Enferm Infecc Microbiol Clin. 2017;35(6):331–332

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Editorial

Should screening programs for carbapenemase-producing strains be implemented in ICU patients?☆

¿Deben implantarse programas de cribado de cepas productoras de carbapenemasas en pacientes que ingresan en la UCI?

Jesús Oteo

Reference and Research Laboratory for Resistance to Antibiotics and Healthcare-associated Infections, National Microbiology Centre, Instituto de Salud Carlos III, Madrid, Spain

ARTICLE INFO

Article history:
Received 9 December 2016
Accepted 10 December 2016
Available online 19 May 2017

In the last 10 years, Carbapenemase-producing Enterobacteriaceae (CPE), mainly *Klebsiella pneumoniae*, have broken out in most of the world's hospitals.[1,2] This outbreak poses a great challenge in the management of patients colonised or infected by CPE, which significantly affects the daily work of health professionals and even the structural organisation of hospital centres. The severe therapeutic limitations that usually occur in CPE infections lead to a delay in the initiation of adequate treatment, and often the impossibility of recommending an optimal treatment.[1] In general, infections caused by bacteria resistant to multiple antibiotics generate more prolonged hospitalisations, more frequent complications, including death, and a higher costs than infections caused by sensitive bacteria.[3] Invasive infections by strains of carbapenemase-producing *K. pneumoniae* are associated with higher mortality rates than those caused by sensitive strains.[4–6] Although the attributable mortality rate is difficult to establish, as CPE often cause infections in patients with significant underlying disease, crude mortality rates ranging from 20% to 60% have been reported.[4–7]

In addition to being one of the bacterial families that cause greater pathology in humans, enterobacteria, mainly *Escherichia coli* and *K. pneumoniae*, are part of our normal microbiota, which means that colonisation by CPE is not rare. The presence of colonised patients is one of the main routes for dissemination of CPE, as well as one of the causes of the persistence of outbreaks and endemics produced by this type of bacteria.[8,9]

Enterobacterial infections are usually autoinfections caused by the same strains that colonise the human body, although there is little published evidence of CPE infections in previously colonised patients.[10] Colonisation by multi-resistant bacteria may be a risk factor for poorer patient progress, as previously demonstrated with *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.[11,12] According to a recent study carried out in two Greek intensive care units (ICU),[13] patients colonised by CPE have a 1.79 times greater risk of dying than non-colonised patients.

Early detection of CPE carriers therefore has a dual purpose: epidemiological, to establish effective and early measures that limit rapid and widespread dissemination[9,14]; and clinical, to prevent and control the possible downward progression of each patient.

Management of colonisation by CPE becomes even more complex in special risk units such as ICUs. The existence of increased antibiotic-related selective pressure, the presence of critical patients with multiple underlying pathologies particularly susceptible to infection, and an elevated risk of transmission between patients increase the impact of CPE in these units.[15] In a study conducted in 2014 in 11 Spanish hospitals, the average incidence of colonisation during ICU stays was 1.35%, although 36% of the participating hospitals presented an incidence higher than 3%.[16] These figures were obtained in a nation-wide epidemiological context of "regional CPE dissemination",[16,17] a situation that has worsened to an "endemic" epidemiological context (unpublished personal data) in the last 3 years, which increases the risk of patients colonised by CPE being admitted to the ICU.

In this issue of *Enfermedades Infecciosas y Microbiología Clínica*, Maseda et al.[18] publish a study conducted in a surgical ICU from January 2012 to December 2013.[18] Out of the 254 patients over the age of 14 admitted to that ICU in the study period, 16.1% were CPE carriers.[18] According to the authors, factors associated with

☆ Please cite this article as: Oteo J. ¿Deben implantarse programas de cribado de cepas productoras de carbapenemasas en pacientes que ingresan en la UCI? Enferm Infecc Microbiol Clin. 2017;35:331–332.

