Bulletin of the *Transilvania* University of Braşov
Series VI: Medical Sciences • Vol. 5 (54) No.2 - 2012

THE SPECTRUM OF INFECTIONS AND THE RESISTANCE TO ANTIBIOTICS OF ENTEROBACTER SPECIES

G. RADU[1] M.L. ŞTEFAN[2] M. IDOMIR[1]

Abstract: *The study was retrospective and included 112 Enterobacter strains isolated from the prelevates of the patients hospitalized in the Clinical County Emergency Hospital Braşov during 6 months (1.01.2010-31.06.2010). The aims of our study were to analyze the spectrum of infections caused by Enterobacter spp. and the assessment of the resistant strains isolated from the prelevates of the hospitalized patients.The etiological spectrum of infections produced by Enterobacter species was large, these germs being most frequent implicated in urinary tract infections (48%) and wound infections (27%). The resistance of Enterobacter spp. to beta-lactams was high, especially to ampicillin (94,92%). The level of resistance to quinolones was relatively high, but the role of these antibiotics is still important in the therapy of Enterobacter spp. infections. The resistance to amynoglicosides was different, being higher in case of gentamicin (51,56%). The sensitivity of Enterobacter spp. to carbapenems and colistin was very high, these antibiotics representing the therapeutical solution even in infections produced by Enterobacter ESBL-producing strains. The selection of resistant strains for these antibiotics is however worrying. The obtained results sustain the need of implementing coherent strategies for the monitoring of the occurrence and spread of the resistance phenomenon.*

Key words: *Enterobacter spp., antimicrobial resistance, infections.*

1. Introduction

Enterobacteriaceae family includes Gram-negative bacilli with wide spread in nature, classified in 44 genres, from which 25 are of medical interest. The Enterobacter genre includes 14 species, the most implicated in pathology being E cloacae, E. aerogenes, E. sakazakii and E. gergoviae. Species as E. hormaechei, E. cancerogenus, E. asburiae and E. taylorae may lead to human infection but in much smaller proportion [1].

Enterobacteriaceae are an important cause of nosocomial infections. These germs are also involved in community infections, especially in the urinary tract infections. [1], [5], [15], [18].

Enterobacter species can be the etiological agent of respiratory tract infections, skin and soft tissue infections, biliary tract infections, catheter infections, meningitis [1,2], [7,8],[10].

[1] Faculty of Medicine, *Transilvania* University of Braşov
[2] Clinical County Emergency Hospital of Braşov

More rarely, strains of Enterobacter spp. are isolated from patient with endocarditis, osteomyelitis, septic arthritis, bacteremia and meningitis [3], [9].

Enterobacter species are intrinsic resistant to aminopenicilins, cefazolin and cefoxitin due to the AmpC beta-lactamase production, typically encoded on the chromosome [4],[13]. The resistance of Enterobacter strains to the third generation of cephalosporins is usually caused by the production in excess of AmpC beta-lactamase [15].

ESBL (extended spectrum beta lactamases) are enzymes that hydrolyze the oximino - group of the beta-lactamic ring having the ability to inactivate penicillins, oximino - cephalosporins and monobactams [4],[15].

Studies showed that the administration of broad-spectrum cephalosporins represent an independent risk factors for resistance. [12]

The presence of ESBL producing strains is often associated with therapeutic difficulties because these germs are often resistant to various classes of antibiotics (e.g. cephems, quinolones, aminoglycosides, tetracyclines, trimethoprim-sulfamethoxazole) [5,6],[11].

Carbapenems still represent the best choice for the tratament of infections with ESBL producing strains but the increasing of the resistant strains number is a great concern. [5]

Colistin (polymyxin E) is also considered an effective and safe drug for the therapy of severe infections due to multidrug-resistant gram-negative bacteria [17].

During the last decade, the emergence and the dissemination of ESBL strains became a concerning problem worldwide [14],[16].

All the physicians should understand the importance of the problem and practice a rational prescribing of antibiotics [19].

Surveillance of antibiotic resistance must be performed in hospitals [20,21].

The aims of our study were to analyze the spectrum of infections caused by Enterobacter species and the assessment of the resistant strains isolated from the prelevates of the hospitalized patients.

2. Material and methods

Our study was retrospective and included 112 Enterobacter strains isolated from the prelevates of the patients hospitalized in the Clinical County Emergence Hospital Braşov during 6 months (1.01.2010-31.06.2010).

