Enferm Infecc Microbiol Clin. 2013;**31(Supl 4)**:16-24

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

How to measure and monitor antimicrobial consumption and resistance

Santiago Grau[a,b,c,*], Germán Bou[d,e], Esther Fondevilla[f], Jordi Nicolás[g], Manuel Rodríguez-Maresca[h] and Luis Martínez-Martínez[i,j]

[a]*Departamento de Farmacia, Hospital del Mar, Barcelona, Spain*
[b]*Comité VINCat, Barcelona, Spain*
[c]*Universitat Autònoma de Barcelona, Barcelona, Spain*
[d]*Servicio de Microbiología, Complejo Hospitalario Universitario de A Coruña (CHUAC), A Coruña, Spain*
[e]*Instituto de Investigación Biomédica de A Coruña (INIBIC), A Coruña, Spain*
[f]*Centro Coordinador VINCat, Barcelona, Spain*
[g]*Departamento de Farmacia, Hospital Son Llàtzer, Palma de Mallorca, Spain*
[h]*Servicio de Microbiología, Hospital Complejo Hospitalario Torrecárdenas, Almería, Spain*
[i]*Servicio de Microbiología, Hospital Universitario Marqués de Valdecilla-IFIMAV, Santander, Spain*
[j]*Departamento de Biología Molecular, Universidad de Cantabria, Santander, Spain*

Keywords:
Antimicrobial consumption
Defined daily dose
Antimicrobial resistance
Surveillance
Bacterial fitness

ABSTRACT

Collateral damage caused by antibiotic use includes resistance, which could be reduced if the global inappropriate use of antibiotics, especially in low-income countries, could be prevented. Surveillance of antimicrobial consumption can identify and target practice areas for quality improvement, both in the community and in healthcare institutions. The defined daily dose, the usual adult dose of an antimicrobial for treating one patient for one day, has been considered useful for measuring antimicrobial prescribing trends within a hospital. Various denominators from hospital activity including beds, admissions and discharges have been used to obtain some standard ratios for comparing antibiotic consumption between hospitals and countries. Laboratory information systems in Clinical Microbiology Services are the primary resource for preparing cumulative reports on susceptibility testing results. This information is useful for planning empirical treatment and for adopting infection control measures. Among the supranational initiatives on resistance surveillance, the EARS-Net provides information about trends on antimicrobial resistance in Europe. Resistance is the consequence of the selective pressure of antibiotics, although in some cases these agents also promote resistance by favouring the emergence of mutations that are subsequently selected. Multiple studies have shown a relationship between antimicrobial use and emergence or resistance. While in some cases a decrease in antibiotic use was associated with a reduction in resistance rates, in many other situations this has not been the case, due to co-resistance and/or the low biological cost of the resistance mechanisms involved. New antimicrobial agents are urgently needed, which coupled with infection control measures will help to control the current problem of antimicrobial resistance.

Medición y monitorización del consumo de antibióticos y resistencias bacterianas

Palabras clave:
Consumo de antimicrobianos
Dosis diaria definida
Resistencia a los antimicrobianos
Vigilancia
Coste biológico

RESUMEN

El daño colateral más importante derivado del uso de los antibióticos es la aparición de resistencias bacterianas. La prescripción inadecuada de los antibióticos está íntimamente relacionada con este efecto, observado globalmente a nivel mundial, pero principalmente en países con recursos económicos limitados. La estrecha vigilancia del consumo de los antibióticos puede ser de gran ayuda para identificar cuáles son los problemas relacionados con la prescripción de estos fármacos e introducir las estrategias necesarias para evitarlos, tanto en el ámbito ambulatorio como en el hospitalario. La dosis diaria definida, referida a la dosis usual de un antimicrobiano concreto, destinada al tratamiento diario de un paciente, se ha considerado útil para el estudio de las tendencias de consumo de los antibióticos en el hospital. Esta unidad se ha introducido en diversas fórmulas que incluyen diversos denominadores correspondientes a la actividad hospita-

*Corresponding author.
E-mail: sgrau@parcdesalutmar.cat (S. Grau).

0213-005X/$ - see front matter

laria, entre ellos el número de camas, ingresos y altas. Todo ello, con el objetivo de obtener una serie de indicadores estandarizados que se utilizan para efectuar comparaciones sobre el uso de antibióticos entre distintos hospitales y países. Los sistemas de información del laboratorio son las fuentes primarias de datos para la preparación de informes acumulados de sensibilidad. Esta información es útil para planificar tratamientos empíricos y adoptar medidas de control de infección. Entre las iniciativas supranacionales de vigilancia de la resistencia, la red EARS-Net proporciona información acerca de las tendencias de resistencia en Europa. La resistencia es consecuencia de la presión selectiva de los antimicrobianos, aunque en ocasiones estos agentes también promueven la resistencia al favorecer la aparición de mutaciones seleccionadas posteriormente. Múltiples estudios indican la relación entre el uso de antimicrobianos y la aparición de resistencias. Aunque en algunos casos una disminución del uso de un antimicrobiano se asocia a una reducción en las tasas de resistencia a este, en muchas otras situaciones no sucede así, debido a la corresistencia o al bajo coste biológico del mecanismo implicado. Son necesarios nuevos antimicrobianos, que junto con medidas de control de infección ayudarán a paliar el problema de la resistencia.