E-mail address: jesus.oteo@isciii.es

colonisation by this type of bacteria included: previous treatment with broad-spectrum cephalosporins and to a lesser extent with β-lactams/β-lactam inhibitors, abdominal surgery and previous digestive or biliary endoscopy.[18]

In light of the above data, active screening for carbapenemase-producing strains in patients admitted to the ICU is a desirable and beneficial measure to reduce person-to-person transmission, prevent outbreaks and improve the prognosis of individual patients.[10,13,19,20] However, in practice, the decision to establish universal active screening in all patients entering the ICU should be considered in terms of another set of closely-linked factors. The epidemiological situation of the hospital and its health area can influence the utility and cost-benefit ratio of this intervention, which would be highly recommended in epidemic situations with active outbreaks caused by CPE.[9,10] However, selective screening for patients with certain risk factors for carrying a CPE could be considered as an alternative in situations of low prevalence.[10,15] These risk factors include, but are not limited to, previous hospital admissions in the last 6–12 months, previous hospitalisation in risk units (such as ICUs), coming from geographical areas with a high prevalence of CPE, having been previously colonised by CPE, prolonged use of antibiotics in the last 3 months or suffering from chronic pathologies susceptible to colonisation.[9,10,15] In addition, following the emergence of a first case of CPE in an ICU, it is recommended to conduct studies to detect colonisation in all hospitalised patients on a weekly basis up to 4 weeks after the last detected case.[19,20]

Proper screening for CPE results in a significant workload at different levels, especially in the microbiology laboratories, which require an essential infrastructure and allocation of resources for this purpose. In addition, screening is only the first step in a chain of actions that lead to the control of CPE dissemination. It is a fundamental and necessary first step, whose effectiveness is entirely dependent on the degree of completion of interventions that should occur as a result of said screening.[10] Therefore, before designing and implementing a CPE screening program in an ICU, each health centre must assess its actual capability for response in light of the information generated by the program. Furthermore, channels must be established for the early implementation of appropriate measures to become a reality. At times, the general, functional and even architectural structures of health systems are not specially prepared to address situations where there is a high prevalence of CPE.

The active monitoring of carriers has been successfully used in multifactorial strategies to control the spread of CPE,[13,21,22] although the specific contribution of this measure is difficult to assess given the largely "activating" nature of the other actions.

ICUs are units with specific characteristics that require individualised consideration. However, they are also integrated in a hospital setting with which they have important and inevitable interactions, so any activities aimed at controlling the dissemination of CPE require adequate coordination throughout the hospital as a whole.

The biological and transmission characteristics of CPE as well as the great clinical impact they can generate, especially in high-risk units such as ICUs, make the early detection of colonised patients highly recommendable. Therefore, even though the individual impact of active screening is difficult to establish since it is closely linked to the development of other measures, its use for the detection of CPE in ICUs is widely supported.[9,10,14,15,19,20] Ideally, although universal screening of all patients admitted to the ICU would be advisable in a situation where the prevalence of CPE is high, as is currently the situation in Spain, the target population included in such screening could be adjusted according to epidemiological circumstances, care and structural aspects of both the ICU and hospital.

