Official journal of the Spanish Society of Chemotherapy

Update in infection diseases 2020

Javier E. Cañada-García[1]
María Pérez-Vázquez[1,2]
Jesús Oteo-Iglesias[1,2]

RedLabRA; a Spanish Network of Microbiology Laboratories for the Surveillance of Antibiotic Resistant Microorganisms

[1]Reference and Research Laboratory on Antibiotic Resistance, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain.
[2]Coordinating Committee of the Spanish Network of Laboratories for the Surveillance of Resistant Microorganisms (RedLabRA), Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain

Revista Española de Quimioterapia
doi:10.37201/req/s01.03.2021

ABSTRACT

There is an urgent need to control the clinical and public health impact that antibiotic resistance (AR) causes worldwide. Any measure for its control must be based on an up-to-date and comprehensive knowledge of the situation. However, it is difficult to determine the current dimension of AR because a large part of the available information is based on heterogeneous, insufficiently unified and retrospective data. The integration of genomic information in the surveillance of AR is another important factor for improvement. The Spanish Network of Laboratories for the Surveillance of Resistant Microorganisms (RedLabRA) is a structured network of interconnected microbiology laboratories developed within the Spanish National Plan against Antibiotic Resistance. Its main objective is to support the diagnosis of resistance to antibiotics, integrating molecular characterization in the surveillance.

Keywords: Antibiotic resistance, antibiotic resistance mechanisms, surveillance, RedLabRA.

INTRODUCTION

Multiple factors such as inaccurate antibiotic treatment regimens, self-medication, low adherence to the treatment, use of antibiotics in food industry, inability to access to clean water, and bad hygiene habits, among others, contribute to the selection and dissemination of microorganisms presenting antibiotic resistance (AR) to commonly used antibiotics [1,2].

An estimation based on the European Antimicrobial Resistance Surveillance Network data, showed that the clinical impact of selected antibiotic resistant bacteria in Europe could be quantified in generated 671,689 infections, 33,110 deaths, and 874,541 disability-adjusted life-years (DALYs) (which is a composite health measure estimating years lived with disabilities following the onset of a disease and of years of life lost due to pre-mature mortality compared to a standardized life expectancy) [3]. These infections generated an additional health expenditure of €1,500 million. It is estimated that more than 4 million people in Spain are infected annually, causing around 2,800 deaths [4], implying an expense of €150 million [5].

Current therapeutic options are being compromised by the emergence of novel resistance mechanisms such as, for instance, *optr*A and *poxt*A linezolide resistance genes [6] and *mcr* colistin resistance genes [7]. Changes in dissemination patterns of already known resistance mechanisms and high risk multidrug resistant clones, such as the *Escherichia coli* ST131/CTX-M-15 [8], *Klebsiella pneumoniae* ST258-512/KPC [9] and *K. pneumoniae* ST307/OXA-48 [10] are of great concern.

Resistance to carbapenems in *K. pneumoniae* and *E coli* has been increasing during the last years [11], enhancing the emergence of nosocomial infections that do not have optimal treatment options [2].

It is difficult to determine the current dimension of RA due to many available data come from heterogeneous, fragmented, and retrospective reports, showing issues of concern in the implementation of an agile and effective surveillance. An active genomic surveillance allows a better understanding of bacterial dynamics and to stablish strain/mechanism associations [12], facts that are crucial to carry out fast interventions in public health [13].

If measures are not implemented, effectiveness of antibiotic treatments against bacterial infections will decrease, and medical procedures such as organ transplants, chemotherapy and great surgeries could be also compromised [5]. In 2050, about 10 million deaths are expected to occur worldwide due to AR, becoming the leading cause of death [14], what could deeply compromise global economy, as World Bank estimated in 2017 [15].

