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MULTIDRUG-RESISTANT MICROORGANISMS AND SURGICAL ANTIBIOTIC PROPHYLAXIS – PREVALENCE AT THE UNIVERSITY HOSPITAL CENTRE SESTRE MILOSRDNICE

Višestruko otporni mikroorganizmi i kirurška antibiotska profilaksa – prevalencija u Kliničkom bolničkom centru Sestre milosrdnice

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Abstract

Aim

Emergence and spread of multidrug-resistant (MDR) microorganisms in healthcare settings, especially in Intensive Care Units (ICUs), cause concern worldwide. A particular problem is a lack of therapeutic options. One of the inducement factors for MDR microorganisms spread is antibiotic over- and wrong-prescribing. Surgical antibiotic prophylaxis is one of the misused antibiotic prescribing indications. The aims of our study were to determine the prevalence of five key MDR bacteria from blood and urine in order to establish surgical antibiotic prophylaxis compliance with the Croatian National Guidelines.

Methods

A point prevalence study was conducted. We present a laboratory-based WHO designed survey on MRSA, VRE, ESBL and CRE-producing *Enterobacteriaceae*, multi-resistant *Acinetobacter spp.*, isolated from blood and urine of hospitalised patients. Surgical prophylaxis data were gathered from patients who had undergone operative procedures in the General Surgery Ward and Gynecology Ward.

Results

The prevalence of MRSA bloodstream infections was 1.64%, other MDR microorganisms were not isolated.

The prevalence of urine MDR isolates was MRSA 0.07%, *E. coli* ESBL 1.43% (5.79% of overall *E. coli* isolates were ESBL producers), *K. pneumonie* 1.79% (26.3% of *K. pneumoniae* were ESBL producers) and *Acinetobacter spp.* 0.38%. The proportion of patients who continued surgical prophylaxis was 6.4%.

Conclusion

MDR microorganisms' prevalence in our institution is low, but the proportion of resistant strains within isolated species corresponds to European reports. Surgical antibiotic prophylaxis compliance with the Croatian National Guidelines is high.

Constant and recent surveillance data are a significant guide for empiric antimicrobial therapy, an indicator for activities concerning the prevention of MDR microorganisms spread and proper antibiotic stewardship.

Keywords

drug resistance, multiple, bacterial, Gram-positive bacteria, Gram-negative bacteria, prevalence, antibiotic prophylaxis

Sažetak

Cilj

Pojava i širenje višestruko otpornih mikroorganizama (MDR) u okruženju zdravstvene njege, posebice u jedinicama za intenzivno liječenje, uzrokuju zabrinutost diljem svijeta. Poseban problem je nedostatak terapeutskih mogućnosti. Jedan od uzročnih faktora širenja MDR mikroorganizama je pretjerano ili pogrešno

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propisivanje antibiotika. Ciljevi ove studije bili su utvrditi prevalenciju pet najvažnijih MDR bakterija iz krvi i urina da bi se kirurška antibiotička profilaksa uskladila s Hrvatskim nacionalnim smjernicama.

Metode

Provedena je studija prevalencije infekcija u određenom vremenu. Prikazani su laboratorijski podaci o sljedećim bakterijskim uzročnicima infekcija: MRSA, VRE, ESBL i enterobakterije koje produciraju karbapenemaze, te višestruko otporna *Acinetobacter spp.*, izolirane iz krvi i urina hospitaliziranih pacijenata. Podaci o kirurškoj profilaksi prikupljeni su od pacijenata koji su bili podvrgnuti operativnim zahvatima na Odjelu opće kirurgije i Odjelu ginekologije.

Rezultati

Prevalencija MRSA infekcija krvi bila je 1,64%, drugi MDR mikroorganizmi nisu bili izolirani. Prevalencija urinarnih MDR izolata bila je sljedeća: MRSA 0,07%, E. coli ESBL 1,43% (5,79% ukupnih *E. coli* izolata bilo je onih koji proizvode ESBL), *K. pneumonie* 1,79% (26,3% *K. pneumoniae* bilo je proizvođač ESBL-a) i *Acinetobacter spp.* 0,38%. Udio pacijenata koji su nastavili s kirurškom profilaksom bio je 6,4%.

Zaključak

Prevalencija MDR mikroorganizama u našoj instituciji je niska, no udio otpornih izolata među izoliranim vrstama odgovara europskim izvješćima. Usklađenost kirurške antibiotičke profilakse sa Smjernicama je visoka.

Kontinuirani i aktualni podaci važna su uputa za provođenje empirijske antimikrobne terapije, pokazatelj za načine sprečavanja širenja MDR mikroorganizama i ispravno korištenje antibiotika.