References

1. Lee CR, Lee JH, Park KS, Kim YB, Jeong BC, Lee SH. Global dissemination of carbapenemase-producing *Klebsiella pneumoniae*: epidemiology, genetic context, treatment options, and detection methods. Front Microbiol. 2016;7:895.
2. Oteo J, Miró E, Pérez-Vázquez M, Navarro F. Evolution of carbapenemase-producing Enterobacteriaceae at the global and national level: what should be expected in the future? Enferm Infecc Microbiol Clin. 2014;32 Suppl 4:17–23.
3. Neidell MJ, Cohen B, Furuya Y, Hill J, Jeon CY, Glied S, et al. Costs of healthcare- and community-associated infections with antimicrobial-resistant versus antimicrobial-susceptible organisms. Clin Infect Dis. 2012;55:807–15.
4. Gasink LB, Edelstein PH, Lautenbach E, Synnestvedt M, Fishman NO. Risk factors and clinical impact of carbapenemase-producing *Klebsiella pneumoniae*. Infect Control Hosp Epidemiol. 2009;30:1180–5.
5. Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem resistant *Klebsiella pneumoniae* infection and the impact of antimicrobial and adjunctive therapies. Infect Control Hosp Epidemiol. 2008;29:1099–106.
6. Sánchez-Romero I, Asensio A, Oteo J, Muñoz-Algarra M, Isidoro B, Vindel A, et al. Nosocomial outbreak of VIM-1-producing *Klebsiella pneumoniae* isolates of multilocus sequence type 15: molecular basis, clinical risk factors, and outcome. Antimicrob Agents Chemother. 2012;56:420–7.
7. Palacios-Baena ZR, Oteo J, Conejo C, Larrosa MN, Bou G, Fernández-Martínez M, et al. Comprehensive clinical and epidemiological assessment of colonisation and infection due to carbapenemase-producing Enterobacteriaceae in Spain. J Infect. 2016;72:152–60.
8. Bou-Arevalo G, Chaves-Sánchez F, Oliver-Palomo A, Oteo-Iglesias J. Métodos microbiológicos para la vigilancia del estado de portador de bacterias multirresistentes. 55. Oteo-Iglesias J (coordinador). Procedimientos en Microbiología Clínica. Cercenado-Mansilla E, Cantón-Moreno R (editores). Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). 2015.
9. Centers for Disease Control and Prevention (CDC). Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE). 2015 CRE ToolKit. CDC; 2015. Available from: http://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf [accessed 24.11.16].
10. Tacconelli E, Cataldo MA, Dancer SJ, de Angelis G, Falcone M, Frank U, et al. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. Clin Microbiol Infect. 2014;20 Suppl 1:1–55.
11. Maragakis LL, Perl TM. *Acinetobacter baumannii*: epidemiology, antimicrobial resistance, and treatment options. Clin Infect Dis. 2008;46:1254–63.
12. Zhuo H, Yang K, Lynch SV, Dotson RH, Glidden DV, Singh G, et al. Increased mortality of ventilated patients with endotracheal *Pseudomonas aeruginosa* without clinical signs of infection. Crit Care Med. 2008;36:2495–503.
13. Dautzenberg MJ, Wekesa AN, Gniadkowski M, Antoniadou A, Giamarellou H, Petrikkos GL, et al. The association between colonization with carbapenemase-producing enterobacteriaceae and overall ICU mortality: an observational cohort study. Crit Care Med. 2015;43:1170–7.
14. European Centre for Diseases Prevention and Control. Risk assessment on the spread of carbapenemase-producing Enterobacteriaceae (CPE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer. Stockholm: ECDC; 2011. Available from: http://ecdc.europa.eu/en/publications/publications/110913_risk_assessment_resistant_cpe.pdf [accessed 22.11.16].
15. Montero JG, Lerma FA, Galleymore PR, Martínez MP, Rocha LA, Gaite FB, et al. Combatting resistance in intensive care: the multimodal approach of the Spanish ICU "Zero Resistance" program. Crit Care. 2015;19:114.
16. Oteo J, Alcaraz R, Bou G, Conejo C, Díaz-Lamas AM, Fernández-Martínez M, et al. Rates of faecal colonization by carbapenemase-producing Enterobacteriaceae among patients admitted to ICUs in Spain. J Antimicrob Chemother. 2015;70:2916–8.
17. Glasner C, Albiger B, Buist G, Tambić Andrasević A, Canton R, Carmeli Y, et al. Carbapenemase-producing Enterobacteriaceae in Europe: a survey among national experts from 39 countries, February 2013. Euro Surveill. 2013;18:20525.
18. Maseda E, Salgado P, Anillo V, Ruiz-Carrascoso G, Gómez-Gil R, Martín-Funke C, et al. Risk factors for colonization by carbapenemase-producing enterobacteria at admission to a Surgical ICU: a retrospective study. Enferm Infect Microbiol Clin. 2017;35:333–7.
19. Comunidad Autónoma de Madrid. Plan de prevención y control frente a la infección de las bacterias productoras de carbapenemsas. Available from: http://www.madrid.org/cs/Satellite?blobcol=urldata&blobheader=application%2Fpdf&blobheadername1=Content-disposition&blobheadername2=cadena&blobheadervalue1=filename%3DPLAN+PREVENCI%C3%93N+Y+CONTROL+EPC+CM_v1_sept+2013.pdf&blobheadervalue2=language%3Des%26site%3DPortalSalud&blobkey=id&blobtable=MungoBlobs&blobwhere=1352838664739&ssbinary=true [accessed December 2016].
20. PIRASOA. Programa para el control de las enterobacterias productoras de carbapenemasas en el SSPA. Available from: http://safh.org/wp-content/uploads/2014/10/Programa-para-el-control-de-las-EPC_SSPA.pdf [accessed 2.12.16].
21. Kochar S, Sheard T, Sharma R, Hui A, Tolentino E, Allen G, et al. Success of an infection control program to reduce the spread of carbapenem-resistant *Klebsiella pneumoniae*. Infect Control Hosp Epidemiol. 2009;30:447–52.
22. Ben-David D, Maor Y, Keller N, Regev-Yochay G, Tal I, Shachar D, et al. Potential role of active surveillance in the control of a hospital-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* infection. Infect Control Hosp Epidemiol. 2010;31:620–6.