Carbapenem-resistant Klebsiella pneumoniae

- The Impact of Clinical Pharmacist Consultation on the Treatment of Multi-Drug Resistant Organisms (MDRO) Infections: A Retrospective Observational Study
- Postoperative Meningitis Caused by Multidrug-Resistant Pathogens: A Case Report
- Molecular epidemiological analysis and research on resistance and virulence of carbapenem-resistant Klebsiella pneumoniae in a tertiary hospital from 2016 to 2023
- A single-center retrospective study of the molecular epidemiological characteristics of different Klebsiella pneumoniae infections in northern China
- Meropenem-vaborbactam as intrathecal-sparing therapy for the treatment of carbapenem-resistant K. pneumoniae shunt-related ventriculitis: two case reports and review of the literature
- Correlation between intestinal CRE colonization and consequent systemic infection in hospitalized patients in China
- Pharmacodynamic target attainment at infection site during treatment of post-neurosurgical ventriculitis caused by carbapenem-resistant klebsiella pneumoniae with ceftazidime-avibactam-based regimens: a case report
- Epidemiological characteristics of ventilator-associated pneumonia in neurosurgery: A 10-year surveillance study in a Chinese tertiary hospital

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Carbapenem-resistant Klebsiella pneumoniae (CRKP) is a critical issue in neurosurgery due to its high resistance to antibiotics and its association with severe healthcare-associated infections. Managing such infections in neurosurgical patients can be particularly challenging because these patients are often immunocompromised, require prolonged hospital stays, and have invasive devices such as external ventricular drains (EVDs), shunts, or catheters that increase the risk of infection.

1. Clinical Impact of CRKP in Neurosurgery

Infections: CRKP can cause meningitis, ventriculitis, surgical site infections (SSIs), and bloodstream infections in neurosurgical patients.

Mortality: CRKP infections carry a high mortality rate, especially when affecting critical brain or central nervous system (CNS) tissues.

Risk Factors:

Prolonged ICU stay and mechanical ventilation.

Use of invasive devices (EVDs, shunts, central lines).

Previous antibiotic exposure, especially carbapenems and cephalosporins.

Neurosurgical interventions with CSF leakage.

2. Mechanisms of Resistance

CRKP produces enzymes like carbapenemases that inactivate carbapenems:

Klebsiella pneumoniae carbapenemase (KPC).

New Delhi metallo-β-lactamase (NDM).

OXA-48-like enzymes.

These enzymes confer resistance not just to carbapenems but often to all beta-lactam antibiotics, severely limiting treatment options.

3. Prevention Strategies in Neurosurgery

Strict Infection Control Measures:

Hand hygiene and aseptic technique during invasive procedures.

Use of antibiotic-coated or impregnated catheters/shunts.

Limiting the duration of invasive devices like EVDs.

Surveillance: Routine screening for CRKP in high-risk patients and ICUs.

Antibiotic Stewardship:

Restrict the use of carbapenems unless absolutely necessary.

Implement protocols for appropriate empirical therapy.

4. Management of CRKP Infections

Treatment is challenging and often involves combination therapies:

Colistin: Often a last-resort antibiotic despite nephrotoxicity.

Tigecycline: Can be used, although CNS penetration is limited.

Ceftazidime-avibactam: Effective against KPC-producing CRKP but less so against NDM.

Meropenem-vaborbactam and imipenem-relebactam: Newer options targeting carbapenemase-producing bacteria.

For CNS infections:

Intrathecal or intraventricular administration of antibiotics like colistin may be considered for direct CNS delivery.

5. Specific Recommendations for Neurosurgeons

Preoperative Screening: High-risk patients should be screened for CRKP colonization.

Intraoperative Measures:

Use meticulous aseptic technique.

Antibiotic prophylaxis guided by local resistance patterns.

Postoperative Care:

Monitor for early signs of infection (fever, neurological decline, CSF changes).

Optimize the duration of invasive devices.

Multidisciplinary Approach:

Collaborate with infectious disease specialists, microbiologists, and infection control teams.

Consider CNS-penetrating antibiotics and advanced therapies when CRKP is detected.

6. Research and Innovation

New Antibiotics: Development of new agents targeting CRKP.

Phage Therapy: Investigational use of bacteriophages to treat CRKP infections.

Immunotherapy: Enhancing immune response to resistant pathogens.

Managing CRKP infections in neurosurgery requires vigilance, prevention, and timely intervention to reduce morbidity and mortality. Surveillance and stringent infection control measures are essential to prevent the spread of these multidrug-resistant pathogens in neurosurgical units.

