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ORIGINAL ARTICLE

Impact of implementing a stewardship program in the pediatric population: cohort study in a quaternary hospital in Brazil

Impacto da implementação de um programa de stewardship na população pediátrica: estudo de coorte em um hospital quaternário do Brasil

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ABSTRACT

Introduction: Strategies to mitigate the advance of antimicrobial resistance span actions in veterinary medicine, agriculture, and healthcare settings. Among these measures is the antimicrobial stewardship program aimed at the rational use of antimicrobials. The appropriate antimicrobial management program in pediatrics is a multidisciplinary initiative that results in the unnecessary use of antimicrobials, decreased resistance, treatment failure, reduced healthcare costs, and optimized diagnostic strategies. **Objective:** To describe satisfactory data on the reduction of DOT (Days of Therapy) and DDD (Defined Daily Dose) in two pediatric and neonatal intensive care units following the implementation of an antimicrobial stewardship program. **Method:** This is a longitudinal study of DOT and DDD reduction conducted in a quaternary hospital in Brazil after the implementation of the antimicrobial stewardship program in the pediatric and neonatal populations. **Results:** During the study period, there was a reduction of approximately 24% in the global DOT of antimicrobials in the studied units. **Conclusion:** The present work demonstrates that through a multidisciplinary methodology, it is possible to achieve a reduction in the unnecessary use of antimicrobials and provide safe care to the population.

Keywords: Stewardship; Antimicrobials; Multidrug resistance.

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RESUMO

Introdução: Estratégias para mitigar o avanço da resistência antimicrobiana perpassam por ações na veterinária, agricultura e ambientes de assistência em saúde. Dentre essas medidas está o programa *stewardship* de uso racional de antimicrobianos. O programa de manejo antimicrobiano adequado em pediatria é uma iniciativa multidisciplinar que resulta em utilização desnecessária de antimicrobianos, diminuição da resistência, falha do tratamento, diminuição dos custos de saúde e otimização de estratégias de diagnóstico. **Objetivo:** Descrever dados satisfatórios de redução de DOT (Dias de Terapia) e DDD (Dose Diária Definida) em duas unidades de terapia intensiva de linha de cuidado pediátrico e neonatal, após implementação de programa *stewardship* de uso racional de antimicrobianos. **Método:** Trata-se de um estudo longitudinal de acompanhamento e redução de DOT e DDD conduzido em um hospital quaternário no Brasil após implementação do programa *stewardship* de antimicrobianos na população pediátrica e neonatal. **Resultados:** Houve no período do estudo redução de cerca de 24% no DOT (dias de terapia) global de antimicrobianos nas unidades estudadas. **Conclusão:** O presente trabalho mostra que através de metodologia multidisciplinar é possível alcançar a redução do uso desnecessário de antimicrobianos e fornecer um atendimento seguro à população.

Palavras-chave: Stewardship; Antimicrobianos; Multirresistência.

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The authors declare no conflicts of interest.

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Introduction

Multidrug-resistant (MDR) bacteria are microorganisms resistant to different classes of antimicrobials. The World Health Organization (WHO) estimates that in Europe, infections by MDR bacteria in the pediatric population represent 30% of the total cases. In sub-Saharan Africa, 66% of neonatal sepsis cases were caused by antibiotic-resistant bacteria[1].

Several factors are associated with the spread of MDR bacteria, including: i) breakdowns in precautionary barriers; ii) use of antimicrobials to ensure animal health in the prevention and control of diseases and parasites in veterinary medicine; and iii) inappropriate use of antibiotics due to diagnostic errors, patient pressure, errors in prescribed doses, non-adherence to treatment by patients, and even self-medication[2,3].

Among these factors, excessive and inappropriate use of antibiotics is most related to the accelerated spread of resistant bacteria. Inappropriate antibiotic prescriptions are common in pediatrics, such as misuse in viral respiratory infections, as well as excessive use of broad-spectrum antibiotics in urinary tract infections and respiratory tract infections[4].

Reducing unnecessary antibiotic use is an important step in slowing antibiotic resistance. Institutional policies on rational antimicrobial use, known as stewardship programs, should be promoted and disseminated to optimize the use of these drugs, especially in the pediatric population. Thus, this study evaluated the quality of antibiotic prescriptions and analyzed consumption among hospitalized children after the implementation of the stewardship program in a quaternary hospital in Brazil.

