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Drug-related problems in oral pharmacotherapy of hospitalized pediatric patients in Rio de Janeiro

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Abstract

Objectives: To evaluate the occurrence of drug-related problems (DRP) associates to the use of oral drugs in hospitalized pediatric patients. **Method:** A cross-sectional study, with data collection performed on the prescriptions of patients using oral medications admitted to the pediatric ward at a reference institute in maternal and child care in Rio de Janeiro. Data collection was carried out from September/2020 to November/2020. Convenience sample was used. Patients aged 0 to 18 years, with oral medications prescribed during the hospitalization period and with a hospital stay of more than 48 hours, were included. DRP were collected and classified based on the pharmacotherapy clinical review guide. Data related to drug interactions were collected in order to identify a possible association with the occurrence of DRP. Pharmaceutical interventions were performed when necessary. **Results:** Thirty-eight patients were evaluated in this study, most of them male (57.9%) and aged between 0 and 4 years (65.8%). Sixteen patients (42.1%) had at least one DRP. We found 50 DRP, representing a rate of 131.6 DRP per 100 patients. Among the oral medications used, 42.4% were related to DRP. Drugs with action on the nervous system were related to most DRP (37%), with emphasis on the class of antiepileptics. **Conclusion:** The number of medications used during hospitalization and the number of drug interactions showed statistically significant differences in patients who had DRP. The review of oral pharmacotherapy identified drug classes and profiles of patients with greater susceptibility to the occurrence of DRP and demonstrated its importance in promoting safety in the use of drugs in the pediatric population.

Keywords: pediatrics; drug interactions; pharmaceutical services; medication errors; administration, oral drug.

Problemas relacionados a medicamentos na farmacoterapia oral de pacientes pediátricos hospitalizados no Rio de Janeiro

Resumo

Objetivo: Avaliar a ocorrência de problemas relacionados a medicamentos (PRM) associados ao uso de medicamentos por via oral em pacientes pediátricos hospitalizados. **Método:** Estudo transversal, com coleta de dados realizada nas prescrições dos pacientes em uso de medicamentos orais internados na enfermaria pediátrica num instituto de referência no atendimento materno infantil no Rio de Janeiro. A coleta de dados foi realizada no período de setembro/2020 a novembro/2020. Foi utilizada amostra de conveniência. Foram incluídos pacientes de 0 a 18 anos, com medicamentos orais prescritos durante o período de internação e com tempo de permanência no hospital acima de 48h. Os PRM foram coletados e classificados com base no guia de revisão clínica da farmacoterapia. Foram coletados dados relativos às interações medicamentosas, visando identificar possível associação com a ocorrência de PRM. Intervenções farmacêuticas foram realizadas quando necessário. **Resultados:** Foram avaliados 38 pacientes neste estudo, a maioria do sexo masculino (57,9%) e na faixa etária de 0 a 4 anos (65,8%). Dezesseis pacientes (42,1%) apresentaram pelo menos um PRM. Foram encontrados 50 PRM, representando uma taxa de 131,6 PRM por 100 pacientes. Entre os medicamentos de uso oral utilizados, 42,4% esteve relacionada com PRM. Os medicamentos com ação no sistema nervoso estiveram relacionados com a maior parte dos PRM (37%), com destaque para a classe dos antiepiléticos. **Conclusão:** O número de medicamentos utilizados durante a internação e número de interações medicamentosas apresentaram diferenças estatísticas significativas nos pacientes que apresentaram PRM. A revisão da farmacoterapia oral identificou classes de medicamentos e perfis de pacientes com maior suscetibilidade à ocorrência de PRM e demonstrou sua importância na promoção da segurança no uso de medicamentos na população pediátrica.

Palavras-chave: pediatria; interações medicamentosas; assistência farmacêutica; erros de medicação; administração, medicamento oral.

Introduction

As in other countries, Brazil has a considerably lower number of medications registered for pediatric use than those for use in adults[1]. A study showed that only 159 medications were registered for pediatric use in the ten-year period from 2003 to 2013, where 25 of these were discontinued and one third were classified as unsuitable for patients up to six years of age. In addition to that, this study showed that age is related to the number of these registrations, in which the number of medications registered is lower the younger the children are[2]. They constitute a vulnerable group of patients because they have physiological characteristics quite different from adults, and which change as they grow up. In conform to ethical issues, such characteristics limit participation of this population in clinical trials performed with drug candidates for new medications[3,4]. This scenario leads to low availability of information on the safety and efficacy of the medications used in children.