Correspondence:
Jesús Oteo-Iglesias
Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain.
E-mail: jesus.oteo@isciii.es

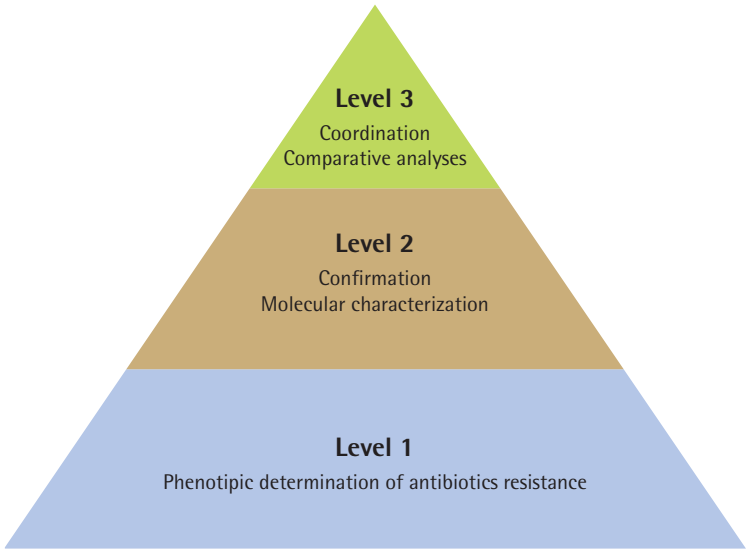

Figure 1 | **Network structure of RedLabRA.**

PRAN

The Spanish National Plan against Antibiotic Resistance (PRAN) is a strategic and action plan aimed to reduce the risk of selection and spread of AR and, consequently, to reduce its clinical and public health impact. The ultimate goal is to sustainably preserve the efficacy of antibiotics [5]. The PRAN is coordinated by the Agencia Española del Medicamento y Productos Sanitarios (AEMPS) and has the participation of all the autonomous communities, nine Spanish Ministries, and more than 70 scientific societies, collegiate organizations, professional associations and universities.

The PRAN addresses in a multidisciplinary way the AR threat from six strategic lines for action: 1) surveillance of consumption and resistance to antibiotics; 2) control of the emergence and spread of antibiotic resistant microorganisms; 3) prevention measures to reduce infections and promote the use of tools for an early diagnosis; 4) research to improve the knowledge of causes and consequences of AR and development of new therapeutic and diagnostic alternatives; 5) training of health professionals; and 6) awareness of the population about a prudent use of antibiotics through communication campaigns [5].

The PRAN considers a priority the implementation of a national network of laboratories that allows early and accurate diagnosis of healthcare-related infections (HAI) caused by multi-resistant microorganisms. This fact contributes to the establishment of early and effective treatments, as well as to the application of control measures [16].

REDLABRA

The Spanish Network of Laboratories for the Surveillance of Resistant Microorganisms (RedLabRA) has been created as a network of microbiology laboratories, coordinated and interconnected at a national level, to work together in the diagnosis and molecular study of infectious diseases caused by antibiotic resistant microorganisms. After being approved by the Interterritorial Board and the Public Health Commission of the Spanish National Health System, this network is working led by a Coordinating Committee dependent on the Ministry of Health, Consumer Affairs and Social Welfare (MSCBS) and the Instituto de Salud Carlos III (ISCIII) [16].

The general aim of RedLabRA is to achieve a complete and quality diagnosis of every case of infection or colonization by resistant microorganisms included in the epidemiological surveillance of the National Health System. This network aims to carry out a molecular study of the infectious diseases, including the next generation genome sequencing as a gold standard, allowing the better understanding of bacterial evolution, outbreaks, and transmission events avoiding the current temporal gaps. For its full implementation, there is a remarkable need of shared databases, agile informatics systems and political implication to acquire resources and health professionals.

RedLabRA is structured in three levels of action (Figure 1). Level 1 laboratories include all clinical microbiology laboratories of the National Health System, both public and private, being a key element of the Network. These laboratories must have the capability to phenotypically detect resistant pathogens and resistance mechanisms. Level 2 laboratories must have the capacity to support level 1 laboratories by performing an agile molecular characterization of resistance mechanisms and clones, as well as being able to address the study of outbreaks. Level 2 laboratories are designated by each autonomous community; the Centro Nacional de Microbiología

(CNM) can provide support in the performance of level 2 functions in those cases deemed necessary.

The third level will be restricted to the CNM (ISCIII) and certain laboratories designated by the Network for specific diagnoses. They must have the same capabilities and functions as level 2 laboratories, but their specific functions are to coordinate the Network, to carry out quality controls, to elaborate protocols and to perform comparative and evolutionary national studies with representative strains of circulating clones by whole genome sequencing.

In RedLabRA, a continuous feedback of information between laboratories of all levels is required; as well as the communication of the obtained results to the National Epidemiological Surveillance Network (RENAVE).