Diagnosis

The objective of a study was to develop a rapid prediction method for carbapenem-resistant Klebsiella pneumoniae (CRKP) and colistin-resistant K. pneumoniae (ColRKP) based on routine MALDI-TOF mass spectrometry (MS) results in order to formulate a suitable and rapid treatment strategy. A total of 830 CRKP and 1462 carbapenem-susceptible K. pneumoniae (CSKP) isolates were collected; 54 ColRKP isolates and 1592 colistin-intermediate K. pneumoniae (ColIKP) isolates were also included. Routine MALDI-TOF MS, antimicrobial susceptibility testing, NG-Test CARBA 5, and resistance gene detection were followed by machine learning (ML). Using the ML model, the accuracy and area under the curve for differentiating CRKP and CSKP were 0.8869 and 0.9551, respectively, and those for ColRKP and ColIKP were 0.8361 and 0.8447, respectively. The most important MS features of CRKP and ColRKP were m/z 4520-4529 and m/z 4170-4179, respectively. Of the CRKP isolates, MS m/z 4520-4529 was a potential biomarker for distinguishing KPC from OXA, NDM, IMP, and VIM. Of the 34 patients who received preliminary CRKP ML prediction results (by texting), 24 (70.6%) were confirmed to have CRKP infection. The mortality rate was lower in patients who received antibiotic regimen adjustment based on the preliminary ML prediction (4/14, 28.6%). In conclusion, the proposed model can provide rapid results for differentiating CRKP and CSKP, as well as ColRKP and ColIKP. The combination of ML-based CRKP with preliminary reporting of results can help physicians alter the regimen approximately 24 h earlier, resulting in improved survival of patients with timely antibiotic intervention [1)].

Risk factors in univariate analysis were: Immunosuppression OR: 2.186 (1.754-2.724), nasogastric catheter OR: 3.562 (1.317-9.634), peripheral arterial catheter OR: 2.545 (1.027-6.307), and being admitted to the neurosurgical unit OR: 4.324 (1.110-16.842) [2)].

Pektezel MY, Isikay I, Gocmen R, Inkaya AC. Carbapenem-resistant Klebsiella pneumoniae meningitis and abscess treated with ceftazidime-avibactam. Enferm Infecc Microbiol Clin (Engl Ed). 2022 Jun-Jul;40(6):332-333. doi: 10.1016/j.eimce.2021.03.007. PMID: 35680351.

Ceftazidime-avibactam (CZA) is a novel antibiotic with activity against serine-lactamase. Chen et al. investigated the sensitivity of carbapenem-resistant Klebsiella pneumoniae (CRKP) to CZA and the mechanisms of drug resistance in Fujian Provincial Hospital, Fuzhou, China.

Patient characteristics were obtained from medical records. Klebsiella pneumoniae and its antibiotic susceptibility were determined using the Vitek-2 Compact instrument. The antimicrobial resistance genes KPC, NDM, OXA-48, VIM, IMP, CIM, SPM, TMB, SMB, SIM, AIM, and DIM were detected using Real-Time PCR. Multilocus sequence typing was used for genetic RELATEDNESS analysis. In total, 121 CRKP strains were isolated from patients in the intensive care unit (51.2%), senior ward (12.4%), and neurosurgery department (10%). With an average age of 72.5 years, most patients were in care for respiratory (34.7%), brain (20.7%), digestive tract (13.2%), and cardiovascular (8.3%) diseases. Specimens were predominantly obtained from sputum (39.67%), urine (29.75%) and blood (6.61%).

Of 23 CZA-resistant CRKP strains (19.01%), ST11 being the most common at 56.52%, eleven NDM-1-positive (47.83%) and four NDM-5-positive (17.39%) strains were detected.

The study indicates that CZA resistance occurs in ~19.01% CRKP strains and that blaNDM-1 and blaNDM-5 might be critical for resistance [3)].

Retrospective cohort studies with a comparative therapeutic analysis

One hundred and fifty cases of KPN treated in the neurosurgery department of our hospital from January 1, 2019 to December 31, 2021 were selected, 50 of which were found to be infected with CRKP and the other 100 were detected with carbapenem-sensitive Klebsiella pneumoniae (CSKP) by culture, analysis of factors associated with infection with CRKP. Subsequently, CRKP-infected patients were randomized into a group treated with Ti (group Ti) and a group treated with PB (group PB). The clinical efficacy, bacterial clearance, adverse reactions, and pre- and post-treatment hepatorenal function were comparatively analyzed.

