The prevalence of infections and colonisation with *Klebsiella pneumoniae* strains isolated in ICU patients

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Abstract

**Background:** *Klebsiella* spp. are among the bacteria most commonly isolated from patients with infections in ICUs. The source of these infections may be the microflora of the patient or the hospital environment. Increasingly, *Klebsiella* strains are also being isolated from epidemic outbreaks. This situation is largely the result of widespread, irrational antibiotic use, the virulence of the bacterial strains and their ability to survive in the hospital environment. The purpose of this dissertation was to estimate the prevalence of *Klebsiella pneumoniae* strains isolated from patients hospitalised in a single ICU.

**Methods:** Seventy-eight isolates of *K. pneumoniae* were studied. The identification and the susceptibility to selected antibiotics were tested by an automated system, VITEK2 Compact. For the analysed strains, the production of different beta-lactamases was noted.

**Results:** Production of ESBL was detected in 64.1% of the *K. pneumoniae* strains isolated from infections and 74.4% from rectal swabs. Most of the strains were susceptible to imipenem (97.7%) and meropenem (96.1%). Sixty-nine (57.0%) of the analysed strains were identified as multidrug resistant.

**Conclusion.** Most of the analysed *Klebsiella pneumoniae* strains produced ESBL-beta-lactamases. The frequency of colonisation and infection with multidrug resistant strains of *K. pneumoniae* in patients hospitalised in the ICU is very high.

Key words: infection, colonisation; *Klebsiella*, ICU

Infections in patients treated in intensive care units (ICUs) are of interest not only to clinicians but also to microbiologists and epidemiologists. The ongoing research studies on microbiological analysis focus on types of microorganisms, phenotypes of drug susceptibility, evaluation of genetic relationships among strains, clinical symptoms and antibiotic therapy. Each ICU is characterised by a specific profile of microorganisms that cause infections. A significant problem for patients treated in ICUs is infection with *Klebsiella pneumoniae*, which produces various types of beta-lactamases [1–4]. The majority of *K. pneumoniae* strains are multidrug resistant (MDR), and the therapeutic options for such infections are extremely limited. *K. pneumoniae* bacteria are among the three most common species of Gram-negative bacteria responsible for infections in ICU patients [5, 6].

Once a patient is admitted to a hospital, the patient’s physiological microflora is replaced with hospital microflora, which can cause infections. Colonisation and development of MDR infections is significantly affected by long hospitalisations (in the ICU, in particular) and broad-spectrum antibiotic therapy. Therefore, the aim of the present study was to evaluate the prevalence of colonisation and infections with *K. pneumoniae* in ICU patients.
METHODS

The study involved *K. pneumoniae* strains isolated from patients treated in the Department of Anaesthesiology and Intensive Therapy between January, 2010 and December, 2012. Each strain was isolated from a different patient. The ages of the patients ranged from 29 to 94 years. Strains were isolated from bronchoalveolar lavage (BAL) — 38 (48.7%), urine — 15 (19.2%), wound swabs — 10 (12.8%), blood — 8 (10.2%), vascular catheters and peritoneal fluid — two strains each, as well as pleural fluid, abdominal fluid and sputum — 1 strain each. Additionally, rectal swabs were taken from 46 patients to evaluate *K. pneumoniae* colonisation of the gastrointestinal (GI) tract. For samples other than rectal swabs, the susceptibility to the following antibiotics was determined: amoxicillin with clavulanic acid, piperacillin with tazobactam, ceftazidime, cefepime, imipenem, meropenem, amikacin, tobramycin and ciprofloxacin using the AST-N259 cards in the automated system VITEK2 Compact (bioMérieux). Species-level identification was performed using the GN cards in the system mentioned above. The capacity to produce extended-spectrum beta-lactamases (ESBL) was determined for each strain. For *K. pneumoniae* strains of lower susceptibility or resistant to at least one carbapenem, the ability to produce metallo-beta-lactamases (MBL) and carbapenemases (KPC) was evaluated according to the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) [7] and the National Reference Centre for Antimicrobial Susceptibility [8].

RESULTS

The study included 578 patients: 206 (35.6%) in 2010, 180 (31.2%) in 2011 and 192 (33.2%) in 2012. *K. pneumoniae* strains were isolated from 78 (13.5%) patients from various material samples: in 2010 — 19 (24.3%), in 2011 — 23 (29.5%) and in 2012 — 36 (46.2%) strains. Amongst 78 *K. pneumoniae* strains isolated, 50 (64.1%) strains produced ESBL enzymes: in 2010 — 10 (20.0%), in 2011 — 12 (24.0%) and in 2012 — 28 (56.0%) strains.

*K. pneumoniae* strains were cultured from 43 (93.5%) samples from rectal swabs; 32 (74.4%) of them produced ESBL enzymes. Among 43 (55.1%) patients with *K. pneumoniae* strains identified in rectal swabs or other samples, strains of ESBL-positive phenotype were found in 31 (67.4%) cases whereas the ESBL-negative phenotype were detected in 8 (17.4%) cases. Among strains of different phenotypes, ESBL-positive strains isolated from urine and blood, plus ESBL-negative ones isolated from wound swabs, were detected in three patients; one patient had an ESBL-negative strain from a wound swab and an ESBL-positive strain from a rectal swab.

