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ORIGINAL ARTICLE

Clinical Intervention of Pharmaceutical Care as an Indicator of Quality of Hospital Care in Pediatrics

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Abstract

Objective: To determine the frequency and nature of drug-related problems in hospitalized patients of a public pediatric hospital in Fortaleza/Ce. **Metodology:** Cross-sectional and retrospective study from the records of pharmaceutical interventions available in the database of the clinical pharmacy service. **Results:** Fifty-eight patients were included in the study. A total of 75 drug-related problems were identified with a frequency of 76.2% related to safety and these involved antimicrobial drugs (45.8%). Dose adequacy (35.7%) was the most frequent pharmaceutical intervention. The acceptability profile of the interventions was 64.4% for physicians and 100% by nurses. **Final considerations:** By analyzing the drug-related problems and pharmaceutical interventions, it was possible to know which aspects of the pediatric patients therapy were explored in the clinical pharmacist follow-up. We emphasize the importance of documentation of clinical practice for the construction of indicators and evaluation of the quality of pharmaceutical care in pediatrics.

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INTRODUCTION

Due to the complexity of drug therapies, hospitalized patients are prone to experiencing drug-related problems (DRPs) arising from errors in therapeutic processes related to the prescription, dispensation, and administration of medication.[1]

If neglected, DRPs may interfere with desirable clinical outcomes, cause and extend hospitalization, and increase mortality and healthcare costs.[2]

Given the physiological immaturity of pediatric patients, weight changes and off-label drug prescriptions are factors that contribute to the occurrence of DRPs. Errors involving medications in a hospital context occur more frequently in neonatal and intensive care units. It is estimated that between 2.5% and 5.7% of hospitalized children have experienced some form of drug-related problem.[3,4]

International organizations such as the American Academy of Pediatrics, the American College of Clinical Pharmacy, and the Joint Commission International have endorsed collaborative and interprofessional work between pediatricians, intensivists, and clinical pharmacists as a way to encourage and strengthen the practices of clinical services delivered by pharmacists in a hospital environment, aiming to minimize the impacts caused by adverse events associated with the use of medications.[5]

It is believed that DRPs are quite common among pediatric patients and in intensive and neonatal care units in particular, given the infectious diseases, neurological conditions, and respiratory dysfunctions for which patients are prescribed complex medical interventions and drug therapies. This study aimed to describe the interventions implemented by clinical pharmacists in the management of DRPs involving patients in pediatric and neonatal intensive care units and neonatal intermediate care units.

METHOD

This quantitative cross-sectional study with retrospective data collection included data from patients staying in three units of the Albert Sabin Children's Hospital in Fortaleza, Northeastern Brazil, namely the Pediatric Intensive Care Unit of the emergency department (PICU 3), the Neonatal Intensive Care Unit (NICU), and the Neonatal Intermediate Care Unit (NIMCU).

The Albert Sabin Children's Hospital is a public hospital that provides tertiary care to children and adolescents and a referral center in the Brazilian North and Northeast for the diagnosis and treatment of rare diseases, cleft lip and palate surgery, and outpatient care in various clinical and surgical medical specialties. The hospital is equipped with 310 beds, 306 of which are for inpatients, four are hospice beds, and 41 are intensive care beds. Pharmacy services are delivered via a central hospital pharmacy, a satellite pharmacy in the surgical center, a pharmacy in the emergency department, and an outpatient pharmacy.

All hospitalized newborns, infants, children, and adolescents admitted to the NICU, NIMCU, and PICU 3 between April and September 2021 who were prescribed at least one pharmaceutical intervention were included in the study. Patients not prescribed pharmaceutical interventions from pharmacotherapy monitoring were excluded from the study.

Data was extracted from the drug-related problem registration database developed by the pharmacists at the Pharmacy Department. The database was created to document pharmaceutical interventions carried out on inpatients and collect indicators for evaluating the quality of pharmaceutical care.

It consists of a list of DRPs categorized into Necessity, Safety, and Effectiveness. A total of 19 DRPs and 21 pharmaceutical recommendations were recorded within these categories. In the period covered by the study, the identification of DRPs and the pharmaceutical interventions carried out were recorded by four pharmacists – two hospital pharmacists and two pediatrics resident pharmacists – during daily clinical practice, primarily with the medical and nursing teams.

