Mini Review

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2021.39.006285

Overview of Carbapenem-Resistant Enterobacteriaceae

Min Shi* and Xiang-qun Fang

Department of Respiratory and Critical Care Medicine, Second Medical Center of Chinese PLA General Hospital, China

***Corresponding author:** Min Shi, Department of Respiratory and Critical Care Medicine, Second Medical Center of Chinese PLA General Hospital, No. 28 of Fuxing Street, Haidian District, Beijing, 100853, China

ARTICLE INFO

Received: October 05, 2021

Published: October 11, 2021

Citation: Min Shi, Xiang-qun Fang. Overview of Carbapenem-Resistant Enterobacteriaceae. Biomed J Sci & Tech Res 39(2)-2021. BJSTR. MS.ID.006285.

ABSTRACT

This article provides a comprehensive review of carbapenem-resistant Enterobacteriaceae (CRE). Carbapenem-resistant Enterobacteriaceae have emerged, which confer broad resistance to most ß-lactam antibiotics including last-line carbapenems. Infection with Carbapenem-resistant Enterobacteriaceae is emerging as an emerging and serious global public health threat. Carbapenem-resistant Enterobacteriaceae is widely spread and is now a major factor in morbidity and mortality in health-care settings. Continued research is desperately needed to determine the most appropriate treatment for serious Carbapenem-resistant Enterobacteriaceae infections.

Keywords: Carbapenemases; Carbapenem-Resistant Enterobacteriaceae; Carbapenems; Resistant Infections; Treatment

Introduction

Respiratory infection is one of the most common diseases in the world, with high incidence and mortality. Enterobacteriaceae is the most clinically important gram-negative pathogenic bacteria, which are increasingly being reported worldwide. Antimicrobial resistance is globally recognized as one of the greatest threats to public health. For years, carbapenems have been used successfully to treat infections due to resistant Enterobacteriaceae, such as Escherichia coli and Klebsiella pneumoniae. However, recently Carbapenem-resistant Enterobacteriaceae have emerged, which confer broad resistance to most ß-lactam antibiotics including last-line carbapenems. Carbapenem-resistant Enterobacteriaceae refers to Enterobacteriaceae that are resistant to any drug of ertapenem, Doripenem, imipenem, meropenem, or enterobacteriaceae that produce carbapenemase. Infection with Carbapenem-resistant Enterobacteriaceae is emerging as an important challenge in health-care settings and a growing concern worldwide, it is very easy to spread in patients with long-term hospitalization or low immunity, leading to nosocomial infection, and may even cause a small- or large-scale outbreak [1-3]. Most Enterobacteriaceae belong to the normal flora in the intestinal tract and can become opportunistic pathogens once the body's immunity declines. Enterobacteriaceae obtain genetic material mainly by horizontal gene transfer mediated by plasmids and transposons [4] Carbapenem-resistant Enterobacteriaceae can cause a number of serious infection types (such as pneumonia, abdominal cavity infection, urinary tract infections, Bloodstream infection, skin and soft tissue infection, central nervous system infection, and device-associated infections) or asymptomatic colonization, among which Ventilator-associated pneumonia (VAP) was the most common [5]. Severe pneumonia has always been a common respiratory disease, which can endanger life. Statistics [6] show that infectious diseases account for 30% of all deaths worldwide, with severe pneumonia leading the way. Carbapenem-resistant Enterobacteriaceae infection was reported in 68.8% of patients with hospital acquired bacterial pneumonia [7]. Consistent mortality rates of 40-50% are observed among inpatients with infections caused by CRE in hospitals worldwide, while the mortality rate from CRE infection in pneumonia patients is as high as 60% [8]. Carbapenem-resistant Enterobacteriaceae infection is a very difficult problem in clinical practice.

Risk Factors of Acquisition of CRE Infection

There are a number of factors that predispose persons to infections by CRE. Exposure to these resistant organisms can cause serious infections in patients with the following reported risk factors: immune-suppression, advanced age, admission to intensive care unit (ICU), mechanical ventilation, previous exposure to antimicrobials, organ or stem-cell transplantation and prolonged hospital stays. Healthcare associated infections caused by CRE, mainly Klebsiella pneumoniae, have been encountered most commonly in ventilator-associated pneumonia, bacteremia, urinary tract and surgical site infections. Growing evidence suggests early detection of CRE-colonized patients on admission to long-term care facilities may help to prevent institutional outbreaks and limit regional spread of this emerging public health threat. Respiratory disease is one of the risk factors for CRE infection, probably because a variety of bacteria grow in the respiratory tract and maintain a dynamic balance in the body. Elderly patients with respiratory diseases have low immunity and are vulnerable to infection. Moreover, most patients with respiratory diseases have a history of invasive operation. When tracheotomy or endotracheal intubation is performed, the respiratory mucosa will be damaged, resulting in a variety of complications. Some bacteria are easy to form biofilm in the open airway, which leads to abnormal expression of outer membrane pore protein and bacterial drug resistance. In particular, frequent aerosol inhalation and other operations change the airway environment, requiring frequent contact with patients by medical staff, which makes patients susceptible to colonization and infection by multi-resistant bacteria.