Ključne riječi

otpornost na lijekove, višestruki, bakterijski, Gram-pozitivne bakterije, Gram-negativne bakterije, prevalencija, antibiotska profilaksa

Introduction

Global emergence and spread of multidrug-resistant (MDR) microorganisms in healthcare settings, especially in Intensive Care Units, cause concern worldwide. Healthcare-associated infections in already critically ill patients are associated with prolonged length of hospitalisation and increased morbidity and mortality [1, 2]. National or multicentre point prevalence surveys of healthcare-associated infections performed in developed countries have shown that the percentage of patients with a nosocomial infection on any given day in acute care hospitals is on average 7.1%, ranging from 3.5% to 10.5%, with main infections of urinary tract (27%), lower respiratory tract infections including pneumonia (24%), surgical site infections (17%) and bloodstream infections (10.5%) [3]. The most frequent cause of these infections are Gram-negative bacteria *Escherichia coli, Klebsiella pneumonie*, other *Enterobacteriaceae* species, *Acinetobacter spp*. and Gram-positive bacteria *Staphylococcus aureus* and *Enterococcus spp*. All these pathogens have the ability of developing effective resistance mechanisms to antimicrobial agents used and becoming multidrug-resistant (MDR) strains presenting a significant problem in therapy optimization because the initial empirical antibiotic choice can be inadequate and there will be a lack of antimicrobial therapeutic options in the future, since no new class of antimicrobials has been developed recently [4]. Surveillance of MDR microorganisms is a fundamental part of an effective response to this threat and surveillance results constitute the essential source of information on magnitude and trends in resistance [5]. It has been identified that one of the inducement factors for selection of bacterial strains with diverse resistance mechanisms and their consequent spread is hospital environment with antibiotic selective pressure [6]. An additional problem is over- and wrong- prescribing of antibiotics within healthcare facilities, despite guidance being available. Surgical antibiotic prophylaxis is one of the misused antibiotic prescribing indications.

World Health Organisation (WHO) recognized the potentially devastating consequences of these issues and has put the spread of antibimicrobial resistance into focus of 2014 WHO – SAVE LIVES: Clean Your Hands global campaign. Since 2009, on May 5th (Hand Hygiene Day), the campaign has launched a call to action to implement and sustain hand hygiene improvement worldwide, to reduce transmission of MDR pathogens causing healthcare-associated infections. WHO proposed a global survey on MDR microorganisms burden and surgical antibiotic prophylaxis use, to raise awareness and promote activities in restraining the beginning of postantibiotic era, such as hand hygiene and antibiotic stewardship [7]. Since our institution is taking part in WHO – SAVE LIVES: Clean Your Hands campaign, the aims of our study were to determine the prevalence of five key Gram-positive and Gram-negative multidrug-resistant microorganisms from blood and urinary specimens and to establish the prevalence of compliance with surgical antibiotic prophylaxis guidelines determining the proportion of patients who continue surgical antibiotic prophylaxis after operative procedures in absence of any infections, either surgical or non-surgical, in order to describe the types of antibiotic prophylaxis prescribed and to ascertain the reasons for prophylaxis prolongation.

Materials and methods

A point prevalence study on multidrug-resistant bacteria and surgical antibiotic prophylaxis was conducted. A laboratory-based study, using WHO

designed survey, was conducted during one week (from March 21st to 28th, 2014) at the University Hospital Centre Sestre Milosrdnice Department of Microbiology, Parasitology and Hospital Infection. Gram-positive multidrug-resistant bacteria (methicillin-resistant *Staphylococcus aureus* – MRSA and vancomycin-resistant enterococci – VRE) and Gram-negative multidrug-resistant bacteria (extended-spectrum β-lactamase ESBL producing *Enterobacteriaceae* – ESBL, carbapenem-resistant *Enterobacteriaceae* – CRE and multi-resistant *Acinetobacter spp.* – MRAB) isolated from blood culture (aerobic and anaerobic blood culture sets) and urine (mid-stream or catheter specimen) of hospitalised patients routinely submitted to our microbiology laboratory, excluding copy strains, were registered in electronic form. Susceptibility patterns of phenotipically identified microorganisms were determined using disk diffusion method. Minimum inhibitory concentration (MIC) of vancomycin was determined by E-test (bioMerieux, France). European Committee on Antimicrobial Susceptibility Testing (EUCAST) antibiotic susceptibility interpretative criteria were used [8]. ESBL is a beta-lactamase that mediates resistance to all cephalosporins and monobactams (aztreonam), but does not effect carbapenems and cephamycin. CRE *Enterobacteriaceae* produce any beta-lactamase that hydrolises carbapenems (any or all of ertapenem, doripenem, imipenem and meropenem). MRAB *Acinetobacter spp.* isolate is resistant to at least three classes of antimicrobials (penicillins, cephalosporins, flouroquinolones and aminoglycosides).