Descriptive analysis of the data was performed using relative and absolute frequencies, proportion estimates, and mean proportions with a 95% confidence interval (95% CI). Statistical analysis was carried out on SPSS® 29.0 (Statistical Package for Social Science for Windows). The study was approved by the Research Ethics Committee of the Albert Sabin Children's Hospital as per opinion no. 5,458,237.

RESULTS

During six consecutive months, clinical pharmacy services were delivered to 58 pediatric patients by two pediatric resident pharmacists assigned exclusively to bedside care and two hospital pharmacists.

As described in Table 1, the main demographic groups provided care were males (51.0%), infants aged from one to 12 months (47.9%), patients with neurological conditions (47.3%), and patients with infectious diseases (28.3%).

A total of 75 DRPs were recorded during the study period (Table 2). PICU 3 was the unit with the largest number of DRPs identified (n=47; 62.6%) and the NICU was the unit with the fewest (n=8; 10.6%).

Statistical analysis revealed that safety DRPs (76.2%) accounted for most of the problems identified in the three units. The analysis of the solutions given to the DRPs recorded in each unit demonstrated that all DRPs identified in the effectiveness category in the three units were solved. Twenty (54.0%) of the 37 (78.7%) DRPs recorded in PICU 3 in the safety category were managed by the clinical pharmacist in charge. In the NICU, four (66.6%) of six (75.0%) DRPs in the same category were solved, while in the NIMCU the ratio was six (40.0%) of 15 (75.0%) DRPs.

Table 1. Distribution of demographic and clinical variables of children hospitalized in a Brazilian pediatric hospital from April to September 2021 (n =58).

Demographics	**PICU 3 (n= 32)**	**NICU (n=8)**	**NIMCU (n=18)**	**Mean**
Sex	%	%	%	%
Male	65.6	37.5	50.0	51.0
Female	34.3	62.5	50.0	48.9
Chronological age				
Newborns (0-28 days)	9.3	37.5	50.0	32.2
Infants (1-12 months)	43.7	50.0	50.0	47.9
Children (1-12 years)	25.0	-	-	8.3
Adolescents (12-18 years)	21.8	-	-	7.2
Clinical Diagnosis				
Neurological conditions	51.0	50.0	41.0	47.3
Gastrointestinal conditions	1.0	10.0	12.0	7.6
Cardiovascular disease	5.0	5.0	25.0	11.6
Infectious disease	40.0	30.0	15.0	28.3
Respiratory disease	3.0	5.0	7.0	5.0

Source: The authors.

Table 2. Characterization of drug-related problems and main drug classes involved (n=75).

DRP	**PICU 3 (n=47)**	**NICU (n=8)**	**NIMCU (n=20)**	**Mean %**
Necessity	7 (14.8)	-	3 (15.0)	9.9
Safety	37 (78.7)	6 (75.0)	15 (75.0)	76.2
Effectiveness	3 (6.3)	2 (25.0)	2 (10.0)	13.7
Solved DRPs				
Necessity	5 (71.4)	-	2 (66.6)	46.0
Safety	20 (54.0)	4 (66.6)	6 (40.0)	53.5
Effectiveness	3 (100.0)	2 (100.0)	2 (100.0)	100.0
Drug Class				
Antidepressants	2 (4.2)	-	-	1.4
Anticonvulsants	2 (4.2)	1 (12.5)	1 (5.0)	7.2
Antiarrhythmics	-	1 (12.5)	2 (10.0)	7.6
Antiacids. Antiulcer agents	-	-	3 (15.0)	5.0
NSAIDS, Steroids	1 (2.1)	-	-	0.7
Antimicrobials	13 (27.6)	4 (50.0)	12 (60.0)	45.8
Electrolytes	8 (17.0)	-	1 (5.0)	7.3
Diuretics	5 (10.6)	-	-	3.5
Vasoactive drugs	5 (10.6)	-	-	3.5
Sedatives/analgesics	11 (23.4)	-	1 (5.0)	9.4
Lung surfactant	-	2 (25.0)	-	8.3

Source: The authors.

