INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

GUIDE TO INFECTION CONTROL IN THE HOSPITAL

CHAPTER 47:

Carbapenem-resistant Enterobacteriaceae

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Topic Outline

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KEY ISSUES

Carbapenem-resistant Enterobacteriaceae (CRE) are increasingly prevalent pathogens in hospitalized patients and can cause a variety of infections such as urinary tract infections, wound infections and respiratory tract infections. Their importance derives from the fact that they can spread rapidly in the hospital setting, and that they are commonly multidrug-resistant (MDR). In contrast to Gram-positive MDR-pathogens such as MRSA, there are still few therapeutic options available to treat these MDR pathogens.

KNOWN FACTS

- *Enterobacteriaceae* like *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Citrobacter* spp. or *Proteus* spp. are Gram-negative rods that can be part of the normal enteric flora. Previous antibiotic therapy, underlying systemic illness, and prolonged hospital stays have been identified as risk factors for colonization of patients with carbapenem-resistant strains. The use of catheters and mechanical ventilation is also associated with an increased risk of CRE colonization. In addition, CRE can be transmitted through direct contact with contaminated surfaces, colonized or infected patients, or more frequently by the hands of health care workers and other hospital personnel. Some species, such as *Klebsiella* spp., have demonstrated a propensity to cause large nosocomial outbreaks. Since most *Enterobacteriaceae* are part of the normal intestinal flora, asymptomatic colonization with CRE is common, however, as with other resistant organisms, CRE colonization increases the risk of CRE infection. This is of special importance in neonates, ICU patients and immunocompromised patients.
- The prevalence of CRE varies widely between different species and different geographical regions. In the U.S., carbapenem-resistance rates

are quoted as 0.1% and 5.3% for *E. coli* and *K. pneumoniae,* respectively, while in Europe, most countries report resistance rates below 1% for both pathogens. However, local and regional differences can be enormous: All over the world, several regions have been identified where CRE are endemic, e.g. in Greece, parts of South-east Asia or the northeastern region of the USA. Even in settings where resistance rates are still low, a steady rise pan-resistant CRE has been observed over the past decade.

- Depending on the virulence of the particular pathogen, the site of colonization, and a variety of host-related factors, CRE can cause nearly all kinds of infections, most commonly urinary tract infections, pneumonia (usually ventilator-associated (VAP)), wound infections, or bloodstream infections. As CRE are commonly multidrug-resistant, comprehensive antimicrobial susceptibility testing is mandatory and treatment should be adapted accordingly, however, in most cases there are very few remaining options and infectious diseases consultation is highly recommended.
- In most countries, scientific societies and/or public health agencies have published guidelines and recommendations on how to handle CRE colonization and infection, and how to prevent transmission and limit spread. These can be used as a basis and should be adapted to local circumstances to implement an effective program in the hospital or other health care facilities.

Controversial Issues

- Generally, there are still only limited data available on a number of important issues regarding detection, management and treatment of CRE. There is as of now no generally agreed recommendation for the laboratory detection of carbapenem resistance. Currently available methods include screening via routine antibiotic susceptibility testing using ertapenem, meropenem or faropenem and/or the cultivation of

bacteria on different CRE-selective media. For confirmation, several methods including the modified Hodge test, inhibitor-based assays, molecular methods or mass spectrometry (MALDI-TOF) may be used. Molecular methods, while having a high specificity and sensitivity, are becoming more common in the routine detection but are mostly used for confirmation due to various practical and financial issues.

- The impact of routine surveillance cultures throughout the hospital stay is currently not supported by strong evidence and therefore not generally recommended. They may, however, be useful during outbreak situations and in high-risk patients with prolonged hospital stays.
- While cohorting patients and staff in an outbreak setting seems to be beneficial, it is uncertain if the spread of CRE in non-outbreak situations can be successfully limited by these practices as well.
- There is currently no decolonization strategy with proven efficacy, even though attempts have been made to eradicate CRE from the gastrointestinal tract through selective digestive decontamination. The long-term effectiveness and adverse effects of this approach, especially in an endemic setting, are unclear so that it is not a generally recommended measure. Similarly, daily chlorhexidine bathing has been performed to contain outbreaks, but its value in eradicating CRE and limiting spread is still under investigation.

SUGGESTED PRACTICE

- Identify high-risk patients on admission to the hospital and/or on admission to high-risk areas such as intensive care units. High-risk patients should include those from regions, countries or institutions where CREs are endemic, patients with a recent history of CRE colonization, and those who have had a recent contact with a known CRE carrier (e.g., shared a hospital room).

- Screen high-risk patients on admission to the hospital. Pre-emptive single-room isolation should be performed until a negative screening result is confirmed.
- Work together with a laboratory that uses fast and accurate methods for CRE detection and is able to provide rapid notification of the results. Early identification is vital both for effective therapy and infection control measures.
- Notify the hospital infection control team if transmission on the ward is suspected and suggest appropriate control measures, including potentially additional screening on the ward affected.
- Observe hand hygiene as suggested by the WHO at all times, with all patients, and with all procedures. Of special importance are hand disinfection before and after contact with a patient and his or her surroundings, and the correct use of gloves.
- Use full contact precautions for CRE patients, including the wearing of gowns and gloves and single-room isolation. If care in a single room is not possible, at least provide a separate toilet for the patient and perform barrier precautions at the bedside.
- Perform daily decontamination of the patient environment, using effective disinfectants. Single-use equipment should be preferred where possible. All other equipment must be properly decontaminated before use on another patient.
- Restrict the use of devices (venous catheters, urinary catheters etc.) as far as possible and review their need on a daily basis.
- Implement an antimicrobial stewardship programme in the hospital to improve antimicrobial therapy and decrease the development of resistance and therefore colonization pressure.
- Make sure all staff are aware of the standard hygiene measures and additional barrier precautions and know when and how to perform them. Regular training is important; monitoring of compliance with infection control measures is recommended. CRE measures should be part of a comprehensive institutional infection control program.

- Be aware of national guidelines and notification systems as appropriate. If CRE patients are transferred to other hospitals or care facilities, ensure CRE status is communicated before transfer.

SUGGESTED PRACTICE IN UNDER-RESOURCED SETTINGS

- Recommendations listed above are also feasible for application in resource-poor settings.

SUMMARY

Carbapenem resistance has increased in all regions of the world over the past decade. Colonization and infection rates are rising and have reached endemic levels in some regions. Although there is little specific evidence for many infection control measures, there is agreement on the general components of an adequate control programme. These include surveillance and rapid identification of CRE carriers, barrier precautions for all CRE patients (single-room care, wearing protective equipment), adherence to hand hygiene and standard hygiene regimes, safe and effective disinfection measures, education, and continuous training of all staff, organizational awareness of the problem of multidrug-resistant organisms and the implementation of appropriate infection control and antimicrobial stewardship programmes.

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