sa Nacionalnim vodičem i međunarodnim smernicama, u tercijarnoj ustanovi koja se bavi abdominalnom hirurgijom. AP je primenjena kod 84,1% bolesnika u našoj studiji, što potvrđuje procene da je profilaktička primena zastupljena sa 30 – 50%, u ukupnoj potrošnji antibiotika u bolničkim uslovima

in (18.5%) patients. The application of antibiotic prophylaxis was completed within 24 hours in 30 (13.1%) patients. In total, 20 (74%) patients declared an allergy to penicillin, of whom 6 (30%) patients received a beta-lactam antibiotic as prophylaxis. Patients without a reported allergy to penicillin statistically more significantly received cephalosporins as prophylaxis (145 (58%) versus 6 (30%); $\chi^2 = 5.89$; $p = 0.019$). The compliance of clinical practice in the application of antibiotic prophylaxis with the guidelines, by type of surgery, is presented in **Table 2**. The method of administering antibiotic prophylaxis is presented in **Table 3**.

DISCUSSION

The results of this study indicate a very low level of compliance of clinical practice with the National Guide and international guidelines, in the tertiary health institution involved in abdominal surgery observed in the study.

Tabela 3. Karakteristike bolesnika i operacija i način primene antibiotske profilakse**Table 3.** Characteristics of patients and surgeries and the pattern of antibiotic prophylaxis

Varijabla / Variable	
Vrsta hirurgije / Type of surgery	
Hernioplastika / Hernioplasty	52 (19.3%)
Laparoskopska holecistektomija / Laparoscopic cholecystectomy	47 (17.5%)
Ezofagektomija / Esophagectomy	4 (1.5%)
Laparoskopska antirefluks operacija / Laparoscopic anti-reflux surgery	8 (3.0%)
Gastrektomija / Gastrectomy	12 (4.4%)
Hepatobilijarna hirurgija / Hepatobiliary surgery	24 (8.9%)
Pankreasna hirurgija / Pancreatic resection	7 (2.6%)
Kolorektalna hirurgija / Colorectal surgery	53 (19.6%)
Proktološka intervencija / Proctological surgery	26 (9.6%)
Operacija tankog creva / Small intestine surgery	5 (1.8%)
Multiorganska resekcija / Multiorgan resection	3 (1.1%)
Splenektomija / Splenectomy	3 (1.1%)
Ostalo / Other	26 (9.6%)
Trajanje operacije (min) / Length of surgery (min)	
100 [60 – 160]	
Alergije / Allergies	
Beta-laktamski antibiotik / Beta-lactam antibiotic	20 (7.4%)
Ostalo / Other	16 (5.9%)
Profilaksa primenjena / Prophylaxis administered	
227 (84.1%)	
Vreme primene profilakse / Timing of prophylaxis	
Više od 1 h pre operacije / More than 1 h before the beginning of surgery	24 (8.9%)
Unutar 1 h pre početka operacije / Within 1 h before the beginning of surgery	8 (3.0%)
Unutar 30 min od početka operacije / Within 30 min after the beginning of surgery	174 (64.4%)
Nakon 30 min od početka operacije / 30 min after the beginning of surgery	19 (7.0%)
Intravenski put primene antibiotika / Intravenous route of administration	
227 (100.0%)	
Potreba za redoziranjem / Redosing required	
27 (10.0%)	
Dužina profilakse (dani) / Duration of prophylaxis (days)	
4 [2 – 6]	

Podaci su prikazani kao broj (procenat) i kao medijana [interkvartilni opseg]

Data are presented as number (percentage) and median [interquartile range]

[7]. Podaci iz literature ukazuju da je obuhvat hirurških bolesnika antibiotskom profilaksom u većini razvijenih zemalja visok i iznosi preko 95% [8].

U našoj studiji, antibiotik kao profilaksa je najmanje primenjivan u grupi bolesnika podvrgnutih operaciji hernije (69,2%). Elektivna operacija preponske kile je tipičan predstavnik „čiste“ hirurgije za koju AP nije potrebna. Iako rezultati randomizovanih studija ne daju jasan zaključak po pitanju efikasnosti antibiotske profilakse u smanjenju učestalosti infekcije rane, vodiči preporučuju da se antibiotik primeni kao profilaksa kada se planira ugradnja protetskog materijala (mrežica) kao i za reparaciju kompleksnih hernija, posebno u centrima sa manje iskustva u ovoj vrsti hirurgije [9].

