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Short Communication: Prevalence of multidrug resistant bacteria in General Surgery Hospital, Ukraine

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Abstract. *Kon K. 2015. Prevalence of multidrug resistant bacteria in General Surgery Hospital, Ukraine. Nusantara Bioscience 7: 102-106.* Rising antibiotic resistance is a serious concern worldwide and during prescribing antibiotic treatment it is important to know general and regional tendencies in spread of multidrug resistant strains. The aim of the present study was to evaluate regional specificity of the prevalence of multidrug resistant strains among agents of surgical infections, to determine the most common microbial associations and to detect the most active antibiotics against multidrug resistant bacteria. More than 60% of strains were multidrug-resistant, with the highest prevalence of resistance among *Klebsiella pneumoniae*, *Enterobacter* spp., *Proteus* spp., and *Pseudomonas aeruginosa*. Isolated multidrug-resistant bacteria showed susceptibility mainly to carbapenems and fluoroquinolones. The high prevalence of multidrug-resistant bacteria indicates the need for continuous monitoring of resistance in each hospital and to search for new methods to coping with this problem.

Keywords: Antibiotics, microbial associations, multidrug resistance, surgical infections

INTRODUCTION

The prevalence of resistance to antibiotics currently reaches significant proportions among agents of hospital infections, and among bacteria of non-hospital origin (Livermore et al. 2009; Arias and Murray 2012; Cantón et al. 2012; Ashiru-Oredope and Hopkins 2015; Izadpanah and Khalili 2015). Despite progress in the technology of surgery, anaesthesia and technical equipment in surgical hospitals, the morbidity and mortality caused by various infectious processes is not reduced, and therefore this problem needs attention from both practitioners and clinical microbiologists (Mulier et al. 2003). Studying the etiological structure of microorganisms causing infectious processes and understanding antibiotic resistance patterns is a major focus in the prevention of nosocomial infections (Farshad et al. 2012).

Many researches are devoted to evaluation of the prevalence of multidrug resistant bacteria in different countries. Thus, the European project ARMed (Antibiotic Resistance Surveillance and Control in the Mediterranean region) conducted comparison of the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) among invasive isolates in nine European Mediterranean countries and found the overall prevalence of MRSA 39%, which in some countries exceeded 50% (in Jordan, Egypt and Malta) in 2003-2005 (Borg et al. 2007). Another study conducted by the European Antimicrobial Resistance Surveillance System found that in a third of European countries, the prevalence of MRSA among blood isolates exceeded 25% in 2008 (Johnson 2011). Alarming is not only a significant prevalence of multidrug resistant pathogens, but the rapid growth of their distribution. Mainous et al. analyzed the dynamics of the spread of resistant pathogens in USA hospitals from 1997 to 2006 and found a 2.5 times increase in the number of strains resistant to antibiotics during this period (Mainous et al. 2011).

Researches have shown that etiologic structure and antibiotic sensitivity of microorganisms varies in different countries, so there is a need to examine regional data. However, increasing popularity of tourism and international job companies contributes exchanging of microbial pathogens between different countries and makes it necessary to know general tendencies of antibiotic resistance in other countries. In spite of European location of Ukraine, European surveillance programs did not include gathering data on its territory and reports on antibiotic resistance of Ukrainian pathogens are published only in locally available journals and are not accessible to international society.

The aim of the present study was to evaluate the prevalence of multidrug resistant bacterial pathogens among surgical infections, to determine the most common microbial associations and to detect the most active antibiotics against multidrug resistant bacteria.

MATERIALS AND METHODS

The survey was conducted on 307 patients treated in the surgical clinic of the Department of General Surgery N2, Kharkiv National Medical University, Kharkiv, Ukraine. The specimens were taken from purulent wounds (139 patients), content of the gallbladder and bile ducts (115 patients), abdominal cavity (12 patients), abscesses of internal organs (liver, pancreas, appendix) (9 patients), sputum (8 patients) and other sources (24 patients). Bacteriological examination of the material was carried out by conventional bacteriological methods (Patrick et al. 2007). Isolated bacterial cultures were tested for susceptibility to 34 antibiotics by the disc-diffusion method (CLSI 2006).

Statistical analysis of the data involved the use of standard methods of descriptive statistics. To determine the prevalent associations of microorganisms in patients, I proposed to use the correlation analysis: the presence of a microorganism in a patient was designated as "1", absence-as "0", then nonparametric gamma-correlation coefficients (r) were calculated, correlations were considered as statistically significant at $p<0.05$.