As most of the medications available on the market are presented in doses based on clinical studies conducted with adults, it becomes necessary to perform pharmaceutical calculations to estimate pediatric doses (lower doses)[5]. These calculations are based on age, weight and/or body surface of the child and is a fundamental stage for a safety pharmacotherapy. Solid pharmaceutical forms (tablets and capsules, for example) for oral administration shows closed/standardized doses for the adult population; therefore, they need to be turned into extemporaneous formulations to meet the demand of pediatric patients[1,6].

In hospital routine, the oral administration is the most used of administration route[4]. Therefore, it appears to be a route that is non-invasive, convenient, easy to administer, economical[10] and safe, as it is believed that oral medications cause fewer serious Adverse Drug Reactions (ADRs) in relation to intravenous drugs[7]. In cases such as the treatment of digestive problems related to enzymatic insufficiency, intestinal infection, parasites and/or need for gastric protection, the oral administration becomes the only possible administration route[4]. In addition to that, the use of oral pharmaceutical presentations avoids the accumulated water balance of patients polymedicated with intravenous medications during the hospitalization period[1].

The pharmacotherapy follow-up evaluation has origin in the context of pharmaceutical care and comprises actions aimed at health promotion and recovery in an integrated way with the health team[4,8]. This practice provide rational pharmacotherapy and the achievement of defined and measurable results aimed at improving safety patient, reflecting on their quality of life. Thus, defined results are understood to be the cure, control, or delay of disease's aggravating. Encompassing aspects related to effectiveness and safety in oral administration of drugs[9-13].

This method of health evaluation also is an important component of the pharmaceutical care process for solving Drug-Related Problems (DRPs) in a systematic, continuous, and documented way.

Thus, the objective of this study is to describe and analyze the occurrence of DRPs related to the use of oral medications in hospitalized pediatric patients.

Methods

The analysis of drug-related problems in hospitalized pediatric patients in use of oral medications was performed through a prospective cross-sectional study, using medical prescriptions as main data source.

The research was conducted in the Pediatric ward of a federal medium-size teaching and research hospital located in the city of Rio de Janeiro, which is a reference for maternal and children healtcare. The institution has 116 beds (18 in the Pediatric ward) and serves medium- and high-complexity cases.

The profile of the population hospitalized in the Pediatric ward is made up of chronically ill children and adolescents, most of them with genetic diseases (such as cystic fibrosis, mucopolysaccharidosis, *osteogenesis imperfecta*, other genetic syndromes and neurological diseases) and/or rare illnesses. Due to treatment complexity and to dependence on health technologies, these patients require even more specialized professional care because they may remain hospitalized for years.

The study participants were patients of both genders, aged from 0 to 18 years old, hospitalized in the Pediatric ward and in use of oral medications during the data collection period. Convenience sampling was employed, that is, all the patients hospitalized in the Pediatric ward from September 2020 to November 2020 and that met the inclusion criteria were analyzed. Therefore, the patients included in this study were those aged from 0 to 18 years old whose prescriptions contained oral medications prescribed during the collection period, and whose hospitalization time was equal to or greater than 48 hours. The data were prospectively collected within the research collection period, performing daily analyses of the prescriptions.

The first stage corresponded to the analysis of the patient's prescriptions for screening based on the inclusion criteria. Subsequently, each prescription was evaluated from the technical point of view to review each patient's oral pharmacotherapy. To such end, the Pharmacotherapy Review Form (PRF) and another form for pharmaceutical interventions were used. Both are already implemented and used in the institution's work routine.

The following variables were collected: sociodemographic characteristics, the drug prescribed with its respective presentation, dose, administration route and use frequency; as well as the pharmacotherapy-related problems and their resolutions. The problems identified by the researchers were written down in the forms for subsequent data compilation and analysis. Data related to the drug interactions were also collected, with the objective of identifying possible associations with the occurrence of DRPs. The *UpToDate*® and *Micromedex*® databases were used to analyze the drug interactions[16,17]. The medications prescribed were organized according to the Anatomical, Therapeutic and Chemical (ATC) classification[14] and the main diagnosis, according to the International Classification of Diseases and Related Health Problems (CID-10).[15]

The pharmaceutical interventions were performed based on the severity level, evidence and course of action recommended in *UpToDate*®[16], according to the interaction identified. In the cases high severity, the course of action was to consider changing the therapy and when moderate severity the course of action was to monitor the patient. Regarding the level of evidence, the interactions were classified based on published studies on the topic and they were divided into high, moderate, or weak levels of evidence.