Based on the Logistic regression analysis, tracheal intubation (or mechanical ventilation), combination of multiple underlying diseases, presence of impaired consciousness, and use of carbapenem antibiotics are independent risk factors for CRKP infection ($P < .05$). Ti and PB groups had no evident differences in clinical efficacy and bacterial clearance ($P > .05$); however, Ti group presented a worse hepatorenal function and a higher incidence of adverse reactions than PB group ($P < .05$).

Tracheal intubation (or mechanical ventilation), multiple underlying diseases, consciousness disturbance, and use of carbapenem antibiotics are related factors affecting CRKP infection in neurosurgical patients. Both Ti and PB have excellent therapeutic efficacy, but the former has more obvious toxicity and side effects [4)].

Cohort studies

Xiao et al. conducted a cohort study and analyzed various clinical characteristics of inpatients with intestinal CRE colonization. A risk prediction model for consequent CRE infection was established and externally validated. The prediction model is freely available online at https://creinfection.shinyapps.io/dynnomapp/ . 839 intestinal CRE colonization samples from inpatients were included. 317 cases of intestinal CRE colonization were enrolled, 25.9% of whom developed systemic infections. The consequent CRE infection rates of Klebsiella pneumoniae and Escherichia coli were 27.0% and 32.3%. The departments at high risk for subsequent CRE infection were respiratory medicine, hematology, and intensive care unit. Secondary infection after intestinal CRE colonization in inpatients can significantly prolong the length of hospital stay (26 days vs. 33 days, $P < 0.001$), increase the total medical cost (144735.34 vs. 281852.34, $P < 0.001$), and has poor (85.11% vs. 52.44%, $P < 0.001$) efficacy and high mortality (5.96% vs. 18.29%, $P = 0.001$). Our study makes a significant contribution to comprehensively specify CRE infection, because these results can facilitate early identification of high-risk hospitalized patients, timely implementation to decolonize treatment interventions, ultimately achieve the goal of CRE nosocomial infection prevention and control [5].

Single-center retrospective observational studies

There has been an upward trend in carbapenem-resistant K. pneumoniae infections in China. This epidemiological trend needs to be examined to enable better disease control. Chen et al. sought to analyze the genomic characteristics, including the prevalent sequence type (ST), resistance, virulence, and evolutionary relationship, of K. pneumoniae strains isolated from patients with different types of infections in northern China to provide theoretical support for the effective prevention and control of the evolution and transmission of K. pneumoniae.

The STs were analyzed using multi-locus sequence typing (MLST). Drug susceptibility tests were used to examine the resistance of these STs to various antibiotics. A phylogenetic tree of these isolates was constructed using the National Center for Biotechnology Information genome as the reference. Antibiotic resistance genes were identified by comparing the genomic sequences against those in the Comprehensive Antibiotic Resistance Database. Virulence genes were identified using the Virulence Factor database, while the pathogenicity of the isolates was predicted using PathogenFinder.

In total, 38 clinical isolates of K. pneumoniae were identified and sequenced by high-throughput sequencing. Multidrug-resistant ST11 and hypervirulent ST23 were found to be the prevalent K. pneumoniae strains. The distribution of the ST11 strains was strongly correlated with stays in the neurosurgery department (chi square test, P=0.02), while the ST23 strains were more frequently isolated from patients with liver abscesses and gallbladder infections. The ST23 strains were significantly more pathogenic than the other STs (Wilcox test, P<0.001). The resistance analysis showed that the rmtB genes were significantly correlated with amikacin resistance (P<2.2e-16, R2=1). The ST11 strains were also found to co-harbor the KPC-2, rmtB, and TEM-1 genes. To the best of our knowledge, this is the first study to report on the dissemination of such multidrug-resistant K. pneumoniae ST11 strains in Tianjin.

The carbapenem-resistant K. pneumoniae (CRKP) ST11 may become highly virulent K. pneumoniae (CR-hvKP) due to the acquisition of virulence plasmids. Attention should be paid to the evolutionary pressure of a caused by the overuse of antibiotics, which may trigger the further development of

multidrug-resistant K. pneumoniae infections [6].

This study provides a valuable contribution to understanding carbapenem-resistant K. pneumoniae infections, particularly the roles of ST11 and ST23 strains in northern China. Despite its limitations, the genomic analysis highlights critical issues regarding antibiotic resistance, virulence, and the potential evolution of CR-hvKP. Future research incorporating larger sample sizes, clinical data, and experimental validation will further solidify these findings and support effective prevention and control strategies.

Carbapenem-resistant Klebsiella pneumoniae meningitis

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Carbapenem-resistant Klebsiella pneumoniae ventriculitis

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Carbapenem-resistant Klebsiella pneumoniae surgical site infection

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