Surgical prophylaxis data were gathered using WHO designed survey with a "closed-question" questionnaire by a hospital infection control professional in one day (March 27th, 2014), from patients hospitalised in the General Surgery Ward and Gynecology Ward at the University Hospital Centre Sestre Milosrdnice Clinic for Tumors. Data were collected from patient records (and by asking clinical ward staff if necessary) on all patients who had operative procedure in the previous three consecutive working days excluding the day of the survey (March 24th, 25th and 26th, 2014). Surgical antibiotic prophylaxis was defined as administration of systemic antibiotics before surgical procedure optimally within 60 minutes (exceptions are vancomycin and flouroquinolones), with possible repetition during the operation depending on its duration. Surgical procedures were classified according to the National Healthcare Safety Networklist of Operative Procedures Categories (CDC). Surgical wounds were classified using Wound Classification. Type 1 are clean, non-traumatic, uninfected operative wounds in which no inflammation is encountered. There is no break in (sterile) technique and the respiratory, alimentary, or genitourinary tracts or the oropharyngeal cavities are not entered. Clean wounds are primarily closed and, if necessary, drained with closed drainage. Type 2 is an operative wound that enters the respiratory, GI, genital or urinary tract under controlled conditions without unusual contamination when no infection or major break in technique has occurred. Type 3 are contaminated wounds which occur when the operation is associated with open, fresh and accidental wounds. In addition, this is a surgical procedure in which a major break in sterile technique occurs or gross spillage from the gastrointestinal tract and incisions in which acute, non-purulent inflammation is encountered. Type 4 are dirty or infected wounds involving old traumatic wounds with retained or devitalised tissue and those that involve an existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the surgical procedure [9]. Each operative procedure was compared with the Interdisciplinary Section for Antibiotic Resistance Control (ISKRA) of the Croatian National Guidelines for Antimicrobial Prophylaxis in Surgery [10].

Results

During the study period 61 blood culture sets were processed. In 6.56% blood cultures of different microorganisms were isolated. The prevalence of MRSA bloodstream infections was 1.64%, while other MDR microorganisms were not isolated. Other isolated microorganisms were *E. coli* and *K. pneumoniae*, both with a wild type susceptibility pattern (susceptible to all antibiotics tested) and *Candida glabrata* (Figure 1). The total number of inpatient urine specimens processed during the study week was 279. The proportion of urine specimens with isolated pathogens was 39.78%. The prevalence of MRSA was 0.35%, ESBL *E. coli* 1.43%, ESBL *K. pneumonie* 1.79% and multidrug-resistant *Acinetobacter spp.* 0.38%. The frequency of multidrug-resistant strains within isolated Gram-positive and Gram-negative species was diverse. One third (33.3%) of overall isolated *Staphylococcus aureus* were methicilin-resistant (MRSA), 5.79% of *E. coli* isolates and 26.3% *K. pneumoniae* were ESBL producers. No vancomycin-resistant *Enterococcus spp.* and carbapenem-resistant *Enterobacteriaceae spp.* were isolated (Figure 1). On the day of the surgical antibiotic prophylaxis survey 31 patients were registered. Seventeen patients (54.83%) had breast surgery, four (12.9%) had thyroid surgery, four (12.9%) had vaginal hysterectomy, two (6.45%) had neck surgery and one (3.22%) had colon surgery, bile duct surgery, abdominal hysterectomy and ovarian surgery. Type 1 were 67.74% operative procedures, Type 2 were 32.25% operative procedures. The patients who had Type 1 procedure and administred prophylaxis had breast surgery. The proportion of patients who had Type 2 procedure and received prophylaxis according to the Croatian National

Guidelines (single pre-operative dose of 1 g cefazoline, 600 mg clindamycin and 1 g cefazoline plus 500 mg metronidazole depending of the operative procedure) was 80%. Other patients received prolonged antibiotic therapy during the day of the operative procedure following departmental guidelines for patients with specific risk factors (Table 1). Overall proportion of patients who continued surgical prophylaxis, overstepping guidelines, was 6.4%.

Discussion

Our study shows that multidrug-resistant micro-organisms' prevalence in our institution is comparable to other prevalence studies on MDR microrganisms. In 2012 a large nationwide study in German hospitals showed MRSA was the most frequently reported causative pathogen in all healthcare-associated infections with prevalence 1.53%, ESBL *E. coli* 0.97%, ESBL *K. pneumoniae* 0.27%, VRE 0.27% and *Acinetobacter spp.* 0.1% [11].