Laparoskopija niskog rizika ne predstavlja indikaciju za profilaktičku primenu antibiotika, prema preporukama domaćeg i međunarodnog vodiča. Činjenica da je nekada teško preoperativno definisati rizik kod laparoskopije, verovatno je uslovlila relativno veliki obuhvat profilaksom kod bolesnika podvrgnutih laparoskopskoj holecistektomiji (87,2%).

U našoj studiji, pokazano je ogromno variranje u izboru antibiotika ili antibiotskih kombinacija

AP was applied in 84.1% patients, which confirms the estimations that prophylactic administration accounts for 30% – 50% of the overall intrahospital antibiotic consumption [7]. Data found in literature indicate that the coverage of surgical patients with AP is very high in most developed countries, amounting to over 95% [8].

In our study, antibiotics, as prophylaxis, were least used in the group of patients who underwent hernia repair surgery (69.2%). Elective inguinal hernia surgery is a typical example of 'clean' surgery, which does not require AP. Although results of randomized studies do not offer a clear conclusion regarding the efficiency of antibiotic prophylaxis in the decrease of wound infection frequency, guides recommend that the antibiotic should be applied as prophylaxis when prosthetic material (mesh) implantation is planned, as well as in cases of complex hernia repair, especially in medical centers where there is less experience in this type of surgery [9].

Low-risk laparoscopy does not indicate prophylactic antibiotic use, according to the recommendations of the national and international guides. The fact that it is sometimes difficult to preoperatively define the risk in laparoscopy has probably resulted in a relatively

primenjenih za profilaksu. Iako preporuke sugerišu primenu cefazolina za većinu operacija u abdominalnoj hirurgiji, ovaj lek je bio tek na petom mestu po učestalosti primene, a dobilo ga je 17 (6,3%) bolesnika. Najčešće primenjivani antibiotski režimi bili su: ceftriakson i metronidazol (24,8%), ceftriakson (21,9%), metronidazol (13,7%) i ciprofloksacin (10,7%). Kao AP, primenjeno je ukupno 14 različitih antibiotskih režima.

Istraživanje sprovedeno u 14 bolnica u Nemačkoj, pokazalo je da je kao AP korišćeno čak 29 antibiotskih režima, a da je variranje u praksi i odstupanje od preporuka bilo posebno izraženo u abdominalnoj hirurgiji [10]. Ta studija je pokazala i značajnu zastupljenost antibiotika širokog spektra i tzv. rezervnih antibiotika, što je bio slučaj i u našem istraživanju. Iznenadjuće je da je u našoj sredini ciprofloksacin bio veoma zastupljen izbor, i pored preporuke da se hinoloni, zbog neželjenih efekata, koriste samo za lečenje životno ugrožavajućih infekcija.

Razlozi za nisku usaglašenost izbora antibiotske profilakse sa preporukama iz vodiča nisu sasvim poznati. Moguće je da je tome doprinela i relativno velika učestalost samoprijavljenih alergija na antibiotike. Prethodno istraživanje sprovedeno u ovom centru je pokazalo da gotovo 40% pacijenata pre operacije prijavljuje alergiju na neki lek, pri čemu je navodna alergija na penicilin najčešća [11]. Ipak, ni u jednom slučaju kao AP nije primenjen klindamicin, kao prva preporučena alternativa cefazolinu, kod alergičnih na beta-laktamske antibiotike, pa je ukupna usaglašenost sa vodičima po pitanju izbora antibiotika iznosila svega 22,6%.

Svi bolesnici u našoj studiji dobili su antibiotik intravenskim putem, što je u skladu sa smernicama. Slične rezultate prikazuju i drugi autori, posebno kada je u pitanju abdominalna hirurgija [12].