From the prelevated samples, Gram smears and insemination in culture media (Columbia Blood Agar, McConkey Agar, U.T.I. Agar) were made. The calibrated loop method was used for the quantitative urine culture.The identification of Enterobacter strains were made using biochemical identification tests (Triple Sugar Iron Agar, SIM Medium, Simmons Citrate Agar) and the automated Vitek 2 Compact system. The testing of sensitivity to antibiotics was made by difusimetric method and automated Vitek 2 Compact system. The interpretation of the results of the antibiograms was made according to CLSI 2010 (Clinical Laboratory Standard Institute).

3. Results and discussions

The first objective of our study consisted in the evaluation of the spectrum of infections produced by Enterobacter spp.

The results are presented in Table 1.

Table 1

Pathological products	No. of samples
Urine	54
Wound secretions	30
Sputum	13
Puss	8
Peritoneal fluid	5
Pleural fluid	1
Vaginal discharges	1
Total	**112**

The etiological spectrum of the infections produced by Enterobacter species was large. These germs were most frequent implicated in urinary tract infections (48%) and wound infections (27%).

More rarely, the Enterobacter strains were isolated from sputum, puss, peritoneal and pleural fluids and vaginal discharges in the case of our study.

The graphical representation of the data is illustrated in Figure 1.

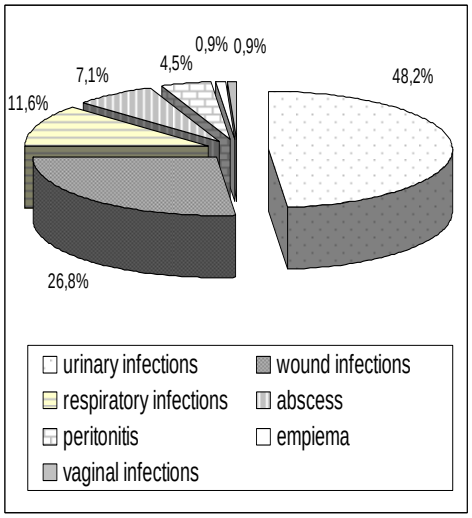

Fig. 1. *The spectrum of infections produced by Enterobacter spp.*

During the study, according to the isolated germ, different antibiotics were tested: beta-lactams (ampicillin – Amp; amoxicillin –clavulanic acid – Amc; ceftriaxone – Cro; ceftazidime - Caz), quinolones (ciprofloxacin – Cip; norfloxacin – Nor; levofloxacin - Lev), aminoglycosides (gentamicin – G; amikacin - Ak), carbapenems (imipenem; Ipm, meropenem - Mem) and polimixines (colistin - Co).

Another objective of our study consisted in the evaluation of antimicrobial resistance of Enterobacter species strains isolated from different pathological products, during the studied period.

Initially, we have analyzed the level of resistance to beta-lactams of Enterobacter strains isolated from different pathological products.

The obtained results are illustrated in Figure 2. It can be observed the high level of resistance of Enterobacter strains to the tested beta-lactams antibiotics, especially to ampicillin.

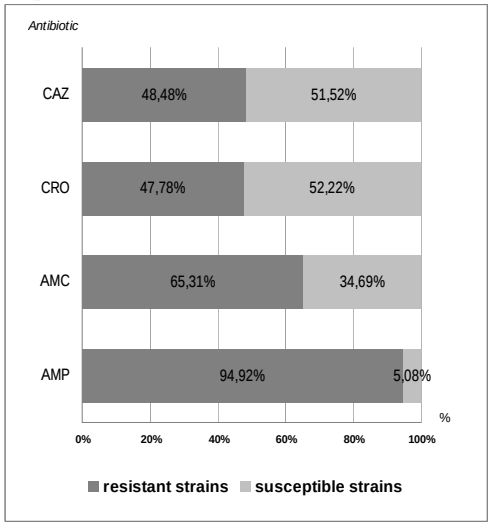

Fig. 2. *The resistance to beta-lactams of Enterobacter strains*

It has been also analyzed the level of the resistance of Enterobacter spp. to the usual quinolones, as shown in figure 3.

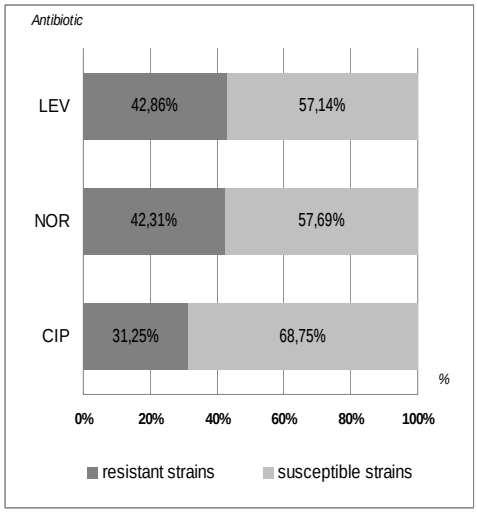

Fig. 3. *The resistance to quinolones of Enterobacter strains*

The level of resistance is relatively high but these antibiotics can still be used with success in therapy. Further, we have evaluated the sensitivity to aminoglycosides of Enterobacter strains, as shown in figure 4.