The most frequent drug class cited in the DRPs was antimicrobials, present in 13 (27.6%) of the 47 DRPs identified in PICU 3, four (50.0%) of the eight DRPs identified in the NICU, and 12 (60.0%) of the 20 DRPs identified in the NIMCU. We found that neonatology patients (NICU and NIMCU) were involved mostly in DRPs related to antimicrobials. The average proportion was 45.8%.

Table 3 outlines the implemented pharmaceutical interventions. Dose adjustments accounted for 29.7% of the interventions in PICU 3, 37.5% of the interventions in the NICU,

and 40.0% of the interventions in the NIMCU. Interventions related to drug dilution/reconstitution varied more widely in neonatal units (NICU and NIMCU), a phenomenon not observed in PICU 3.

Table 3 also lists the healthcare personnel targeted in the pharmaceutical interventions. The importance of this correlation lies in the fact that DRPs can occur at any stage of care and have the involvement of medical doctors and nurses. Our analysis found that a higher proportion of interventions were aimed at medical doctors in the three units (78.3%). This finding can be explained by the fact that medical doctors prescribe medication, which is statistically correlated with the main DRP found in this study, drug dosage.

We found a variation in intervention acceptance between care units. All interventions involving nurses in the three units were accepted. Acceptance among medical doctors varied between units, with every pharmaceutical intervention in the NICU being accepted, differently from what was observed in PICU3 and the NIMCU. In our view, acceptance levels were generally reasonable and contributed to the attainment of positive results, which prevented potential cases of harmful drug interaction, incompatible drugs in intravenous solutions, and medication errors.

Table 4 lists the drugs involved in most DRPs based on prescription frequencies. The medications with the highest frequency of DRPs were: Meropenem (7), Fentanyl (6), Dexamethasone (6), and Methadone (6). Underdosing issues were present in almost every drug class, with antibiotics topping the list.

DISCUSSION

Hospitalization is a frequent event among young children and preschoolers. When the groups of patients included in our study were split by age group, we found a predominance of infants (aged between one and twelve months).

A Brazilian study enrolling 92 children admitted to a public hospital in the interior of the state of Rio de Janeiro found that infants aged from 29 days to two years accounted for most admissions (n=47; 51.1%).[6] This can be explained by the characteristics peculiar to this age group, in which the immune system is not yet fully developed, which makes them more susceptible to disease and complications that require hospitalization. Most of the admissions were due to neurological conditions, followed by infectious diseases.

Table 3. Types of pharmaceutical intervention for patients hospitalized in a Brazilian pediatric hospital from April to September 2021 (n =75)

Pharmaceutical intervention	PICU 3 (n= 47)	NICU (n=8)	NIMCU (n=20)	Mean %
Dose adjustment	14 (29.7)	3 (37.5)	8 (40.0)	35.7
Administration adjustment	3 (6.3)	-	1 (5.0)	3.7
Timing adjustment	6 (12.7)	2 (25.0)	-	12.5
Dilution/reconstitution	-	3 (37.5)	5 (25.0)	20.8
Infusion time	1 (2.1)	-	2 (10.0)	4
Medication addition	4 (8.5)	-	-	2.8
Contraindication	4 (8.5)	-	-	2.8
Medication replacement	-	-	1 (5.0)	1.6
Medication withdrawal	10 (21.2)	-	2 (10.0)	10.4
Prescription correction	3 (6.3)	-	-	2.1
Advice about prescription	2 (4.2)	-	1 (5.0)	3
Medical Doctors	40 (85.1)	6 (75.0)	15 (75.0)	78.3
Nurses	7 (14.8)	2 (25.0)	5 (25.0)	21.6
Outcome of Interventions with Medical Doctors				
Accepted explanations	21 (52.5)	6 (100.0)	14 (93.3)	81.9
Did not accept	19 (47.5)	-	1 (6.7)	18
Outcome of Interventions with Nurses				
Accepted explanations	7 (100.0)	2 (100.0)	5 (100.0)	100
Did not accept	-	-	-	-

Source: The authors.

