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Editorial

Antimicrobial stewardship programs in pediatrics: A growing reality in our country



Programas de optimización del uso de antimicrobianos en pediatría: una realidad creciente en nuestro país

The current rise in antimicrobial resistance is a well-recognized global health threat. Antimicrobial use in human and animal health, as well as in other activities has been identified as a factor accelerating the emergence of resistance mechanisms. Forecasts for the coming years in this line are alarming, as it is estimated that antimicrobial resistance could lead to the premature death of some 300 million people worldwide, with a significant negative impact on the world economy.¹

Resistance to antibiotics is also an important health problem in children. Data from the annual mortality report in Spain show that the third most frequent cause of mortality in infants younger than one year is infectious disease leading to neonatal early- and late-onset sepsis.² Furthermore, an estimated 30% of deaths from sepsis in neonates worldwide is due to multi-resistant bacterial infections.^{3,4}

In the last decade, efforts have been intensified to deal with what is already considered a silent pandemic at the global level. National and international government agencies have defined strategic plans to curb the growing emergence of resistance to antimicrobials. In this direction, the Spanish Agency for Medicines and Health Products (AEMPS) has published the National Plan against Antibiotic Resistance (PRAN), which establishes an urgent need to put into practice antibiotic stewardship programs (ASPs) at different care levels to improve antimicrobial use.⁵

Although we have clear recommendations regarding ASPs for the adult population,⁶ there are still some unknowns about the best strategies to improve antimicrobial use in children.⁷ Several scientific societies and health organizations have recognized children as a key priority population group for the development of ASPs, and some recommendations have been drawn up for implementation of ASPs in children and newborns.^{8–11} These have been designed taking into consideration existing differences in the etiology and clinical features of infections in children, the pharmacokinetic characteristics of the agents used in this population, the incidence of infections due to resistant microorganisms, and the less extensive evidence regarding the efficacy and safety of some antibiotics in neonates and children.

Antimicrobial prescription in children's hospitals varies considerably between different centers and countries. It is estimated that more than 40% of hospitalized pediatric patients receive at

least one antibiotic during admission, and in pediatric intensive care units (PICUs) the prescription rate may rise above 60%.^{12,13} At the primary care level, several reports have noted an upward trend in inappropriate pediatric use of broad-spectrum antibiotics to treat acute respiratory infections, antibiotic prescription for viral respiratory infections, and treatments of unnecessarily long duration.¹⁴ Thus, there is an evident need for specific ASPs for this population, in which relevant and sustainable indicators for each healthcare level and age group are defined. These programs should allow continuous monitoring of antimicrobial use, but also attend to clinical and microbiological indicators to enable actions for improvement.¹⁵

Recently, Donà et al.¹⁶ conducted a systematic review of studies on pediatric ASPs published between 2007 and 2018, which confirmed that that implementation of these programs in pediatrics also has a significant impact on reducing the use of antibiotics, lowering health costs, and decreasing antimicrobial resistance. To date, pediatric ASPs have been developed mainly in the United States (only 28 of the 113 hospitals identified by Donà et al. were in European countries), but they are now emerging in Europe, although with important differences between countries.¹⁰

Thus, the presence of three articles in this issue of *Enfermedades Infecciosas y Microbiología Clínica* related to various pediatric and neonatal ASPs carried out in Spain is particularly noteworthy. These studies cover both diagnostic aspects (Brotons et al.¹⁷) and monitoring of antimicrobial use in highly vulnerable, pediatric populations: neonatal patients (Villanueva-Bueno et al.¹⁸) and those admitted to PICUs (Simó Nebot et al.¹⁹).

In their study on the use of diagnostic tests in acute respiratory infections (ARIs) in children admitted to the PICU, Brotons et al.¹⁷ note that defining the etiology of ARIs is challenging in this population because of the non-specificity of the symptoms, especially in the youngest patients. The authors evaluate the usefulness of conducting microbiological screening upon admission using molecular biology techniques in respiratory samples, almost exclusively nasopharyngeal aspirates. This approach includes the main causes of viral ARIs in pediatrics, as well as *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*. The authors found that routine addition of this study to their standard of care significantly increased the diagnostic yield, almost

entirely because of virus detection, with a response time of less than 3 h. Despite these results, the impact on antimicrobial prescription was modest, as is usually the case in high-risk patients such as those admitted to the PICU. The authors justify these findings by citing the practice of waiting until bacteriological results from standard studies are available before withdrawing empirical antibiotics. Nonetheless, it seems reasonable to advocate more proactive attitudes in patients who have no other risk factors for bacterial coinfection, which is rare according to the authors' data. Reasoned use of clinical and analytical parameters can be of aid for better prescription of antimicrobials in these patients.¹⁷ In any case, the benefits of incorporating diagnostic stewardship programs to ASPs and infection control programs was demonstrated once again.

Although most objectives of ASPs in children are the same as those in the adult population, one of the main differences for their implementation is the need to use appropriate measures for this age group, especially for calculating antimicrobial consumption, with DOT (days of therapy) being the most widely used indicator.^{9,15}

Regarding this aspect, at the same children's hospital in Barcelona, Simó Nebot et al.¹⁹ quantitatively and qualitatively evaluate the use of antimicrobials in their PICU for one year. Appropriate use of antimicrobials in pediatric and neonatal intensive care units is especially complicated due to several factors: the severity of the patients' clinical course, the higher prevalence of multiresistant microorganisms, and the reluctance of treating physicians to withdraw empirical treatment despite negative microbiological results. This PICU study mainly involved surgical and community-acquired infections within a short time frame. Overall, the quality of prescription was acceptable, but a need to reduce both the spectrum of antibiotics used and their duration was manifested, especially in perioperative prophylaxis. Extension of this type of study to PICUs of other centers in our country would promote suitable benchmarking focused on detecting potential points of improvement in each center.

Finally, Villanueva-Bueno et al.¹⁸ investigate an alternative method to DOT for calculating antimicrobial consumption in the neonatal population, as they did within the KiDDDs group for children in 2018.²⁰ The study was carried out using a Delphi method, and neonatologists and pharmacists from the main neonatal intensive care units in Spain participated. Although DOT is recognized as a standard measure for the pediatric and neonatal population, calculation of this parameter is not a simple task and requires the center to have computerized electronic prescription. As not all centers have data on microbial use in DOT, an adaptation of the defined daily dose (DDD), the measure generally used as the standard unit in adults, could provide them with an approximation of the data required for monitoring antimicrobial consumption in children and neonates. The unit of measurement proposed by Villanueva-Bueno et al.¹⁸ could be an alternative for quantifying antimicrobial consumption in this population at the hospital level, but it will require validation by scientific societies for generalized use.

These valuable studies related to specific ASPs for children and neonates should serve as a stimulus for other groups to develop their own programs and publish their results to bring to light points of improvement from intra- and inter-hospital comparisons. Initiatives such as creation of the VINCat PROA Pediatrics program in Catalonia and the ASP group of the Spanish Society of Pediatric Infectious Diseases (SEIP) are vital to provide a definitive push toward generalization of healthcare quality programs considered essential by national and international healthcare organizations both at the hospital level and in primary care.

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