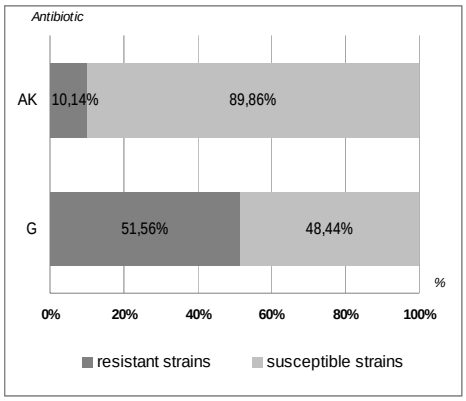

Fig. 4. *The resistance to aminoglycosides of Enterobacter strains*

The level of resistance was different for the two tested antibiotics, probably due to the different using rate in therapy.

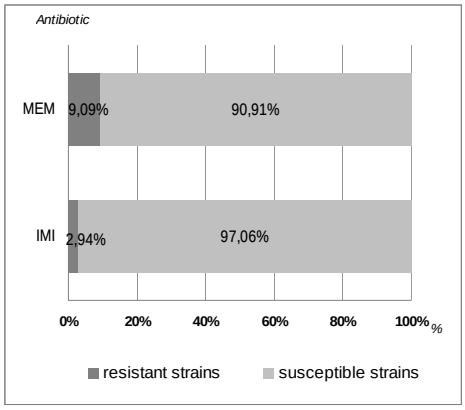

Fig. 5. *The resistance to carbapenems of Enterobacter strains*

As shown in the figure 5, the susceptibility to carbapenems was high, these antibiotics representing the therapeutic solutions even in infections caused by the ESBL-producing strains.

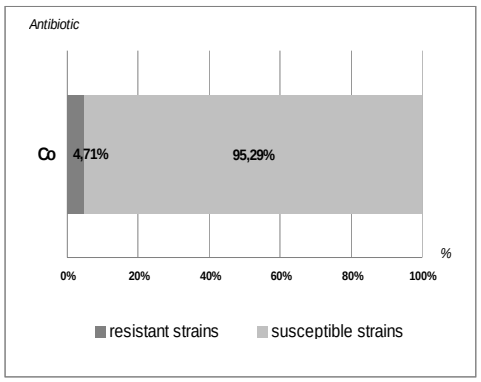

Fig.6. *The resistance to polimixines of Enterobacter strains*

The sensitivity in vitro to colistin of the isolated Enterobacter strains was also very high.

The levels of resistance resulted from the study have been high for the majority of the tested antimicrobial. The values were slightly higher than in previous studies carried out in the same medical facility, fact which is worrying although it could have been influenced by the lower duration of the study.

The resistance levels are comparable with those reported in many international studies for Enterobacter strains isolated in hospitals.

4. Conclusions

1. The etiological spectrum of infections produced by Enterobacter species was large, these germs being most frequent implicated in urinary tract infections (48%) and wound infections (27%).
2. Resistance of Enterobacter strains to beta-lactams was high, especially to ampicillin.
3. The level of resistance to quinolones was relatively high, but the role of these antibiotics must not be ignored since they could be still used with success in the therapy of Enterobacter infections.

4. The resistance to amynoglicosides was different, being a lot higher in case of gentamicin than for amikacin.
5. The sensitivity of Enterobacter spp. to carbapenems and colistin was very high, these antibiotics representing the therapeutical solution even in infections produced by ESBL-producing strains. The selection of nosocomial resistant Enterobacter strains for these antibiotics is however worrying.
6. The obtained results sustain the need of implementing coherent strategies for the discerning practice of antibiotic prescription and for the monitoring of the occurrence and spread of the resistance phenomenon.