Table 4. Drugs involved in most DRPs.

DRP	# of DRPs for each drug			
	Fentanyl	**Dexamethasone**	**Methadone**	**Electrolytes**
Underdose	6	-	1	-
Overdose	-	1	-	-
Inadequate timing of administration	-	5	-	-
Inadequate infusion time	-	-	2	-
Inadequate administration	-	-	1	-
Unnecessary medication	-	-	2	4
Total	**6**	**6**	**6**	**4**
	Vancomycin	**Amikacin**	**Meropenem**	**Piperacillin / tazobactam**
Underdose	1	1	5	-

A similar prevalence was found in another Brazilian study that looked into the anthropometric profile of children in the pediatric intensive care unit of a public hospital in Salvador, Bahia. The authors found that 33.3% of the patients (n=87) had been admitted for neurological causes,[7] a lower proportion than the one found in our study (n=58; 47.3%). Our results differed from those of other studies that described respiratory disease as the main cause of pediatric hospitalizations, with pneumonia topping the list.[8]

Infectious diseases were the second most important cause of hospitalization seen in our study. On average, they accounted for 28.3% of the admissions of the three units, with PICU 3 showing the highest proportion. This result was similar to the one reported in a study that analyzed the hospitalization of children in the first six years of life. The authors found that "influenza and pneumonia" and "chronic lower airway diseases" were listed among the three main causes of hospitalization.[9]

The main finding of the study was the high exposure of newborns and children to DRPs, with an average frequency of 76.2%. Prescription was identified as the most vulnerable stage in the process of medication. An international descriptive study based on information reported by pharmacists at a NICU in Doha, Qatar, found that prescription was the stage with the most errors involving medication.[10]

In a review of the prevalence and nature of DRPs in hospitalized children in the United Kingdom, the authors found that DRPs affect children throughout the entire hospitalization process, with prescription errors ranking as the most frequent.[11] A study performed in a PICU in Hong Kong, China, reported inaccurate dose calculations for intravenous medications, cardiovascular and antimicrobial drugs, fluids and electrolytes, and drugs that require dose adjustments as the main elements in prescription error.[12]

Considering that the prescription of drugs to newborns in intensive care is challenging, given the frequent dose adjustments, compliance with volumes, devices used, and drug incompatibility, the literature stresses the role of clinical pharmacists in this context and the close collaboration that must exist with neonatologists to optimize working processes and mitigate the harm associated with medication errors.[13]

Few studies have analyzed the frequency of DRPs in NICUs. The available studies report substantial variation in the occurrence of DRPs. An important Brazilian prospective cross-sectional study carried out in the NICU of a teaching maternity hospital analyzed the frequency and nature of DRPs involving newborns with heart disease and found a frequency of exposure to DRPs of 76.4% in a group of 122 newborns. A total of 390 DRPs were identified, 49.0% of which were related to treatment effectiveness. Our study found 75 DRPs in total and a proportion of DRPs related to effectiveness in the NICU and the NIMCU of 25.0% and 10.0%, respectively, both much lower than the proportions reported in the literature.[14]

Regarding drug classes, antimicrobials (45.86%) were the most involved in DRPs among newborns and infants, followed by sedatives/analgesics (9.46%). Underdosing was listed as a DRP involving antimicrobial agents vancomycin, amikacin, and meropenem, along with sedatives/analgesics fentanyl and methadone. The authors of a study that described and characterized clinical pharmacist interventions in PICUs found similar results, with antibiotics (34.4%) and sedatives/analgesics (20.3%) atop the list of drug classes tied to DRPs.

