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Editorial

Monitoring of antimicrobial consumption in paediatrics

Monitorización del consumo de antimicrobianos en pediatría

Infectious diseases are the main reason for medical consultation and hospital admission in paediatrics and the first cause of admission to paediatric intensive care units. According to the Antibiotic Resistance and Prescribing in European Children (ARPEC) study, antibiotics are the most prescribed drugs in paediatrics, both within hospitals and primary care.[1] Therefore, the implementation of the Antimicrobial Stewardship Program (ASP) in paediatrics must be a priority for healthcare institutions, especially if we consider that it has been shown, also in paediatrics, a significant impact on the reduction of antibiotic use, and a decrease in healthcare costs and antimicrobial resistance.[2] Thus, several scientific societies and health organisations have focused their efforts on recognizing paediatrics as a key population group that should be prioritised for the development of the ASPs in order to minimise the inappropriate use of antimicrobials.[3–11]

Monitoring the amount of antimicrobial use is one of the key strategies in ASP since it allows to control and evaluate the impact of the actions implemented, as well as establishing benchmarking strategies between health centres or between countries or regions.[12] Currently, several units of measurement have been described for monitoring antimicrobials consumption, with the Defined Daily Dose (DDD) being the most widely used.[13] DDDs have been defined by the World Health Organization (WHO) in collaboration with the Centre for Drug Statistics Methodology in its Anatomical Therapeutic Chemical (WHO/ATC) and correspond to the assumed average maintenance dose per day for a drug used for its primary indication in adults (https://www.whocc.no/atc_ddd_index/). Although there is a broad consensus on the use of DDDs for the definition of quantitative consumption indicators of antimicrobials, they are limited in their application, especially in situations in which a reduced dose from the daily dose administrated is used or if there are different dosing recommendations between countries and administration routes (oral, parenteral).

It is especially important to consider that these limitations for the use of DDD are found in the monitoring of consumption in paediatrics, since, by definition, DDD is not an adequate unit of measurement: it is a unit of measurement expressed in grams that do not reflect the Recommended Daily Doses (RDD) or the Prescribed Daily Dose (PDD). In addition, the great variability of dosing in paediatrics, due to the individualisation of the dose according to the patient's weight and age, means that DDDs do not correctly reflect the real consumption of antimicrobials. Thus, the definition specified that DDDs established by the WHO must not be used for the paediatric or neonatal population.[14] Given this limitation, alternative units of measurement have been suggested. A group of experts established a proposal of 19 possible indicators for monitoring the use of antimicrobials suitable for the paediatric population at the hospital level and clearly stated that the main unit of measurement for antimicrobial consumption in paediatrics should be the Days of Therapy or Days of Treatment (DOT).[13,15]

However, the calculation of DOT in many organisations indeed presents certain difficulties in obtaining computation, especially due to the lack of the implementation of computerised electronic prescribing or e-prescribing. Faced with this reality, many centres have been forced to suggest initiatives to calculate antimicrobial consumption based on data generated by the consumption in physical units of antimicrobials, complementary to DDD. And it is in this direction that Montecatine et al.[16,17] published a proposed definition of DDD adapted to paediatrics and neonates (PeDDD). To date, this unit of measurement is an expert proposal, but it has not been sufficiently validated by the international scientific community and, consequently, the authors suggest that it could only be applied in scenarios where other validated units of measurement are impossible to be calculated.

It is in this context that Castagnola et al.[18] conducted a study, published in this issue of Enfermedades Infecciosas y Microbiología Clínica, in a tertiary paediatric hospital comparing the results obtained in the monitoring of antimicrobial consumption calculated on the basis DDDs *vs.* PeDDDs. For this purpose, they estimated the PeDDDD and DDD calculated from the quantity in physical units of each drug consumed. After this analysis, they found that the PeDDDs values were higher than those of the DDDs, but the most remarkable aspect of their results was that the curves between both calculations were parallel and that they obtained identical AUC. Therefore, the calculation for the consumption of antimicrobials using either unit of measurement as an indicator for the exposure to antimicrobials presented no appreciable differences. These results are particularly relevant as they confirm that the monitoring of antimicrobial consumption from PeDDDs should be performed separately for the adult population but in scenarios where calculating other more appropriate indicators for the paediatric population proves impossible (e.g., DOT), the evaluation of PeDDDs and DDDs would show antimicrobials exposure similarly.

While it is true that, despite attempts to define and use quantitative indicators for antimicrobial use based on units consumed for the paediatric population, in certain circumstances, at the hospital

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level there is an increasing number of hospitals that have developed tools for obtaining DOTs using relatively automated methods. But in primary care setting it is still more difficult to monitor the consumption with indicators that do not come from the calculation of units dispensed. For this reason, in the primary care setting, the calculation is usually made based on the DDDs per 1000 inhabitants per day (DHD) based on data from the units of containers collected in pharmacies. These indicators can be used for the evaluation of ASPs in antimicrobial consumption or for evaluating the impact of the different social situations that occur, such as the COVID-19 pandemic. At the European level from 2019 to 2020, a substantial decrease in antibiotic consumption in primary care has been observed during the COVID-19 pandemic and in the post-pandemic months.[19] This reduction has been much more evident in the paediatric population in our healthcare environment, as was observed in the study by Perez-Solís et al.,[20] also included in this issue of Enfermedades Infecciosas y Microbiología Clínica, in which they evaluated the evolution of paediatric antibiotic consumption in primary care in the community of Asturias. In this study, they use data about antibacterial agents for systemic use dispensed for official prescriptions to children under 14 years in primary care. Antibiotic consumption was expressed as defined daily dose (DDD) per 1000 inhabitants per day (DID). The most relevant results were a lower antibiotic use during COVID-19 pandemic, an important decrease in the use of amoxicillin/clavulanic acid and an increased use of amoxicillin and third-generation cephalosporins.

The current challenge is to establish ASP actions to be able to maintain these low levels of antimicrobial consumption and to monitor the impact of other converging situations such as shortages of paediatric pharmaceutical products, the introduction of rapid diagnostic tests in consultations to rule out a bacterial infection in respiratory tract infections or changes in epidemiological profiles in the seasonality of viral infections. It will be necessary to continue developing and implementing technological tools to automate the collection of consumption indicators that allow calculations to be made from units of measurement that more accurately express the real consumption of antimicrobials in the paediatric population in both primary care and hospital care. These indicators will provide ASP teams with relevant and accurate information to design new strategies to improve the use of antimicrobials in the paediatric and neonatal population.

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Aurora Fernandez-Polo
Servei de Farmàcia, Hospital Infantil, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain
E-mail address: aurora.fernandez@vallhebron.cat