Eighty-two (94.3%) patients received antibiotics during sample collection for microbiological examinations. Twenty-nine (37.2%) received three or more antimicrobial drugs. The most common agents they received were imipenem (24 — 30.8%), vancomycin (22 — 28.2%) and colistin (14 — 17.9%). Thirty-six (46.1%) patients were administered III/IV generation cephalosporins or carbapenems — the drugs essential for the selection of ESBL-positive strains. All *K. pneumoniae* strains were also evaluated for the presence of beta-lactamases other than ESBL. Among 82 (67.8%) ESBL-positive strains, four simultaneously produced AmpC beta-lactamases (strains were isolated from BAL, blood, wound swabs and rectal swabs) and two produced MBL (isolated from BAL and blood). None of the strains had the ability to produce KPC.

Among *K. pneumoniae* strains inducing various mechanisms of resistance, 69 (57.0%) were defined as MDR, 29 of them were isolated from the rectal swabs.

Moreover, the highest number of *K. pneumoniae* strains were susceptible to carbapenems: 76 (97.4%) to imipenem and 75 (96.1%) to meropenem. The percentages of strains susceptible to the remaining antibiotics were as follows: 27 (34.6%) susceptible to ceftazidime; 26 (33.3%) to amikacin; 24 (30.8%) to tobramycin; 23 (29.4%) to ceftriaxone; 20 (25.6%) to ciprofloxacin and 16 (20.5%) to piperacillin with tazobactam. None of the strains were found susceptible to amoxicillin with clavulanic acid and 31 (39.8%) strains were defined as intermediate. During the study period, the guidelines regarding criteria of drug susceptibility to amoxicillin with clavulanic acid were changed. This drug was administered to 4 patients.

Among *K. pneumoniae* strains isolated from BAL and blood, two were susceptible to only one of the antibiotics examined, and another two isolated from urine were resistant to all of the antibiotics considered.

DISCUSSION

According to some authors, *K. pneumoniae* bacilli are second only to the *Escherichia coli* species from the family *Enterobacteriaceae* in their responsibility for infections in ICU patients [5, 6, 9]. The major types of infections that occur with these bacteria include infections of the blood, urinary system, ventilator-associated pneumonia, and surgical wound infections [10].

One of the most common mechanisms of resistance to antibiotics in *Klebsiella* spp. is the production of extended-spectrum beta-lactamases. Although the first species of this phenotype was described in 1983 [11], they still present a serious diagnostic, clinical and epidemiological problem, which is associated with the occurrence of new ESBL variants that have a broader spectrum of action and are non-susceptible to beta-lactamase inhibitors. Initially, the species of this phenotype were resistant to penicillins and cephalosporins of older generations. During evolution
of beta-lactamases, the species able to produce them have been found increasingly resistant to all beta-lactam antibiotics except the carbapenems. Moreover, overlapping of various mechanisms of resistance is of importance.

The therapy for infections caused by the bacteria developing this mechanism of resistance to antibiotics entails increasingly high treatment costs. Target antibiotic therapy does not ensure recovery, and hospital infections with ESBL-positive species are characterised by high mortality. Moreover, the hospital environment favours the survival of the bacteria in question. In the study period, K. pneumoniae were isolated seven times from the environment of three departments (cardiac surgery, vascular surgery and angiology, as well as paediatric, haematology and oncology); in 2010 — 5 species and in 2012 — two species. K. pneumoniae species were also isolated from patients of the above-mentioned departments. Three of the 7 species isolated from the environment produced ESBLs. The findings of the study by Mączyńska and co-workers [12] confirm that epidemic clones of K. pneumoniae can survive in the environment, even for several months.

The epidemiological situation is considerably affected by frequent use of 3rd and 4th generation cephalosporins and carbapenems (due to the patient’s condition). Another problem, which has already been mentioned, is the diversity of these enzymes and their ease of spread, not only within the species of one genus but also within bacterial families or groups. More than 300 variants of ESBLs are known [13]. The most frequently isolated strains are those from the family Enterobacteriaceae producing extended-spectrum beta-lactamas from the families CTX-M, TEM and SHV [14]. The strains producing CTX-M beta-lactamases predominate in Europe, Canada, South America and Asia [14−16]. Although the mechanisms condition the resistance to beta-lactams, it should be remembered that in many cases, the genes conditioning the resistance to antibiotics of other groups (i.e., aminoglycosides, quinolones, tetracyclines) are localised on the same plasmid encoding ESBLs. In such cases, MDR strains are detected. K. pneumoniae strains that exhibit reduced susceptibility or are resistant to carbapenems are increasingly detected, and this is also the case in our hospital. Therefore, the drug susceptibility of bacteria belonging to species that easily acquire resistance genes should be monitored. An additional problem is the eradication of K. pneumoniae strains due to the place of residence. The fact that ICU patients are hospitalised in other departments and wards is also of significance.

Our findings demonstrate that the prevalence of GI tract colonisation with K. pneumoniae strains is high in ICU patients. Over 93% of our patients had GI tracts colonised with K. pneumoniae strains. Over 70% of the strains isolated simultaneously from the site of infection and from a rectal swab from the same patient had the same phenotype of drug susceptibility. Earlier studies [17] confirm that strains with the same drug susceptibility phenotype that are isolated from the GI tract and site of infection of a single patient are identical or closely genetically related.

GI colonisation with the ESBL-positive K. pneumoniae strains is a significant risk factor for infections with strains of this phenotype due to the easy transmission of the genes encoding this phenotype, the survival of these strains in the hospital environment, and hence, difficulties in their eradication.

CONCLUSIONS

1. The majority of K. pneumoniae strains isolated from ICU patients produce extended-spectrum beta-lactamases.
2. The prevalence of infections and colonisation with multidrug-resistant K. pneumoniae strains in ICU patients is high; therefore, monitoring of K. pneumoniae is recommended.

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