Methods

This is a longitudinal comparative study conducted from January 2020 to December 2022 at a quaternary hospital in Rio de Janeiro, Brazil. The hospital has 18 pediatric intensive care unit (PICU) beds and 24 neonatal intensive care unit (NICU) beds.

The antimicrobial stewardship program was implemented in the hospital in 2021. The main objectives of the program are to ensure the therapeutic efficacy of antimicrobials, minimize adverse events, reduce the incidence of bacterial resistance, reduce hospitalization time, and decrease costs related to unnecessary treatment. The team includes an infectious disease specialist and a clinical pharmacist dedicated to the project. In addition to these professionals, the hospital management team included high-level institutional management, an infection control service representative, a medical team representative, a

nursing team representative, a microbiology laboratory, and information technology.

Evaluation and intervention steps included: i) validation of antimicrobial prescriptions by clinical pharmacists using an electronic justification form filled out by the clinical staff; ii) implementation of a unified antimicrobial protocol for the hospital available via QR code; iii) case discussions in multidisciplinary rounds; iv) conducting clinical sessions for reviewing controversial topics that emerged during rounds; v) training the medical team through clinical cases available in Google Forms.

The study population was defined by: i) being admitted to a pediatric or neonatal intensive care unit and having received at least one dose of an antimicrobial; and ii) receiving treatment while hospitalized. A non-probabilistic convenience sample was used. Patients who died or were transferred without prescription validation by the stewardship team, as well as those with insufficient data for statistical analysis and those who used only antivirals and antitubercular, were excluded. Categorical variables were presented as proportions.

From the antimicrobial request form evaluation, the stewardship professionals assessed: i) the need for escalation or de-escalation of empirical or targeted therapy according to the unit's microbiological profile and culture results; ii) the possibility of duration adjustment; iii) checking of dose and drug interactions; iv) switching from intravenous to oral therapy; and v) discontinuation of the drug.

After consulting the form and reviewing records, a database was developed in *Excel* containing the following data: name, age, gender, admission sector, month of evaluation, year of evaluation, prescribed antimicrobial, infection site, collected cultures and results, as well as the stewardship team's assessment, type of intervention needed, and whether the intervention was accepted by the attending team.

According to the infection site, the infection diagnosis was categorized into respiratory tract infection, central nervous system infection, gastrointestinal tract infection, urinary tract infection, skin and soft tissue infection, and primary bloodstream infection. All antimicrobial therapy recommendations described in the care protocols were based on scientific evidence from Brazilian, American, and European infectious disease societies.

Restricted-use antimicrobials were defined as drugs: i) associated with toxicity; ii) promoting pathogenic microorganism selection; iii) developing resistance; or iv) with a high cost. The restricted-use antimicrobials listed by the hospital were: meropenem, ertapenem, imipenem, polymyxin B/E, ceftazidime-avibactam, ceftolozane-tazobactam, tigecycline, linezolid, ceftaroline, teicoplanin, lipid formulations of amphotericin B, voriconazole, posaconazole, and isavuconazole.

Outcome measures included: days of antimicrobial exposure (DOT) and Defined Daily Dose (DDD) of antimicrobials and antifungals. Process measures included antimicrobial prescriptions in the neonatal and pediatric intensive care units, proportion of audited prescriptions, proportion of appropriate and inappropriate prescriptions, number of adjustment interventions performed, and proportion of accepted interventions. Project goals were agreed upon annually by the stewardship team, management, and corporate. A 20% random reduction in global DOT of antimicrobials was agreed upon. Results were published monthly as feedback to the care teams, management, and corporate.

Defined Daily Dose (DDD) is defined as the average daily maintenance dose of the antimicrobial, expressed in grams, for the main therapeutic indication of that medication. However, for optimal medication use in children, several factors, such as age, weight, disease progression, and pharmacokinetics, must be considered. Thus, DDD in the pediatric population should consider the average maintenance dose per unit of body weight for a medication used for its main indication in children[5].

DOT equals the number of days a patient receives an antimicrobial agent (regardless of the dose). Any dose of an antimicrobial received during a 24-hour period represents 1 DOT[5].

Data governance for DDD and DOT was managed using Power BI[6,7]. Notifications of restricted antimicrobial prescriptions were received via text message on the infectious disease specialists' phones and by email for clinical pharmacists through the Knotify[8] application. Weekly case discussions were held in the respective units. Subsequently, data were stored in Excel spreadsheets. The study is part of the stewardship project approved by the Hospital Ethics Committee under number CAAE: 47504821.0.0000.5455.