An explanation for the association of these drug classes with DRPs is that patients in intensive care undergo invasive procedures that cause discomfort and pain and are at increased risk of infection, which call for sedatives/analgesics and antimicrobials, respectively.[15]

The use of antibiotics in the PICU is very high (ranging from 67% to 97%) for reasons such as the high incidence of sepsis, healthcare-associated infections, and postoperative prophylaxis.[16] A study that looked into the impact of a PICU pharmacist-led antibiotic administration program showed that 29 pharmaceutical interventions had been carried out in three months, which resulted in dose adjustments (n=11), changes in the selection of antibiotics (n=15), de-escalation (n =5), and recommendations over monitoring and drug interactions

(n=6). Mortality dropped from 16.2% to 15.7% during the implementation of the program.[17]

Successful experiences of rational use of antibiotics in NICUs have been observed in recent years. A study that evaluated the risk of neonatal sepsis and the use of antimicrobials in low birth weight newborns found that 74.3% (1,254) of the newborns weighing less than 1500 g did not take antibiotics in the first 72 hours of life, which considerably decreased exposure to this drug class and associated risks, which include adverse reactions and antimicrobial resistance.[18]

According to our results, the causes of DRPs were directly related to drug dose. In intensive care environments, inadequate dose and administration are among the most frequent causes of DRPs.[19] The predominance of safety and effectiveness DRPs in our population was primarily due to the prescription of antimicrobial doses below the recommended levels, an issue that may increase therapeutic failure and bacterial resistance.

Meropenem was the main antimicrobial drug implicated in DRPs of safety and effectiveness due to inadequate dosing. A study showed an increase in microbial resistance to carbapenem meropenem in patients hospitalized in a pediatric hospital and higher levels of occurrence of antimicrobial resistance in ward patients (29.1%) when compared to PICU patients (12.1%).[20] Our study did not look into antimicrobial resistance, but the prevalence of underdosing associated with meropenem pointed to the need to assign to a clinical pharmacist the role of managing antimicrobial therapy, enforcing the rational use of medication, and curbing bacterial resistance.

The quantitative and qualitative analysis of pharmaceutical interventions serves as an important indicator of pediatric hospital pharmaceutical care. Pharmaceutical care for critically ill children, in addition to increasing treatment safety and effectiveness, may also decrease the overall cost of healthcare. Our study found 75 pharmaceutical interventions in the three care units included, of which 35.73% were related to dose adequacy, 20.83% to dilution/reconstitution, and 12.56% to the timing of administration. These categories were also among the most common in other studies.[21,22]

A study that evaluated the relationship between the safe use of drugs and clinical pharmacy services in the pediatric intensive care units of a Brazilian hospital found 141 DRPs during the implementation of the program, with more frequent interventions occurring in the prevention of incompatible drugs in intravenous solutions (21%) and inadequate dosing (17%).[5]

Most of the interventions targeted medical doctors. This is probably because in Brazil medical doctors, not nurses, can prescribe drug doses, dilutions, and reconstitutions. A substantial number of the pharmaceutical interventions analyzed in our study were associated with dose adequacy, dilution, and reconstitution.

We also found that nurses were more willing to accept the interventions of clinical pharmacists. Acceptance by medical doctors varied by unit, with an overall percentage of 81.9%. Similar acceptance results were observed in a Brazilian study that analyzed the pharmaceutical interventions carried out by the clinical pharmacists working at the PICU of the University Maternity Hospital in São Luís. The authors found that 98% (983) of the 1003 pharmaceutical interventions were accepted.[23]

The high level of acceptance by nurses and medical doctors seen in our study might speak to the bond formed between clinical pharmacists and the teams involved in providing direct patient care, and the trust deposited in the implemented interventions.

Our study clearly showed that clinical pharmacists have a strategic role in identifying and dealing with potential DRPs, while contributing to drug safety in hospital environments. Although the relevance of clinical pharmacists is well established, underreporting of cases is still an issue, since few experiences have been described in the literature about the success of programs implemented in children and adolescent care.

FINAL CONSIDERATIONS

Despite the limited number of professionals involved exclusively with clinical pharmacy (resident pharmacists working on the bedside usually take on the role of clinical pharmacists), this study analyzed retrospective data that may serve as an indication of the impact of the first six months of implementation of a clinical pharmacy program in a pediatric hospital.

The analysis of DRPs and the most common pharmaceutical interventions shed light on the impact of clinical pharmacy practices in PICU 3, the NICU, and the NIMCU of the Albert Sabin Children's Hospital. We would like to emphasize the importance of documenting clinical pharmacy practices in the construction of indicators and evaluation of the quality of pharmaceutical care in pediatrics.

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