RESULTS AND DISCUSSION

Positive cultures of aerobic and facultative anaerobic microorganisms were obtained in 177 (57.7%) patients; in the remaining 130 (42.3%) patients the growth of microorganisms was not found. The samples yielded in 217 strains belonging to 10 genera. The predominant bacteria were *Staphylococcus* spp.-86 strains (39.6%), which were represented by two species: *S. aureus*-53 strains (24.4%) and *S. epidermidis*-33 strains (15.2%); common bacteria were also *Escherichia coli*-55 (25.4%) strains. Less frequent microorganisms were *Pseudomonas aeruginosa*-16 strains (7.4%), *Klebsiella pneumoniae*-15 (6.9%), *Proteus* spp.-12 (5.5%), *Enterobacter* spp.-11 (5.1%), *Enterococcus faecalis*-10 (4.6%), *Streptococcus pyogenes*-6 (2.8%), *Candida albicans*-4 (1.8%) and *Citrobacter* spp.-2 strains (0.9%). *Proteus* spp. were represented by species *P. mirabilis* (10 strains-4.6%) and *P. vulgaris* (2 strains-0.9%); *Enterobacter* spp. included *E. cloacae* (8 strains-3.7%) and *E. aerogenes* (3 strains-1.4%).

Of the total number of isolated microorganisms, 140 (64.5%) were in a monoculture, and 77 (35.5%)-in associations with other types of organisms, with 37 associations consisted of two microorganisms, and only one-of the three. As it can be seen from Figure 1, in patients with surgical infections there is a direct correlation between the isolation of *Staphylococcus* spp. and *Proteus* spp. (r = 0.55), which is confirmed by the original data: of 12 *Proteus* strains, 9 were in association with *Staphylococcus*; four associations consisted of *S. aureus* and *P. mirabilis*, two-of *S. aureus* and *P. vulgaris*, three-of *S. epidermidis* and *P. mirabilis*. All these nine associations were isolated from purulent wounds. These data suggest that in patients with purulent wounds there is a high probability that these microorganisms would be not only in monoculture, but in associations.

Also of interest are the resulting negative correlations: between the isolation of *Staphylococcus* spp. and *S. pyogenes* (r =-1.0), *Staphylococcus* spp. and *Citrobacter* spp. (r =-1.0), *Staphylococcus* spp. and *K. pneumoniae* (r =-0.88), *Staphylococcus* spp. and *E. faecalis* (r =-1.0); *E. coli* and *Enterobacter* spp. (r =-1.0), *E. coli* and *S. pyogenes* (r =-1.0), *E. coli* and *Proteus* spp. (r =-1.0), and *E. coli* and *E. faecalis* (r =-1.0). Correlation coefficient equal to-1.0 indicates that in the examined patients no associations consisting of a particular pair of microorganisms were isolated.

Sensitivity to antimicrobial agents was studied in 196 bacterial isolates. It is important to note that 123 (62.8%) strains were resistant to more than 50% of the tested antibiotics, which actually corresponded multidrug resistant bacteria (defined as resistant to more than two groups of antibiotics), and 62 (31.6%)-were resistant to more than 80% of antibiotics. These data indicate a very high level of overall microbial resistance.

All isolated 14 strains of *Klebsiella* were multidrug resistant (Figure 2), in *Enterobacter* 7 of 9 strains were multidrug resistant (77.8%), among *Proteus*-7 out of 10 strains (70%), among *P. aeruginosa*-11 of 16 (68.8%). There was a high prevalence of multidrug resistant isolates among *S. pyogenes* and *E. coli*-66.7% (4 of 6 and 34 from 51 strains, respectively). Among the 79 analyzed staphylococci-43 (54.4%) were multidrug resistant. Sensitivity to oxacillin was tested in 38 strains, and the prevalence of methicillin (oxacillin)-resistant staphylococci was 52.6%-20 out of 38 strains (31.6% MRSA and 21.0% methicillin-resistant *S. epidermidis*). The lowest prevalence of multidrug resistant strains was detected among *E. faecalis*-only 22.2% (2 of 9 strains).