Vreme davanja antibiotika za hiruršku profilaksu je od značaja, jer je cilj da se postigne najviša koncentracija leka u plazmi u vreme najveće izloženosti potencijalnim uzročnicima infekcije rane. Ovaj aspekt primene antibiotske profilakse imao je najnižu usaglašenost sa smernicama u našem istraživanju, jer je kod samo 8 (3,0%) bolesnika ispoštovana satnica za davanje doze antibiotika. To je neuporedivo niže u odnosu na rezultate drugih autora, gde je 45% do 94% slučajeva antibiotske profilakse bilo primenjeno u pravilno vreme, u skladu sa preporukama [13]. Mogući uzroci ovako niske usaglašenosti sa smernicama u našem istraživanju leže u organizacionim razlozima, jer operacioni blok na Klinici za digestivnu hirurgiju nema prostor u kome bi bolesnici mogli da dobiju lek venskim putem. Takođe, česte izmene programa otežavaju da bolesnik dobije lek pravovremeno na odeljenju, već se sa ordiniranim antibiotikom upućuje u operacionu salu gde procedure

wide coverage of patients undergoing laparoscopic cholecystectomy with AP (87.2%).

In our study, a huge variability in the selection of antibiotics or combinations of antibiotics used as prophylaxis has been shown. Although recommendations suggest the application of cefazolin for most operations in abdominal surgery, this drug was only the fifth most frequent drug used and was administered to only 17 (6.3%) patients. The most frequently applied antibiotic regimens were the following: ceftriaxone and metronidazole (24.8%), ceftriaxone (21.9%), metronidazole (13.7%), and ciprofloxacin (10.7%). Fourteen different antibiotic regimens were applied as antibiotic prophylaxis.

A study including 14 hospitals in Germany has shown that as many as 29 antibiotic regimens were used as antibiotic prophylaxis, and that variations in clinical practice and deviation from recommendations was especially prominent in abdominal surgery [10]. This study showed significant use of broad-spectrum antibiotics and of so-called reserve antibiotics, which was also the case in our study. It is surprising that in our environment ciprofloxacin was used to a great extent, despite the recommendation that quinolones, due to adverse effects, should be used only for treating life-threatening infections.

The reasons for poor compliance of the choice of AP with recommendations offered in the guides have not completely been elucidated. It is possible that a relatively high frequency of self-reported allergies to antibiotics has contributed to this state of affairs. A previous study carried out in this health center has shown that almost 40% of patients report a drug allergy prior to surgery, wherein the alleged allergy to penicillin is the one most commonly reported [11]. Yet, clindamycin was not used as AP in a single case, even though it is the first recommended alternative for cefazoline in patients allergic to beta-lactam antibiotics, and therefore, the overall compliance with the guidelines with respect to antibiotic choice was a only 22.6%.

All of the patients in our study received the antibiotic intravenously, which is in keeping with the guidelines. Other authors have reported similar results, especially in the domain of abdominal surgery [12].

The timing of antibiotic administration for surgical prophylaxis is significant, since the goal is to achieve the highest concentration of the drug in the blood at the time of the greatest exposure to potential causative agents of wound infection. In our study, this aspect of AP application had the lowest compliance with the guidelines, since the timeline for antibiotic application was observed in only 8 (3.0%) patients. This is far lower than the results reported by other authors, where in 45% to 94% of the cases, AP was applied at the appropriate time, as recommended by the guidelines [13].

oko uvođenja u anesteziju često imaju prioritet. Zato je najveći broj bolesnika (174; 64,4%) antibiotsku profilaksu primio unutar 30 minuta od početka operacije.

Produženo trajanje antibiotske profilakse je jedna od čestih grešaka u mnogim ustanovama. Iako vodiči jasno ističu da je potrebno dati jednu dozu ili završiti sa primenom antibiotika unutar 24 h, u studijama se navodi da se to primenjuje u 5,8% – 91,4% slučajeva [14]. Činjenica da je adekvatno trajanje profilakse u našoj studiji bilo ostvareno u 13,1% slučajeva, može se objasniti strahom hirurga od razvoja infekcije rane nakon velikih, čistih-kontaminiranih operacija, u situaciji u kojoj se drenovi zadržavaju više dana. Ostaje nejasno zašto je dužina profilakse ispoštovana kod samo jednog bolesnika podvrgnutog laparoskopskoj holecistektomiji, za koju davanje antibiotika, u najvećem broju slučajeva, nije potrebno.