No individual, agency, region, or country will be able to control AR on their own. RedLabRA is a tool that arises with the purpose of helping to unify, coordinate and jointly analyze the AR information generated by microbiology laboratories, which will facilitate the implementation of early measures to reduce its impact and dissemination.

REFERENCES

1. WHO. Resistencia a los antibióticos. Organización Mundial de la Salud. 2020 [accessed: 2 April 2021]. Available from: https://www.who.int/es/news-room/fact-sheets/detail/resistencia-a-los-antibióticos
2. WHO. Resistencia a los antimicrobianos [Internet]. Organización Mundial de la Salud. 2020 [accessed: 6 April 2021]. Available from: https://www.who.int/es/news-room/fact-sheets/detail/antimicrobial-resistance
3. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis. 2019;19(1):56–66. DOI: 10.1016/S1473-3099(18)30605-4
4. AEMPs. La cooperación entre investigadores, administración y empresas, clave para ofrecer nuevas alternativas terapéuticas frente a la resistencia a los antimicrobianos. Agencia Española de Medicamentos y Productos Sanitarios, AEMPS. 2018.
5. PRAN. PRAN [Internet]. Plan Nacional de Resistencia a Antibióticos (PRAN). 2021 [accessed: 14 April 2021]. Available from: https://resistenciaantibioticos.es/es
6. Moure Z, Lara N, Marín M, Sola-Campoy PJ, Bautista V, Gómez-Bertomeu F, et al. Interregional spread in Spain of linezolid-resistant Enterococcus spp. isolates carrying the optrA and poxtA genes. Int J Antimicrob Agents. 2020;55(6):105977. doi: 10.1016/j.ijantimicag.2020.105977
7. Ortiz de la Tabla V, Ortega A, Buñuel F, Pérez-Vázquez M, Marcos B, Oteo J. Detection of the high-risk clone ST131 of Escherichia coli carrying the colistin resistance gene mcr-1 and causing acute peritonitis. Int J Antimicrob Agents. 2017;49(1):115–6. doil: 10.1016/j.ijantimicag.2016.10.003
8. Nicolas-Chanoine MH, Bertrand X, Madec JY. Escherichia coli ST131, an intriguing clonal group. Clin Microbiol Rev. 2014;27(3):543–74. doi: 10.1128/CMR.00125-13
9. Oteo J, Pérez-Vázquez M, Bautista V, Ortega A, Zamarrón P, Saez D, et al. The spread of KPC-producing Enterobacteriaceae in Spain: WGS analysis of the emerging high-risk clones of Klebsiella pneumoniae ST11/KPC-2, ST101/KPC-2 and ST512/KPC-3. J Antimicrob Chemother. 2016;71(12):3392–9. doi: 10.1093/jac/dkw321
10. Oteo-Iglesias J, Pérez-Vazquez M, Campoy PS, Moure Z, Romero IS, Benito RS, et al. Emergence of blood infections caused by carbapenemase-producing klebsiella pneumoniae ST307 in Spain. J Antimicrob Chemother. 2020;75(11):3402–5. doi: 10.1093/jac/dkaa301
11. David S, Reuter S, Harris SR, Glasner C, Feltwell T, Argimon S, et al. Epidemic of carbapenem-resistant Klebsiella pneumoniae in Europe is driven by nosocomial spread. Nat Microbiol. 2019;4(11):1919–29. doi: 10.1038/s41564-019-0492-8
12. European Centre for Disease Prevention and Cont. ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations – 2019-2021. 2019. 54 p. Available from: www.ecdc.europa.eu
13. Oteo-Iglesias J. Active surveillance of antimicrobial resistance. Enferm Infecc Microbiol Clin. 2019;37(Supl 1):26–31. doi: 10.1016/S0213-005X(19)30179-X
14. O'Neil J. Tackling drug-resistant infections globally. Arch Pharm Pract. 2016;7(3):110. doi: 10.4103/2045-080x.186181
15. World Bank. Drug-Resistant Infections: A Threat to Our Economic Future. [Internet]. Vol. 2, Washington, DC: World Bank Report. 2017. Available from: www.worldbank.org
16. AEMPS, Dirección General de Salud Pública. Red de laboratorios para la vigilancia de los microorganismos resistentes. 2018. Available from: https://resistenciaantibioticos.es/es/system/files/field/files/red_laboratorios_vigilancia.pdf?file=1&type=node&id=499&force=0