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Editorial

It is time for pediatric antimicrobial stewardship programs

Es el momento de los programas de optimización del uso de antimicrobianos (PROA) en Pediatría

Antimicrobial resistance (AMR) is currently one of the main problems in healthcare. The prevalence of multidrug-resistant bacteria has increased significantly in recent years, being included by the World Health Organization in the list of 10 threats to global health in 2019.[1] Among the factors associated with the growing incidence of AMR is the inappropriate use of antibiotics.[2] Countries with higher consumption of antibiotics also have a higher prevalence of AMR.[3] Therefore, there is an increased interest in programs targeting the prescription of antimicrobials in healthcare settings, including hospitals and primary care centers, which have been named antimicrobial stewardship programs (ASP).[4]

Initially, these programs were mostly applied to adult units, showing impactful results.[5] However, considering the singularities of children, adapting specific pediatric strategies may be relevant to achieve the goals of ASP successfully in this population. Furthermore, there is rising evidence associating early consumption of antibiotics in infants with an increased risk of developing different diseases later in life, such as asthma, allergy or diabetes through alterations in the gut microbiome.[6]

Over the last few years, an increasing number of hospitals have incorporated a pediatric ASP. These programs have achieved notable relevance amongst different healthcare workers, including pediatricians, pediatric pharmacists and nurses. A survey about the state of pediatric ASP in Spain in 2017 showed that 34% of centers had a pediatric ASP, and 45% additional centers were performing some activities related to antimicrobial stewardship (unpublished data by Goycochea-Valdivia). Another recent survey including hospitals with pediatric ASP conducted in the UK showed that 'Audit and feedback' was the most commonly used stewardship model, adopted in 13 out of 17 centers.[7]

The characteristics of infections and the use of antimicrobials in children are different from adults. Notably, children under 3 years of age are the group with the highest cumulative probability of receiving an antibiotic over time.[8] Moreover, two recent studies conducted in Europe and the US revealed that up to one-third of antibiotic prescriptions for children in different hospital settings were inappropriate.[9,10]

The profile of the prescription of antimicrobials in children has several peculiarities that differentiate it from prescriptions in adults. Unlike adults, in which there is an excessive consumption of quinolones, this antibiotic group is not routinely prescribed in children. However, other broad-spectrum antibiotics, such as amoxicillin-clavulanate or non-first-line antibiotics, such as macrolides, are usually overprescribed in children without adhering to clinical guidelines.[4,11] This highlights that the antimicrobials targeted in ASP should differ slightly according to the age group.

There are different resistance patterns in children compared to adults. A study performed in Europe that compared AMR prevalence of bacterial isolations from children reported by a pediatric network (ARPEC) with all-age isolations reported by EARS-Net showed important variations between children and adults.[12] Additionally, within a specific resistance mechanism such as carbapenemase production by Gram-negative microorganisms, some geographical regions have reported different epidemiology among pediatric units compared to adult units.[13]

The standard measurement of the rate of antimicrobial use in adults, defined as daily dose (DDD) per 1,000 occupied bed-days, is not appropriate in children as dosing in this population is based on body weight or body surface area. Using DDD makes the audit and comparison of pediatric antimicrobial prescriptions difficult. Several alternatives, such as a modified DDD[14] or a different index, such as days of treatment (DOT),[15] have been proposed. Notably, DOT is recommended as standard measurement in children by the Infectious Diseases Society of America and the Australian Health Care.[15,16] Therefore, in order to correctly audit the quality and characteristics of prescriptions in children, DOT should be implemented in all pediatric centers.

On the other hand, there are several differences in the physiology, epidemiology and clinical manifestations of childhood infections. Taking these aspects into account, the importance of including professionals with pediatric-specific knowledge in AMS teams should be reinforced.

Recent evidence on pediatric ASP has demonstrated relevant benefits in several aspects: decreased antimicrobial use, prescribing errors and medication costs, improved clinical outcomes, and decreased prevalence of AMR.[17] Key pediatric ASP strategies include improvement in the appropriateness of antimicrobial prescriptions, reduced treatment duration, the use of oral ther-

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apy (including intravenous-to-oral switch strategies), and dose optimization.[16] While a vast majority of pediatric ASP evidence is from hospital settings, it is important to highlight that most antimicrobial prescriptions for children occur in primary care. Therefore, some specific approaches for pediatric primary care should be included in the pediatric ASP.

In the present issue of Enfermedades Infecciosas y Microbiología Clínica, the study by Melendo et al. is another good example of the high impact of these types of interventions.[18] The authors performed activities to monitor treatments with intravenous antibiotics lasting longer than 7 days in non-neonatal pediatric patients through a weekly cross-sectional analysis, followed by recommendations for inappropriate prescriptions. A total of 146 prolonged antibiotic treatments in 81 patients were evaluated. The most common antibiotics prescribed were piperacillin-tazobactam and meropenem. Out of 190 evaluations, 36 (19%) were inappropriate, receiving a persuasive recommendation. Half (52.7%) of these recommendations were followed by the prescriber, and nineteen treatments were optimized (14 suspended and 5 de-escalated).

The low percentage of recommendations that were accepted by the attending physicians highlights the difficulties in advising on antimicrobial treatment in children. Probably, the lack of strong recommendations regarding the duration of antibiotics in children for several infections keeps the prescribers from using shorter durations. It should be taken into account that the success of ASP not only improves individual prescriptions but also helps in training and transferring the habit of a rationalized prescription to other colleagues.

The increasing evidence in favor of early step down to oral treatment is improving the management of several infectious diseases.[19,20] Thus, a specific ASP focused on intravenous antibiotics seems relevant. Intravenous treatment is associated with an increased risk of many adverse outcomes, such as catheter-related infections or longer hospital stay, leading to higher costs and a higher risk of hospital-acquired infections. Intravenous-to-oral switch, de-escalation, or shortening the duration of antimicrobial treatment are key strategies to reduce these risks.

In conclusion, it is time for pediatric ASP. It is necessary to address research gaps in pediatric infectious diseases, such as increasing knowledge in pharmacokinetic/pharmacodynamics of several antimicrobials in children or optimal antimicrobial duration. The development of consensus guidelines on pediatric ASP supported by pediatric scientific societies will encourage clinicians to improve the quality of prescriptions. Investing resources to implement inpatient and outpatient ASP and emphasizing the relevance of including pediatric experts on ASP programs is essential to achieve the goals of pediatric ASP, which will produce relevant improvements in global health.

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Conflicts of interest

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