Moguće je da se uslovi za dobru praksu u primeni antibiotske profilakse stiču usvajanjem znanja iz te oblasti, u toku studija medicine. Istraživanje sprovedeno u bolnici u Kataru je pokazalo da je 51% specijalizanata hirurgije, koji su samostalno izvodili operacije, bilo upoznato sa principima primene antibiotske profilakse [15]. Kliničku praksu, osim poznavanja teorije, oblikuju i neki drugi faktori, koji nisu bili predmet ovog istraživanja. Rezultati ranijih istraživanja ukazuju na značajnu pomoć povratne informacije o primeni antibiotika putem zdravstvenog informacionog sistema, kao i periodičnih unutrašnjih stručnih nadzora, u poboljšanju usaglašenosti prakse sa vodičima za primenu antibiotske profilakse [16,17].

ZAKLJUČAK

Usaglašenost prakse sa preporukama vodiča za AP u abdominalnoj hirurgiji je bila na niskom nivou u tercijarnoj ustanovi za abdominalnu hirurgiju. Činjenica da se nalazimo u eri ekspanzivnog razvoja hirurgije, ali i razvoja multirezistentnosti bakterija prouzrokovao bolničkih infekcija, nameće potrebu za izvesnim merama i postupcima, u cilju racionalnije primene antibiotika. Potrebno je preduzeti mere na institucionalnom nivou, u cilju povećanja svesti kliničara o značaju ovog problema; podržati timove za upravljanje antibiotici u bolnicama; uvesti liste za proveru, kako bi se vršio nadzor nad različitim aspektima primene antibiotske profilakse; te unaprediti nastavu na studijama medicine, kako bi se naglasio značaj ove teme. Promovisanje Nacionalnog vodiča i izrada lokalnih preporuka su takođe neke od mera koje bi mogle doprineti efikasnijoj primeni i sprovođenju antibiotske profilakse u hirurgiji.

Sukob interesa: Nije prijavljen.

The possible causes of such a low compliance with the guidelines, in our study, may be attributed to organizational issues, since the surgical suite at the Clinic for Digestive Surgery does not have a space/room where the patients could receive the antibiotic intravenously. Also, frequent changes in the operating schedule make it more difficult for the patient to receive the antibiotic in a timely fashion while still on the ward, rather the patients are prescribed the antibiotic and then transferred to the operating theatre, where anesthesia procedures are often given priority. This is why the greatest number of patients in our study (174; 64.4%) received AP within 30 minutes of the beginning of the operation.

Prolonged antibiotic prophylaxis is one of the frequent mistakes made in many healthcare facilities. Although guides clearly emphasize that only one dose should be administered or that antibiotic application should be finished within 24 hours, studies report that this recommendation is observed in 5.8% – 91.4% cases [14]. The fact that the appropriate duration of prophylaxis was achieved in 13.1% of the cases may be explained by the surgeons' concern that infections may develop after major, clean-contaminated surgeries, in situations when drains remain in place for a number of days. It remains unclear, why the length of prophylaxis was observed only in one patient who underwent laparoscopic cholecystectomy, for which, in most cases, antibiotic prophylaxis is unnecessary.

It is possible that the conditions for good clinical practice in the application of antibiotic prophylaxis are developed during medical studies, when knowledge and understanding in this area is obtained. A study carried out in a hospital in Qatar showed that 51% of surgical residents, who were performing surgery independently, were aware of the principles of antibiotic prophylaxis application [15]. Aside from theoretical knowledge, clinical practice is shaped by other factors as well, which were not the subject of this study. The results from earlier studies indicate the importance of feedback related to the application of antibiotics, obtained through the health information system, as well as the importance of periodical internal professional supervision, for improving the compliance of clinical practice with AP application guides [16,17].

CONCLUSION

The compliance of clinical practice with recommendations from guides on AP in abdominal surgery was poor at the tertiary health institution for abdominal surgery observed in our study. The fact that this is the era of extensive surgery development, but also the development of multi-drug resistance in bacteria causing intra-hospital infections, necessitates the need for certain

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- measures and procedures, with the aim of achieving a more rational use of antibiotics. It is necessary to implement measures at the institutional level, so as to raise the awareness of clinicians on the importance of this problem; support antibiotic management teams in hospitals; introduce checklists, in order to establish supervision of different aspects of AP application; and enhance the study of medicine, in the sense of emphasizing the significance of this issue. Promoting the National Guide and developing local recommendations are also some of the measures that may contribute to a more effective and efficient application and administration of antibiotic prophylaxis in surgery.

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