Introduction

Antibiotics have increased life expectancy. Self-medication occurs in many countries where antibiotics are classified as prescription-only medicines. Currently, microbial resistance to treatment with antibiotics constitutes an important public health problem, especially in the hospital environment. In this environment we find significant complexity and density of antibiotic use.

Surveillance of antimicrobial resistance can identify trends in resistance patterns and novel resistances. Antimicrobial stewardship initiatives and infection control programmes play an important role in decreasing inappropriate use and halting the dissemination of resistance. Education of professionals and the public should focus on changing behaviour rather than exclusively increasing knowledge, as the latter could have a paradoxical effect by increasing demand and prescription. Behaviour change should target all prescribers, including veterinarians, since microbes know no boundaries between animals and humans and are capable of exchanging resistance genes.[1] This section is focused on certain aspects related to measures of antimicrobial consumption and bacterial resistance.

Ways of measuring antimicrobial consumption

A European Commission press release dated November 17, 2011 outlined an action plan against bacterial resistance to last-line antibiotics, comprising 12 specific measures to be implemented in the next five years.[2] Two of the measures aim to heighten awareness regarding the appropriate use of antimicrobials and to strengthen surveillance systems of bacterial resistance and antimicrobial consumption in medicine.

In order to promote rational use and to avoid the development of resistance, antimicrobial consumption[3] in groups of hospitals and departments must be measured and compared. Trends in antibiotic consumption must also be monitored. For this to be possible, the data must be expressed in the same units of measurement. At present, comparisons with other hospitals or countries are not always possible, as different bibliographic resources may contain different measurement units—a situation that generates a certain degree of confusion.[4-8]

Usually, consumption is expressed as a quotient consisting of a numerator and a denominator. Today, the three measurement units most often used as the numerator are:[9] DDD[10] (defined daily doses), PDD[6] (prescribed daily doses) and DOT[11] (days of therapy, a new unit used in the US). The definitions and the advantages and disadvantages of each unit of measurement are specified in Table 1.

Each year, the WHO's International Working Group for Drug Statistic Methodology of Norway establishes the DDD for each drug and administration route.

At the hospital level, the most frequently used denominators are: 100 (or 1,000) occupied bed-days (OBD) and 100 admissions (or discharges).[12] The calculation of DDD/100 OBD is carried out according to the formula: DDD/100 OBD = consumption/DDD × 100/OBD, where the consumption and the DDD are expressed in the same units (grams).

At the primary care level, the most frequently used unit is DDD/1,000 inhabitants/day.

The monitoring of antimicrobial consumption is usually presented in a report[9] that records: *a)* The periodicity of measurement (e.g., annual, six-month, quarterly, monthly, before and after an intervention); *b)* The department studied (overall, medical or surgical department, ICU, a certain ward); *c)* The clinical indications (e.g., antipseudomonals); *d)* The level of data aggregation (e.g., therapeutic group or subgroup, drug, medicine).

The reports may be cross-sectional (a certain year or month) or longitudinal, in order to track the evolution of consumption over time.

For a correct evaluation of trends of consumption in hospitals over time, the variations in the hospital indicators and consumption must be expressed in DDD/100 OBD and DDD/100 discharges.[12]

Information about trends of hospital consumption of antimicrobials in Spain is scarce. However, in the autonomous community of Catalonia the VINCat monitoring program compiled data from 54 hospitals on antibacterial and antifungal consumption in the period 2007-2011.[13-16]

In Europe, several countries have carried out studies of antibacterial consumption over time. Examples include Denmark (DANMAP[17]), Netherlands (NETHMAP[18-19]), France (CCLIN[20-23]), Sweden (SWEDRES[24,25]) and Ireland (HSE-HPSC[26]) (Fig. 1). In general, antibiotic consumption presents an upward trend in all these countries.

Evolution of human consumption of antimicrobial agents

Although most antimicrobials are prescribed in the community,[27] microorganisms isolated from hospital infections usually show more resistant profiles than microorganisms from community infections,[28] due to the fact that the proportion of patients receiving antimicrobial agents is much higher in hospitals than in the community,[29] and for this reason the exerted selective pressure is much higher in hospitals.

In order to see the evolution of antibiotic consumption in the European Union, we will analyse the data published by the ESAC Net. The European Surveillance of Antimicrobial Consumption (ESAC) network is an international data collection network that aims to improve antimicrobial prescribing by collecting data on patterns of antibiotic prescribing utilizing a standard validated method.[30] ESAC-Net is today a Europe-wide network of national surveillance systems that provides independent reference data on antimicrobial consumption in Europe, reported by 29 EU/EEA countries. It collects and analyses data from the community (primary care) and the hospital sector.