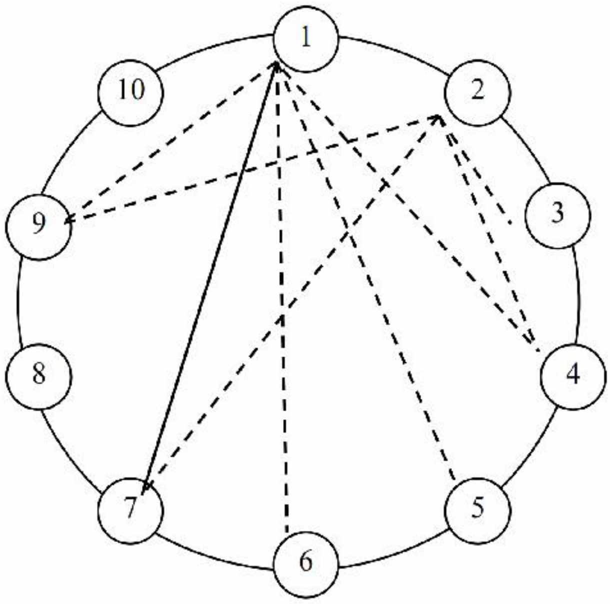

Figure 1. The correlations between the components of associations of microorganisms isolated from patients with surgical infections: 1. *Staphylococcus* spp., 2. *E. coli*, 3. *Enterobacter* spp., 4. *S. pyogenes*, 5. *Citrobacter* spp., 6. *K. pneumoniae*, 7. *Proteus* spp., 8. *P. aeruginosa*, 9. *E. faecalis*, 10. *C. albicans*; solid line-positive correlation, dashed line-negative correlation

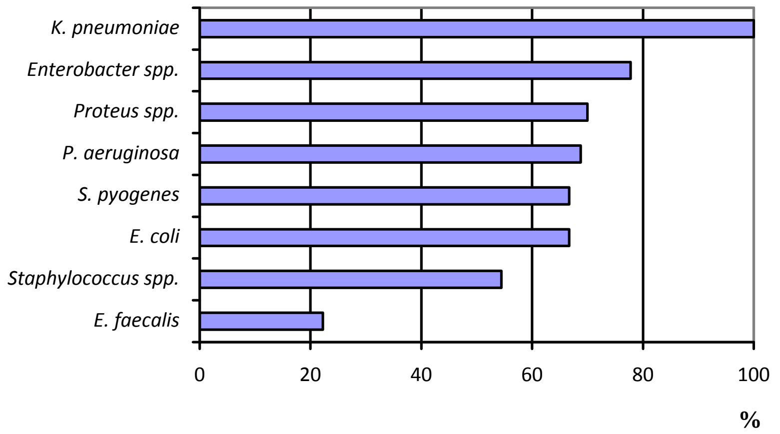

Figure 2. The prevalence of multidrug resistant strains in pathogens causing surgical infections