As opposed to reports, significant and encouraging is the fact that no carbapenem-resistant *Enterobacteriaceae* and vancomycin-resistant *Enterococcus spp.* were isolated (Figure 1). So far carbapenem-resistant *Enterobacteriaceae* species have presented a new global threat to carbapenems, our last-line broad spectrum antimicrobial agents and are in the spotlight of all hospital infection preventionists in Croatia, since there have been reports of their epidemic spread in the region [12]. The proportion of resistant strains within isolated species in our institution corresponds to antibiotic resistance in Croatia and to European Centre for Disease Prevention and Control (ECDC) Earss-Net latest reports, with the exception of high MRSA proportion in overall *S. aureus* isolates (33.3%), since the Croatian average is 13%. The proportion of ESBL producing *K. pneumoniae* strains is lower than the Croatian average (36%) [13]. Although point prevalence studies have limitations, they are a valuable tool for assessment of routine data, they can help raise and maintain awareness of MDR microorganisms and can therefore contribute to planning prevention strategies.

The other part of our study concerning surgical antibiotic prophylaxis showed high compliance with the Croatian National Guidelines. Published data on this subject are in range from appropriate prophylaxis in 18.1% cases as in the Italian study, 28% in the Dutch study to 93% in the Canadian research [14–16]. The interpretation of different compliance rates requires caution. It depends on patient cohorts, studies design and evaluation methods. The prevalence of surgical antibiotic prophylaxis prolongation in our institution is low and with short duration (no longer than 24 hours). The Croatian National Guidelines recommend prophylaxis administration for Type 2 operative procedures. Type 1 are considered clean procedures with low prevalence of surgical site infections and antibiotic prophylaxis is recommended only in cardiovascular surgery and prosthetic implants insertion. No recommendations are given on breast surgery prophylaxis. It is considered clean surgery and the effectiveness of prophylaxis is not clear. In our institution, the decision on prophylaxis is based on the patient's general state and local risk factors for surgical site infection development. Further research of this issue is needed, since recommendations and guidelines are not consistent.

Our study shows that point prevalence studies are an inexpensive and fast way to provide significant data and to unfold new research ground for clinicians and hospital infection practitioners in their efforts for better patient care and prevention of healthcare-associated infections management, using costless tools such as hand hygiene and rational antibiotic prescribing.

Figure 1. Gram-positive and Gram-negative bacteria isolated in blood and urine specimens and the prevalence of antimicrobial drugs' sensitive and multidrug-resistant strains.

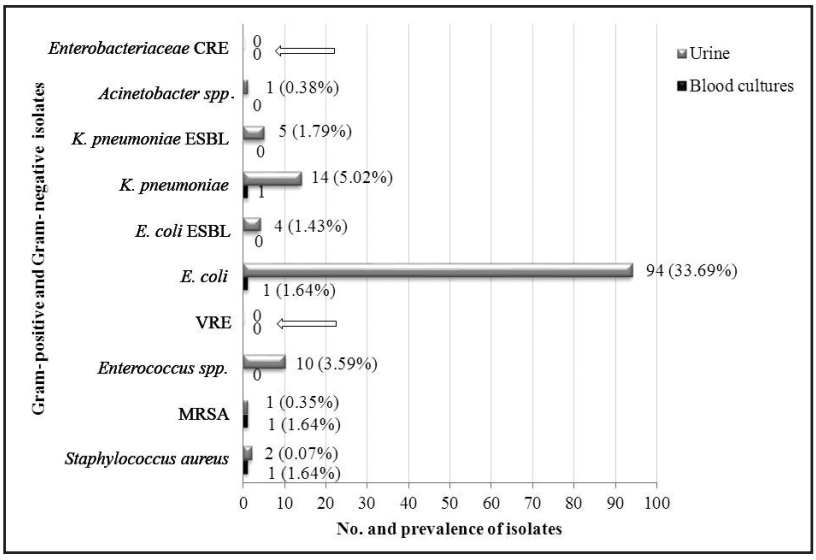

Table 1. Surgical antibiotic prophylaxis according to operative wound classification type.

Wound classification type	No. of operations	Antibiotic Prophylaxis Administered	Antimicrobial Agent Used			Prolongation of Prophylaxis	Reason for prolongation
			cefazoline 1 g	clindamycin 600 mg	cefazoline + metronidazole 1 g + 500 mg		
Wound Type 1.	21 (67.74%)	4 (19.04%)	3	1	0	0 (0%)	
Wound Type 2.	10 (32.26%)	8 (80%)	4	1	3	2 (20%)	Departmental guidelines

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