Prevention and Control measures for CRE Infections

2.1 There are reports which suggest that overuse of carbapenems is closely related to the incidence of CRE infection, and unreasonable use of carbapenems can easily induce bacterial resistance and spread [9]. One of the chief difficulties in the treatment of CRE is the excessive use of antibiotics, not only those acquired by the community but also in hospitals. On the one hand, the use of broad-spectrum antibiotics can kill the sensitive bacteria, and the resistant bacteria can survive and become the dominant growth, thus increasing the probability of CRE infection. On the other hand, drug resistance may occur due to the change of drug binding sites after drug use, resulting in carbapenemases and other drug resistance mechanisms [10]. Growing evidence suggests that carbapenem-resistant Gram-negative bacteria are sufficient to develop in the intestinal flora of intensive care patients just a few days of application of carbapenems antibiotics [11]. Therefore, it is necessary to strengthen the supervision and management of clinical application of carbapenems, and strictly implement the classification of antibiotics and the management of doctors' prescribing rights, limiting the over-use and abuse of antibiotics in humans and agriculture.

Standardized Collection and Correct Interpretation of Microbial Test Reports

Specimens should be collected before antibiotic treatment, sterile site specimens should be collected as far as possible and microbial reports should be correctly interpreted, eliminating contamination and colonization and avoiding unnecessary use of antibiotics. Therefore, clinical microbiology laboratories at all levels of medical institutions should establish the ability to receive and process microbial specimens within 24 hours.

There are reports which suggest that that patient carrying other multidrug-resistant bacteria are mostly in serious and complex conditions, with low immunity and relatively long stay in intensive care units, leading to the development of CRE. Therefore, it is necessary to strengthen the contact and isolation of MDR-resistant bacteria to avoid the spread of MDR-resistant bacteria in hospitals. Hand hygiene is the simplest, most effective, most convenient and economical method to control the infection in hospitals, which can significantly reduce the incidence of CRE infection. Mobile water sinks, non-contact faucets, hand sanitizers, hand drying facilities, quick-drying hand disinfectants, and related charts can reduce the colonization rate of CRE [12].

Studies show that the wash basin and its surrounding environment are seriously polluted, which is an important source of CRE pollution. Therefore, medical institutions should pay attention to the cleaning, disinfection and management of the location of the sink in the diagnosis and treatment area, taking anti-splash measures. Symptomatic colonized patients can become potential sources of infection. The significance of active screening lies in early identification of CRE colonized patients so that timely isolation measures can be taken to reduce the risk of transmission. Stool is the best specimen for active screening, and if not readily available, a rectal swab is taken. If the patient has a definite history of CRE infection, specimens from the infected site should be screened again. Patients with positive initial screening and hospitalized for less than 30 days do not need further screening, while patients hospitalized for more than 30 days were screened once a month. Those who have been screened negative for the first time should be screened regularly, either once a week or every two weeks, or twice a week, depending on the severity of the outbreak. Health care facilities should implement isolation of all CRE infected/colonized persons. Isolation refers not only to the establishment of physical spatial barriers, but also to the strict enforcement of isolation measures.

Treatment Options for CRE Infections

There are numerous different types of carbapenemase enzymes, each conferring varying spectrums of resistance. In

general, the presence of a carbapenemase confers broad resistance to most ß-lactam antibiotics including penicillins, cephalosporins, and the monobactam aztreonam (excluding metallo-β-lactamases [MBLs] and oxacillinases [OXAs]) [13]. At present, the main drugs for the treatment of CRE in the world are polymyxins, Tigecycline, fosfomycin, Ceftazidime-Avibatam and aminoglycoside antibiotics. Polymyxins and tigecycline were highly sensitive to CRE in vitro and were not affected by the type of carbapenemases produced by bacteria. Due to heterogeneous drug resistance and positive correlation between dose and renal toxicity, polymyxins are often used in combination with other antibacterial agents. The conventional dose of tigecycline is difficult to reach sufficient concentration in the areas including the blood flow and alveolar lining fluid, so it is often necessary to increase the dose and use it in combination with other drugs. Ceftazidime-avibactam lacks effective antibacterial activity against metalloenzyme-producing CRE, so it may be an important choice for the treatment of non-metalloenzyme-producing CRE infection. The most common adverse drug reactions of Ceftazidime-avibactam in trials were vomiting, nausea, constipation, and anxiety [14].

Combination therapy for CRE infections may decrease mortality compared with monotherapy. Benefits of combination therapy include reduction of initial inappropriate antimicrobial therapy, potential synergistic effects, and suppression of emerging resistance [15]. For patients who are critically ill or with deep-seated infections, consider empiric and antibiogram-directed combination therapy with 3 drugs, basing on antimicrobial sensitivity results. Polymyxins may be most effective as part of a combination for serious CRE infections [15,16].