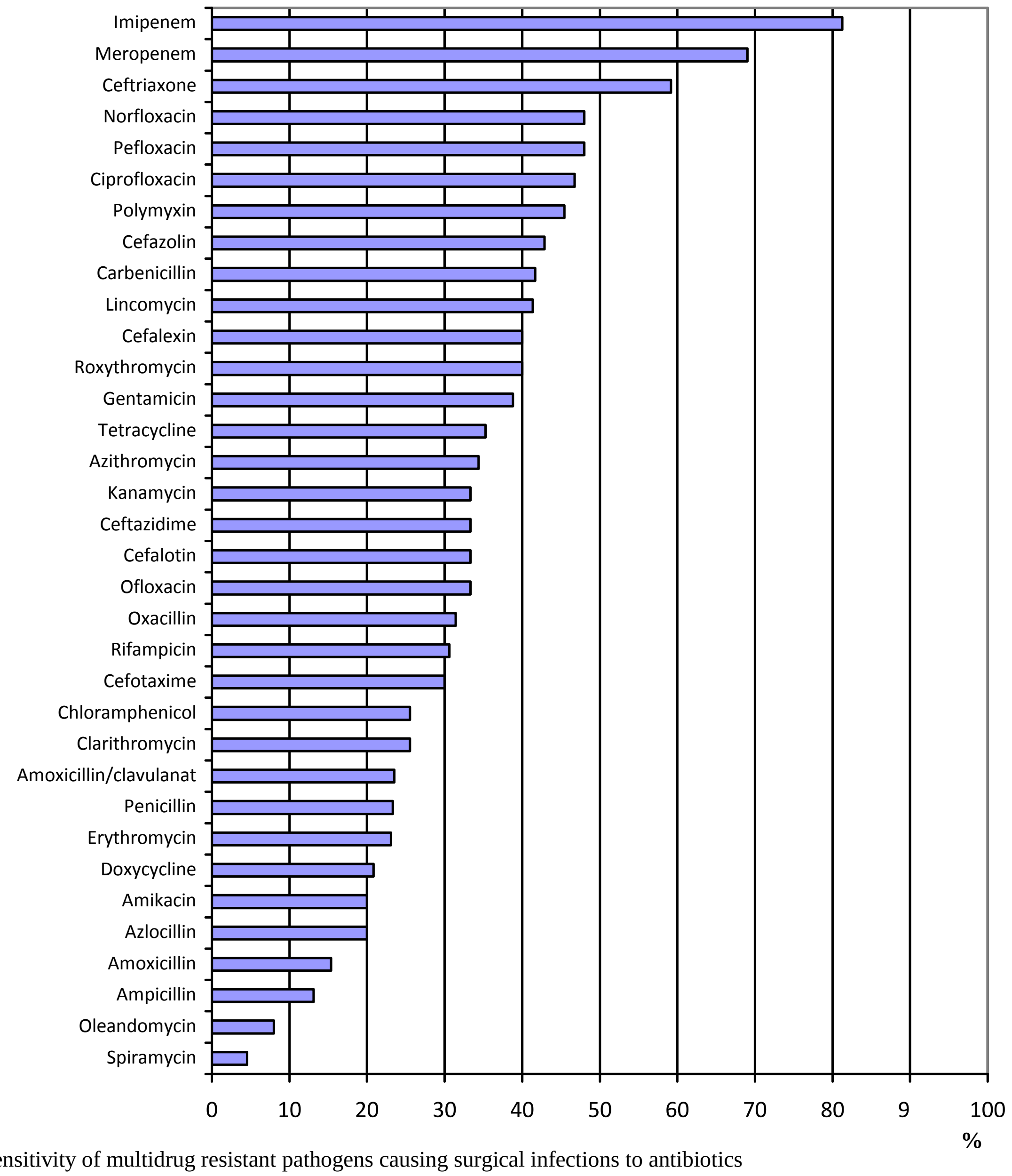

Figure 3. Sensitivity of multidrug resistant pathogens causing surgical infections to antibiotics

Since the greatest difficulties arise in the treatment of infections caused by multidrug resistant strains, we analyzed the sensitivity of multidrug resistant pathogens causing surgical infections to antibiotics (Figure 3). The highest activity was in carbapenems: to imipenem and meropenem 81.3% and 69.1% of multidrug resistant pathogens were susceptible, respectively. Also, high activity was in ceftriaxone (59.2% susceptible strains) and fluoroquinolones: to norfloxacin and pefloxacin 48% of strains were susceptible, to ciprofloxacin-46.8% of strains. The lowest activity was determined in some penicillins (ampicillin and amoxicillin were active only against 13.1% and 15.4% of strains, respectively) and in some macrolides (to rovamycin and oleandomycin were only 4.5% and 8% of susceptible strains, respectively).

High activity of carbapenems against multidrug resistant bacteria, demonstrated in the present study, is in consent with other published studies on antibiotic resistance surveillance: the SMART (Study for Monitoring Antimicrobial Resistance Trends) surveillance program conducted in Spain in 2002-2010 evaluated antibiotic susceptibility of Gram-negative bacteria isolated in patients with intra-abdominal infections with special attention to isolates producing extended spectrum β-lactamases. The most active antibiotic was ertapenem from carbapenem group which therefore was recommended as the empirical choice for treatment (Cantón et al. 2011). However, resistance to carbapenems is also on the rise (Chen and Hsueh 2012; Gutkind et al. 2013; Pitout et al. 2015; Morrill et al. 2015), which emphasizes the need to constant monitoring antibiotic resistance profiles in hospitals.

The results of the study indicate a high prevalence of multidrug-resistance pathogens among surgical infections: more than 60% of the agents of surgical infections in general surgical hospital are multidrug resistant, with the highest prevalence of multidrug-resistance in *Klebsiella*, *Enterobacter*, *Proteus* spp., and *Pseudomonas aeruginosa*. This requires continuous monitoring of antibiotic resistance both in the country level and in every hospital. A positive correlation was revealed between isolation of *Staphylococcus* and *Proteus* spp. in patients with surgical infections. This bacterial association should be further studied for understanding biological mechanisms of relationship between these bacterial species. In spite of general low susceptibility of isolated bacterial strains to antibiotics, carbapenems and fluoroquinolones showed promising activity against multidrug resistant strains, and therefore, their activity against multidrug resistant bacteria should be further evaluated alone and in combinations in *in vivo* and *in vitro* studies. Future researches should also be directed on search for new methods to cope with multidrug-resistance in surgical hospitals, such as to evaluation of combinations of antibiotics and antibiotics with other classes of antimicrobial agents, especially in *in vivo* studies.

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TRANSPARENCY DECLARATION

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. No writing assistance was utilized in the production of this manuscript.

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