References

1. Buiuc., D., Neguţ, M.: *Tratat de Microbiologie clinică*, IIIrd Edition. Editura medicală, 2009, p. 696-700.
2. Choi, S.H., Lee, J.E, et al.: *Prevalence, microbiology, and clinical characteristics of extended-spectrum beta-lactamase-producing Enterobacter spp., Serratia marcescens, Citrobacter freundii and Morganella morganii in Korea.* In: Eur J Clin Microbiol Infect Dis, 2007, 26(8), p. 557 – 561.
3. Deal, E., Micek, S., Ritchie, D., et al.: *Predictors of in-hospital mortality for blood stream infections caused by Enterobacter species or Citrobacter freundii*. In: Pharmaco-therapy, 2007, 27(2), p. 191-199.
4. Dima, L., Idomir, M., et al.: *Infecţii cu Enterobacteriaceae producătoare de ESBL – prevalenţă şi aspecte terapeutice*. In: Jurnal Medical Braşovean, 2010, vol. 3, p. 66-72.
5. Falagas, M.E., Karageorgopoulos, D.E.: *Extended-spectrum b-lactamase-producing organisms*. In: Journal of Hospital Infection, 2009, vol. 73, p. 345-354.
6. Idomir, M., Fiţ, R., Guth, R.: *Dinamica rezistenţei la antibiotice a Enterobacter sp*. In: Acta Medica Transilvanica, 2007, vol. 2, p. 59-61.
7. Idomir, M., Fiţ, R., Nemet, C., Leaşu, T.: *Evaluarea rezistenţei Enterobacter species la substanţe antimicrobiene*. In: Jurnal Medical Braşovean, 2008, nr. 3, p. 40-45.
8. Idomir, M., Gavrilă, et al.: *Infecţiile urinare cu enterobacteriaceae – dificultăţi terapeutice*. In: Jurnal Medical Braşovean, 2010, nr. 3, p. 62-65.
9. Idomir, M., Ionescu, R., et al.: *Rezistenţa la antibiotice a germenilor izolaţi prin hemocultură*. In: Jurnal Medical Braşovean, 2007, nr. 1, p. 40-46.
10. Idomir, M., Nemet, C., Bratu, C., Cheşcă, A.: *Evaluation of etiological spectrum and therapeutically problems in varicose ulcer infections.* In: Bulletin of the Transilvania University of Braşov, Series VI: Medical Sciences, 2010, 3(52), p. 33-36.
11. Idomir, M., Pruteanu, E., Cheşcă, A.: *The dynamics of resistance to quinolones in Gram negative bacteria isolated from the hospitalized patients*. In: Bulletin of the Transilvania University of Braşov, Series VI, 2011, No. 1, 4(53), p. 7-10.
12. Kaye, K.S., Cosgrove, S., et al.: *Risk Factors for Emergence of Resistance to Broad - Spectrum Cephalosporins among Enterobacter spp.* In: Antimicrob Agents Chemother, 2001, 45(9), p. 2628–2630.
13. Kim, J., Lim, Y.: *Prevalence of Derepressed AmpC Mutants and Extended-Spectrum β-Lactamase Producers among Clinical Isolates of* „*Citrobacter freundii*, *Enterobacter* spp." and „*Serratia marcescens"* in Korea: Dissemination of CTX-M-3, TEM-52, and SHV-12, In: J Clin Microbiol, 2005, 43(5), p. 2452–2455.

14. Nedjai, S., Barguigua, A., Djahmi, N., et al.: *Prevalence and characterization of extended spectrum beta-lactamases in Klebsiella – Enterobacter - Serratia group bacteri, in Algeria*. In: Médecine et maladies infectieuses, 2012, vol. 42, p. 20–29.
15. Paterson, D.L.: *Resistance in gram - negative bacteria: Enterobacteriaceae*. In: The American Journal of Medicine, 2006, 119(6 Suppl 1), S20–S28.
16. Pfeifer, Y., Cullik, A., et al.: *Resistance to cephalosporins and carbapenems in Gram - negative bacterial pathogen*. In: International Journal of Medical Micro-biology, 2010, 300(6), p. 371-379.
17. Pintado, V., *et al*.: *Intravenous colistin sulphomethate sodium for therapy of infections due to multidrug-resistant gram-negative bacteria*. In: Journal of Infection, 2008, 56, p. 185-190.
18. Pitout, J.D., Nordmann, P., et al.: *Emergence of Enterobacteriaceae producing extended-spectrum b-lactamases (ESBLs) in the community*. In: J Antimicrob Chemother 2005, vol. 56, p. 52-59.
19. Sharma, L., Sharma, C.L., Kapoor, B.: *Antibacterial resistance: Current problems and possible solutions*. In: Indian J Med, 2005, 59(3), p. 120-129.
20. Truls, E.B.J., Mete, C., et al.: *Hospital acquired urinary tract infections in urology departments: pathogens, susceptibility and use of antibiotics. Data from the PEP and PEAP-studies*. In: International Journal of Antimicrobial Agents, 2006, 28S, S91–S107.
21. Wagenlehner, F.M.E., Niemetz, A.M., et al.: *Spectrum and antibiotic resistance of uro - pathogens from hospitalised patients with urinary tract infections: 1994–2005*. In: International Journal of Antimicrobial Agents, 2008, 31S, S25–S34.