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A step forward in the definition of antimicrobial stewardship indicators: Better measurements, better work

Un paso adelante en la definición de indicadores PROA: Medir bien para trabajar mejor

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The available evidence suggests that there is a causal association between the development of antimicrobial stewardship programs (AMS) and reductions in the incidence of infection and colonization by antibiotic-resistant bacteria[1]. The description of indicators and their monitoring over time is a key pillar of these programs; without an initial assessment, it is impossible to establish the baseline situation, the priorities for action, or the effectiveness of interventions. In addition, in an increasing number of centres, AMSs form part of service management agreements with the centres' management, and hospitals with health services, as in the PIRASOA program in Andalusia (Spain) or the VINCAT program in Catalonia (Spain). This means that the indicators are the best tool for assessing adherence with the agreed objectives.

In response to the evident need in Spanish hospitals, 2012 saw the publication of the PROA (AMS in Spanish) document[2], which represented a starting point for the organization and implementation of these programs in many hospitals. With the participation of intensivists, this document was developed by the Spanish societies of Clinical Microbiology and Infectious Diseases (SEIMC), Hospital Pharmacy (SEFH), and Preventive Medicine, Public Health and Hygiene (SEMPSPH). It established the objectives and guidelines for initiating and developing AMSs in hospitals, and included a description of a set of structure, process, and outcome indicators for their assessment. Among the process indicators, the document proposed the monitoring of antimicrobial consumption as a basic indicator to determine the situation and evolution of antibiotic pressure, and highlighted the importance of measuring not only the global and individual consumption of antimicrobials, but also measuring the consumption of a group of drugs based on prescription indications (e.g. measuring the global consumption of antipseudomals or drugs against resistant gram-positive bacterias). However, it is likely that this type of "strategic" measurement is being used less than it should be in actual practice.

In this issue of *Farmacia Hospitalaria*, Gutiérrez-Urbón *et al.* describe a set of antimicrobial consumption indicators selected by a panel of experts using the Delphi methodology for their use in hospital settings[3]. It is striking that, among the selected indicators, the classic indicators of consumption of specific drugs are in the minority, whereas the majority are indicators that measure what we could be considered the strategic use of drugs. This is the case for indicators based on ratios (e.g. metronidazole/piperacillin-tazobactam + carbapenems, or IV macrolides/IV respiratory fluoroquinolones), or on antipseudomal heterogeneity. Undoubtedly, this approach represents a bold and (in our opinion) wise step forward, given that these indicators provide a relative picture of consumption and can help AMS teams to take decisions in a more specific manner. However, as with many other indicators, caution should be exercised when interpreting the results of these indicators.

Firstly, some of these indicators may be especially dependent on local epidemiology, such as antipseudomonal diversification, which depends on the sensitivity of the local isolates of *Pseudomonas aeruginosa*, or the ratio of anti-methicillin-sensitive *Staphylococcus aureus*/anti-methicillin-resistant *Staphylococcus aureus* (MRSA) agents, which depends on the incidence of MRSA. Thus, their comparative use between centres should take these facts into account.

Perhaps the most debatable aspect of the proposal is that the indicators are based solely on the defined daily dose (DDD). As suggested in the AMS document[2], indicators that use the DDD may overestimate antibiotic pressure in situations in which doses higher than those defined are used, without this involving a greater risk of resistance selection or induction (or even help to prevent resistance). This has become increasingly relevant in recent years, given that the information provided by pharmacokinetic and pharmacodynamic studies have shown the need to use higher dosages for certain microorganisms (e.g. for the treatment of *P. aeruginosa* pneumonia), in multiresistance situations (e.g. the use of meropenem 2 g/8 h for multiresis-

tant isolates with a minimum inhibitory concentration to meropenem 2 mg/L to 8 mg/L), or in critically ill patients with augmented renal clearance when drugs eliminated by this route are used[4]. Therefore, epidemiological changes or changes in dosing recommendations can have a decisive impact on indicators. In addition, in many cases, the DDDs are much lower than the doses recommended in the clinical guidelines. For example, in *Staphylococcus aureus* bacteraemia, the recommended standard doses of cloxacillin would correspond to 6 DDDs[5]. For example, if only 1 more patient with *S. aureus* bacteraemia was treated with cloxacillin instead of vancomycin, the proposed ratio-based indicator would easily overestimate the very modest improvement achieved. An important aspect to consider in relation to the ecological impact of antimicrobials, at least for some microorganisms, is the duration of treatment. This aspect may not be precisely captured by measuring DDDs[6].

The use of patient-days as the denominator is also subject to question. Patient-days are easy to measure objectively, but the turnover rate and average stay must be taken into account. If the hospital stay is short, patients admitted for community infection or scheduled surgery (for treatment or prophylaxis, respectively) will receive antibiotics during a greater percentage of days of admission. Therefore, measurements in DDD/patient-days tends to penalize the units and hospitals with the shortest mean stays and the highest turnover rates (or number of admissions), which are common situations in hospitals or at times of the year with the greatest pressure on healthcare. Therefore, despite greater difficulties in their measurement, we must develop systems that can measure prescribed daily doses and days of treatment as complementary indicators to the DDD. This strategy would help us better understand the above aspects.

The oral/intravenous drug ratio should also take into account the mean stay. A suitable policy for promoting hospital discharges in patients without the need for intravenous treatment would reduce the use of oral drugs and artificially worsen the indicator, given that these drugs would be consumed on an outpatient basis.

Finally, whether these indicators really serve to assess the quality of the prescriptions (although in an aggregate form) is open to question, as the authors themselves point out. The quality of antimicrobial use is assessed by weighing the greatest benefit to the patient against the least adverse effects and taking into account the selected drug, dose, and route, and the duration of the prescription[7,8]. The assessment of the quality of antimicrobial use is always controversial given the difficulty in establishing homogeneous and objective criteria[9,10]. However, taking the foregoing aspects into account, we consider that the quality of prescriptions should continue to be assessed on a case-by-case basis.

Gutiérrez-Urbón *et al.* should be congratulated regarding their proposed indicators, which represent a clear advance over the classic indicators that only take into account drug consumption. The authors and invited panellists have rightly taken into account variables such as the spectrum of drugs, their indications, and their potential strategic use, as well as costs. The methodology used allowed the opinions of the multidisciplinary panel to be incorporated in a structured manner. Furthermore, it appears that the indicators used may be calculated in any hospital. We invite the panellists to go further and establish a line of work to validate the impact of these indicators on decision making in the setting of AMS.

As an additional aspect, we must point out the need for all hospitals to have electronic systems that provide better and faster measurements of indicators, which not only include DDD but also prescribed daily doses and days of treatment. Such systems would lead to a better assessment of AMS activities and marked time-savings in the identification of prescriptions susceptible to intervention. These tools are essential in a setting in which the lack of human resources is the main barrier to the correct development of AMS in Spain.

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