Results

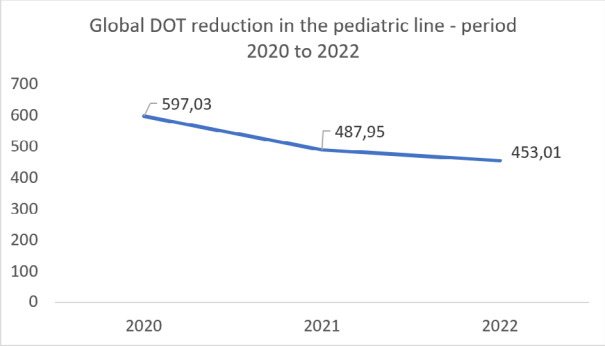
A total of 25,690 patient-days were accounted for during the period, with 11,988 in the pediatric ICU and 13,702 in the neonatal ICU. The average duration of antimicrobial use in the pediatric ICU was 4.22 days, while in the neonatal unit it was 3.91 days. Vancomycin, meropenem, and cefepime were the most prescribed antimicrobials in the pediatric ICU, while in the neonatal ICU, ampicillin, gentamicin, and vancomycin were the most prescribed.

In the pediatric unit, there was a 24.15% reduction in the global DOT of antimicrobials, from 597.03 in 2020 to 453.01 in 2022, as shown in Graph 1.

When analyzing DOT and DDD data by unit, the DOT in the neonatal ICU decreased from 353.87 before the project to 318.91 in 2022. The DOT in the pediatric ICU decreased from 889.13 to 587.94. Compiled data are presented in the following table.

Discussion

This study presents important and successful data from a rational antimicrobial use program aimed at the pediatric population, utilizing the automated Power BI tool. Studies demonstrate that automated tools for obtaining DOT indicators in pediatrics facilitate audits[9]. Additionally,



Graph 1. Global DOT reduction in the pediatric line - period 2020 to 2022

Table 1. Values of DOT and DDD from 2020 to 2022 stratified by follow-up sector

PERIOD/ UNIT	NEO ICU		PED ICU	
	DOT	DDD	DOT	DDD
January 2020 to December 2020	353.87	1,520,000	889.13	1,100,000
January 2021 to December 2021	345.82	1,510,000	662.08	800,640
January 2022 to December 2022	318.91	1,300,000	587.94	718,940

Caption: NEO ICU = Neonatal Intensive Care Unit; PED ICU = Pediatric Intensive Care Unit; DOT = Days of Therapy; DDD = Defined Daily Dose.

well-structured stewardship programs are effective in improving the quality and safety of pediatric health[10].

The fact that the three most prescribed antimicrobials in the pediatric ICU are broad-spectrum is explained by the unit being a referral center for oncohematological patients in the region. Febrile neutropenia is an expected event during chemotherapy[11]. Ampicillin, gentamicin, and vancomycin were prominently used in the neonatal intensive care unit, likely due to diagnostic challenges of sepsis and the relative immunosuppression of newborns, many of whom receive antibiotics due to suspected sepsis. Antibiotics have become the most used therapy in neonatal intensive care units[12].

There was a reduction in DOT in the neonatal ICU from 353.87 to 318.91. These values are consistent with the literature. A study by Newland et al. (2012)[13] demonstrated a reduction from 883 DOTs per 1000 patient-days to 787 DOTs per 1000 patient-days in a neonatal ICU following the implementation of the stewardship program.

A survey conducted in Sergipe, Brazil, in 2012, reported a DOT of 1,530.8 DOTs per 1000 patient-days in the pediatric ICU and emphasized that monitoring is crucial for reducing DOT values. These data underscore the importance of coordinated multidisciplinary actions for the rational use of antimicrobials[14].

The present study is limited by being conducted at only one center and not describing admission reasons and microbiological profiles. Therefore, additional human, technological, and microbiological resources are necessary to promote the safe use of antimicrobials in the pediatric population.

Author's Contributions:

We describe contributions to the papers using the taxanomy (CRediT) provided above:

Conceptualization, Investigation, Methodology, Visualization & Writing–review & editing: JMA; LNHS; CTVB; JMSS; DBS; MBXO. *Project administration, Supervision & Writing–original draft:* PQC; TTD; RFSS; NCZS. *Validation & Software:* JMSS; NCZS. *Data curation & Formal Analysis:* PQC; TTD; RFSS; NCZS.

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