

ON THE ISSUE OF KLEBSIELLA PNEUMONIAE RESISTANCE IN YOUNG CHILDREN WITH CONGENITAL HEART DEFECTS

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Abstract: A prospective study was conducted to study resistance in *Klebsiella pneumoniae* in the intensive care unit of young children. It was revealed that resistance to III-IV generation cephalosporins, fluoroquinolones, aminoglycosides is caused by the production of extended spectrum β -lactamases (ESBLs), and to carbapenems due to a decrease in the permeability of the cell membrane in combination with the production of ESBLs. The characteristics of patients colonized with multi-resistant *K. pneumoniae* strains were identified.

Keywords: *K. pneumoniae*, sustainability, antibiotics, Extended spectrum β -lactamases.

INTRODUCTION: *Klebsiella pneumoniae* is one of the leading causative agents of nosocomial infections (NI), it causes from 2 to 20% of all nosocomial infections [1, 4]. In Uzbekistan, *K. pneumoniae* is the third most common gram-negative pathogen of NI. In a number of hospitals, *Klebsiella* is the predominant causative agent of NI, ranging from 24.5 to 43.6% [2]. One of the main clinically significant mechanisms of acquired resistance to β -lactams in *K. pneumoniae* is multiple resistance caused by the production of ESBLs [1, 3]. Carbapenems, primarily imipenem and meropenem, have the greatest stability to the action of ESBLs [1–4]. Currently, strains of *K. pneumoniae* resistant to carbapenems have been reported. To the mechanisms that determine stability

Carbapenems include both the production of β -lactamases of various molecular classes and the combination of ESBLs with reduced permeability of the cell membrane [3].

MATERIALS AND METHODS: In 2023, we conducted a prospective study to study the mechanisms of resistance in *K. pneumoniae* isolated from young children requiring treatment in an intensive care unit (ICU). The study included pediatric ICU patients colonized and with infections caused by *K. pneumoniae*. A total of 33 strains isolated from 27 patients were studied. The analysis included all successively isolated strains of *K. pneumoniae* in 2023. *K. pneumoniae* with the same resistance (susceptibility), repeatedly isolated from one patient, were excluded from the analysis.

RESULTS AND DISCUSSION: The strain isolated first was analyzed. Strains with moderate resistance (susceptibility) were classified as resistant. Pure cultures of *K. pneumoniae* were used to determine sensitivity. Sensitivity was studied using disks impregnated with antibiotics (BioRad, USA) on Mueller-Hinton agar (BioMerrier, France) using the disk diffusion method in accordance with the recommendations of the National Committee for Clinical and Laboratory Standards of the USA and Methodology - any instructions for determining the sensitivity of microorganisms to antibacterial drugs. Determination of ESBL production by *K. pneumoniae* strains using the double disk method using disks with amoxicillin/clavulanate (20/10 μ g), cefotaxime (30 μ g), ceftazidime (30 μ g). Carbapenem resistance was studied using discs impregnated with meropenem (10 μ g) and imipenem (10 μ g).

To detect metallo- β -lactamase (MBL), the synergy method between imipenem (10 μ g), meropenem (10 μ g), ceftazidime (30 μ g) and ethylenediaminetetraacetic acid (EDTA) was used.

Among the studied *K. pneumoniae*, the prevalence of strains resistant to β -lactam antibiotics was recorded ranging from 3 to 87%. The highest frequency was observed for third- and fourth-generation cephalosporins (cefotaxime and ceftriaxone - 87%, ceftazidime - 81%, cefepime - 78%), somewhat less frequently for inhibitor-protected penicillins (amoxicillin/clavulanate - 48%) and cephalosporins (cefoperazone/ sulbactam – 63%). The lowest frequency of resistant strains of *K. pneumoniae* was registered for carbapenems. At the same time, the greatest activity was observed in imipenem (resistance 6%), two strains were insensitive to it. Resistance to meropenem was 15% (5 strains). All strains were classified as moderately sensitive (Table 1).

Table 1

Antibiotic resistance of *K. pneumoniae*, n = 33

| Antibiotics | Sensitivity, % | Moderate sensitivity, % | Stability, % |
|-------------------------|----------------|-------------------------|--------------|
| Amoxicillin/clavulanate | 46 | 6 | 48 |
| Ceftriaxone | 13 | — | 87 |
| Cefotaxime | 16 | — | 84 |
| Ceftazidime | 16 | 3 | 81 |
| Cefoperazone/sulbactam | 28 | 9 | 63 |
| Cefepime | 22 | — | 78 |
| Imipenem | 94 | 3 | 3 |
| Meropenem | 85 | 15 | 15 |
| Ciprofloxacin | 43 | — | 57 |
| Amikacin | 64 | 6 | 30 |
| Netilmicin | 61 | 6 | 33 |

In our study, in 73.7% of cases, producers were insensitive to ciprofloxacin, in 26.3% to amikacin, and in 31.6% to netilmicin. All *Klebsiella* resistant to III–IV generation cephalosporins were sensitive to imipenem and meropenem, the drugs of choice for empirical treatment of severe and life-threatening infections [1, 2, 4, 9]. Currently, carbapenem-resistant *K. pneumoniae* are registered in North America, Greece, Turkey, Israel, and India [4].

CONCLUSION: This prospective study allowed us to identify carbapenem-resistant *K. pneumoniae* in young children with complex congenital heart disease who require long-term treatment in the ICU after cardiac surgery. In 71.4% of cases (5 patients), patients had previous hospitalization in the ICU and received broad-spectrum antimicrobial therapy. In the medical history of three (42.8%) patients there was evidence of the isolation of ESBL-producing *Klebsiella* during a previous hospitalization. This fact suggests that young children with complex congenital heart disease, who require long-term therapy in the ICU after cardiac surgery and who have a history of previous hospitalization, are at increased risk for isolating carbapenem-resistant strains of *K. pneumoniae*.

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