Conclusion

In summary, the burden of carbapenem-resistant Enterobacteriaceae is increasing rapidly worldwide. CRE is widely spread and is now a major factor in morbidity and mortality in health-care settings. The results at present are still not good, especially in elderly patients with a history of CRE infection. The extremely high mortality rates of patients with CRE infections have driven efforts to prevent the acquisition and spread of these bacteria in hospitals. Although the above measures are simple, they can prevent the spread of CRE to some extent. However, continued research is desperately needed to determine the most appropriate treatment for serious CRE infections.

References

1. Schwaber MJ, Carmeli Y (2008) Carbapenem-resistant Enterobacteriaceae: A potential threat. J Am Med Assoc 300(24): 2911-2913.
2. Nordmann P, Naas, T, Poirel L (2011) Global spread ofcarbapenemase-producing Enterobacteriaceae. Emerg Infect Dis 17(10): 1791-1798.
3. Ola H Moghnia, Vincent O Rotimi, Noura A Al-Sweih (2021) Monitoring antibiotic resistance profiles of faecal isolates of Enterobacteriaceae and the prevalence of carbapenem-resisant isolates carbapenem-resistant isolates among food handlers in Kuwait. Journal of antimicrobial Resistance 25: 370-376.
4. Patrice N, Thierry N, Laurent P (2011) Global Spread of Carbapenemase-Producing Enterobacteriaceae. Emerging Infectious Diseases 17(10): 1791-1798.
5. De Maio CarrilhoCM, de OliveiraLM, GauderetoJ, Juliana Gaudereto, Jamile S Perozin, Mariana Ragassi Urbano, et al. (2016) A prospective study of treatment of Carbapenem-resistant Enterobacteriaceae infections and risk factors associated with outcome. BMC Infect Dis 16(1): 629.
6. Brown SM, Dean NC (2011) Defining Severe Pneumonia. Clinics In Chest Medicine 32(3): 469-479.
7. Pang F, Jia XQ, Zhao QG, et al. (2018) Factors Associated to Prevalence and Treatment of Carbapenem-resistant Enterobacteriaceae Infections: a Seven Years Retrospective Study In Three Tertiary Care Hospitals. Ann Clin Microbiol Antimicrob 17(1): 1-8.
8. Carrilho CMD DM, Oliveira LMD, Gaudereto J, Jamile S. Perozin,3 Mariana Ragassi Urbano, et al. (2016) A Prospective Study of Treatment of Carbapenem-resistant Enterobacteriaceae Infections and Risk Factors Associated with Outcome. Bmc Infectious Diseases 16(1): 1-9.
9. Prakobsrikul N, Malathum K, Santanirand P, Supatat Chumnumwat 1, Pongsathorn Piebpien, et al. (2019) Correlation between antimicrobial consumption and the prevalence of carbapenem-resistant Escherichia coli and carbapenem-resistant Klebsiella pneumoniae at a university hospital in Thailand. J Clin Pharm Ther 44(2): 292-299.
10. Suk KJ, Jongyoun Y, Kyung KM, Soon Ok Lee 1, Jeong Eun Lee, et al. (2019) Prevalence and Risk Factors of Carbapenem-resistant Enterobacteriaceae Acquisition in An Emergency Intensive Care Unit in a Tertiary Hospital in Korea: a Case-Control Study. Journal Of Korean Medical Science 34(18): e140.
11. Kim T, Chong Y P, Park S Y, Min-Hyok Jeon 4, Eun Joo Choo, et al. (2014) Risk Factors for Hospital-Acquired Pneumonia Caused by Carbapenem-Resistant Gram-Negative Bacteria in Critically Ill Patients: a Multicenter Study In Korea [J]. Diagn Microbiol Infect Dis 78(4): 457-461.
12. Viale P, Tumietto F, Giannella M, M Bartoletti, S Tedeschi et al. (2015) Impact of a hospital-wide multifaceted programme for reducing Carbapenem-resistant Enterobacteriaceae infections in a large teaching hospital in northern Italy. Clin Microbiol Infect 21(3): 242-247.
13. Nordmann P, Dortet L, Poirel L (2012) Carbapenem resistance in Enterobacteriaceae: here is the storm! Trends Mol Med 18(5): 263-272.
14. Actavis plc (2015) Actavis Receives U.S. FDA Approval for AVYCAZ™ (CEFTAZIDIME-AVIBACTAM). 2015. Feb 25.
15. Petrosillo N, Giannella M, Lewis R (2013) Treatment of carbapenem-resistant Klebsiella pneumoniae: the state of the art. Expert Rev Anti Infect Ther 11(2): 159-177.
16. Lynch JP 3rd, Clark NM, Zhanel GG (2013) Evolution of antimicrobial resistance among Enterobacteriaceae (focus on extended spectrum beta-lactamases and carbapenemases). Expert Opin Pharmacother 14(2): 199-210.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2021.39.006285

Min Shi. Biomed J Sci & Tech Res