CONSIDERATIONS ABOUT SUSCEPTIBILITY TO ANTIBIOTICS OF UROPATHOGENICS *KLEBSIELLA PNEUMONIAE* STRAINS

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**Abstract. Objective:** This study aimed to determine and analyze the antibiotic sensitivity of Klebsiella pneumoniae strains isolated from urine cultures. **Material and methods:** Retrospective, comparative study, performed within the Craiova Clinical Hospital for Infectious Diseases “Victor Babeş”, determining the evolution of the chemosensitivity of uropathogenic Klebsiella pneumoniae in urinary tract infections, during 2000-2004 and 2005-2008. **Results:** During 2000-2004, we identified 161 pathologic urine samples bacteriologically positive for Klebsiella pneumoniae (15.01% of the total positive urocultures) and we analyzed them through antibiogram testing. Between 2005-2008, we identified 127 pathological bacteriologically positive urine samples (13.23% of all positive urine cultures). The rates of susceptibility to antibiotics tested in the first period of the study were: 33.7% for amoxicillin/clavulanic acid, 77.15% for aztreonam, 89.46% for cefoperazone-sulbactam, 85% for ceftazidime, 84% for amikacin, 79.91% for gentamicin, 74.13% for ofloxacin, 84.25% for norfloxacin, 84.71% for colistin and 96.59% for meropenem. During the second studied period, the rates of susceptibility to antibiotics were: 22.22% for amoxicillin-clavulanic acid, 62.65% for aztreonam, 52.51% for cefoperazone-sulbactam, 76% for ceftazidime, 84.31% for amikacin, 70% for gentamicin, 69.69% for ofloxacin, 65.82% for norfloxacin, 57.14% for nalidixic acid, 80.35% for colistin and 95.96% for meropenem. **Conclusions:** Increased susceptibility of K. pneumoniae to meropenem and certain aminoglycosides (amikacin) is maintained. We noticed an increasing trend in the sensitivity to colistin and a declining trend in that to quinolones and certain IIIrd generation cephalosporins (ceftazidime, cefoperazone-sulbactam). **Keywords:** urinary tract infections, K. pneumoniae, susceptibility

**Introduction**

*U* rinary tract infections (UTIs) represent a widespread pathology for the medical practice and an important public health issue, frequently requiring hospitalization [1,2,8]. *Klebsiella pneumoniae* is one of the pathogen agents commonly involved in the etiology of UTIs [2,8] which currently presents altering of its sensitivity phenotype. Antibiotic resistance is a dynamic phenomenon which permanently requires observational studies according to which the therapeutic recommendations need to be adjusted.

**Objectives**

This study aimed to determine and analyze the antibiotic sensitivity of *Klebsiella pneumoniae* strains isolated from urine cultures.

**Material and methods**

Retrospective, comparative study on the sensitivity phenotype of *K. pneumoniae*, performed within...
the Microbiology Laboratory of the Craiova Clinical Hospital for Infectious Diseases “Victor Babeș” during 2000-2004 and 2005-2008.

We studied the *Klebsiella pneumoniae* strains isolated from urine cultures, through KIRBY-BAUER diffusimetric antibiograms. We analyzed their sensitivity to betalactamines, aminoglycosides, quinolones and colistin.

We considered the strains which presented resistance to at least 3 classes of antibiotics as being multiresistant.

The collected data were statistically processed through the Epi Info software, the statistic significance of the correlations being evaluated through the Fischer test, considering the value of *p* < 0.05 as statistically significant and calculating the relative risk (RR).

**Results**

In the first of the studied intervals, between 2000-2004, 161 *K. pneumoniae* UTIs were diagnosed, representing 15.01% of the total UTIs with positive urocultures.

The rate of sensitivity to the tested antibiotics (see diagram 1) was extremely reduced for amoxicillin-clavulanate (33.70%), reduced for colistin and nalidixic acid (62.71%, 67.16%). Aztreonam, cefoperazone-sulbactam, ceftazidime, amikacin, gentamicin, norfloxacin and ofloxacin presented a median sensitivity, with values ranging from 74.13% to 89.46%. High sensitivity was registered for meropenem (96.59%).

A comparison of the antibiotic susceptibility recorded during the two timelines revealed the same reduced sensitivity to amoxicillin-clavulanate, nalidixic acid, a decreasing tendency of the sensitivity to certain IIIrd generation cephalosporins and to certain fluoroquinolones, an increasing tendency of the sensitivity to colistin and a preserved elevated sensitivity to aminoglycosides and high sensitivity to meropenem.

The meropenem-resistant *K. pneumoniae* strains were analyzed for resistance to colistin, thus revealing a correlation between the two tested antibiotics, so that the risk of developing resistance to colistin is elevated in meropenem-resistant strains (*p*<0.05; 1.93< RR=3.84<7.63).

Out of the 6 strains of meropenem-resistant *K. pneumoniae*, 3 were capable of producing extended spectrum beta lactamase (ESBL). This resistance was noticed in the second interval of our study, only between 2005 and 2006 (see diagram 3).

Multiresistant *K. pneumoniae* (see diagram 4, 5) was encountered with a higher frequency (14.17%) in the second period of the study, compared to the first study interval (9.31%).
Discussion

Nowadays, when the germs’ resistance to antibiotics is continually increasing, a bacteriologic diagnosis is mandatory. The excessive use of antibiotic therapy in the absence of a bacteriologic diagnosis represents one of the factors involved in developing antibiotic resistance.

It has been proven that the intensive use of fluoroquinolones has led to the decrease in the efficiency of this therapeutic class in the treatment of gram-negative UTIs.

Meropenem is an optimal antibiotic in the therapy of *K. pneumoniae* UTIs, but the role of ESBL producing strains is not to be overlooked [1,5]. The resistance of *K. pneumoniae* to carbapenems is nowadays a worldwide spread subject of concern, Greece reporting a resistance of 1% in 2001 and of 20% in 2006, in hospitalized patients [3,4,9]. In the USA, this phenomenon is also treated with utmost interest, new strategies currently being employed for identifying the beta lactamases produced by *K. pneumoniae* [6,7].

Our study showed an increase in meropenem resistance from 3% in the first time span to 4.5% in the second time span, which lead us to the conclusion that the evolution of the resistance to carbapenems is comparable to the South European pattern. Our study only refers to the uropathogenic strains; therefore, there is need for additional, extended studies on *K. pneumoniae* strains of diverse origins.

As such, colistin could remain the optimal therapeutic solution [5], but the risk of developing resistance over time cannot be overlooked and its widespread use requires caution.

Currently, IIIrd generation cephalosporins are not an optimal therapy, being indicated only in the cases with confirmed etiology and chemosensitivity.

Antibiotherapy conducted according to the antibiogram is of utmost importance for all UTIs, the current list of efficient antibiotics being quite limited, and the treatment of UTIs being considerably correlated with a risk of resistance development.

Conclusions

1. We identified significant altering of the sensitivity phenotype of *K. pneumoniae*.
2. The rate of decreased sensitivity of *K. pneumoniae* to amoxicillin-clavulanate and to 1st generation quinolones entails the requirement of avoiding these drugs as first intention therapy in UTIs.
3. Colistin is an efficient therapeutic solution for *K. pneumoniae* UTIs, but its role is controversial when dealing with carbapenem-resistant strains.

4. The role of meropenem in the therapy of UTIs is threatened by the emergence of extended spectrum beta lactamase producing strains.

References