The Pediatric & Neonatal Dosage Handbook[18] was used as a reference for checking the prescribed doses of the medications. The Pharmaceutical interventions performed with the medical team from the Pediatric ward were recorded in both pharmaceutical interventions' forms for further data analysis.

The classification from the Second Granada Consensus on pharmacotherapy failure was used for type categorization of each DRP founded. This is an easily reproducible classification method according to the study design in view of its use by other authors[19], in addition to the availability of information on the pharmacotherapy of the patients in the unit studied. Consequently, the analysis of the type of DRP followed the criteria indicated below:

- DRP type 1 (patients are not using the medications they need): the medications prescribed do not treat the base diagnosis.
- DRP type 2 (patients use medications they do not need): the patients use "unnecessary" medications.
- DRP type 3 (non-quantitative ineffectiveness): despite the prescribed dose being in accordance with the one recommended in the literature, the presence of drug interactions pointed to a reduction in plasma concentrations of the drug by inducing its metabolism and/or increasing its elimination.
- DRP type 4 (quantitative ineffectiveness): the dose prescribed was below the one recommended in the literature.
- DRP type 5 (non-quantitative insecurity): despite the prescribed dose being in accordance with the one recommended in the literature, the presence of drug interactions pointed to increased plasma concentrations of the drug by inhibition of its metabolism and/or reduction of its elimination.
- DRP type 6 (quantitative insecurity): the dose prescribed was above the one recommended in the literature.

The study was approved by the institution's Research Ethics Committee (*Comitê de Ética em Pesquisa*, CEP), under opinion No. 4,131,446.

The statistical analysis expressed the continuous variables through the median and interquartile range because the data did not present normal distribution and the categorical variables through proportions. The Student's t, chi-square, Shapiro Wilk and Wilcoxon tests were performed.

The occurrence of DRPs was measured using the following calculations: rate of patients with drug-related problems (number of patients with at least one DRP/total patients) and DRP rate for every 100 patients (number of DRPs/total patients). In addition to the DRP rates, other outcomes such as the predominant type of DRP, number of drug interactions, number of drugs used during hospitalization and the drug classes involved in the DRPs identified were also evaluated.

The data were processed in EpiData 3.1 and analyzed with the aid of the R software, version 4.04.

Results

A total of 38 patients hospitalized in the institution's Pediatrics ward were analyzed according to the inclusion criteria. The patients that failed to meet the inclusion criteria did not have their prescriptions considered and added to this study. The predominant age group found corresponded to 0 (zero) to 4 (four) years old, with 25 patients (65.8%), most of them male (22; 57.9%). The prevailing diagnoses were cystic fibrosis (6;15.8%), *osteogenesis imperfecta* (5; 13.2%) and unspecified pneumonia (3; 8.0%). Nearly 22 patients (57.9%) presented some other comorbidity. The medians found were age, 2.5 years old (IQR: 1.3 – 5.9) and number of drugs in using, 3.5 (IQR: 2.0 – 5.0) (Table 1).

Table 1. Sociodemographic and clinical characteristics of the patients hospitalized in the Pediatric ward and in use of oral drugs (Rio de Janeiro, 2020).

Variables	% (n=38)
Age	
0-4 years old	65.8 (25)
5-9 years old	23.7 (9)
10+ years old	10.5 (4)
Gender	
Male	57.9 (22)
Female	42.1 (16)
Weight	
0-9 kg	36.8 (14)
10-19 kg	34.2 (13)
20 kg or more	29.0 (11)
Main Diagnosis1	
Cystic fibrosis	15.8 (6)
Osteogenesis imperfecta	13.2 (5)
Uns. 2 pneumonia	8.0 (3)
Others	63 (24)
Presence of comorbidities	
Yes	57.9 (22)
No	42.1 (16)
Presence of DRPs3	
Yes	42.1 (16)
No	57.9 (22)
Presence of drug interactions	
Yes	39.5 (15)
No	60.5 (23)

[1] Main diagnosis according to CID-10; [2] Uns.: Unspecified; [3] DRPs: Drug Related Problems
[4] IQR: Interquartile Range

Regarding presence of DRPs, 16 patients (42.1%) had some DRP in their prescription and 15 patients (39.5%) had at least one drug interaction in their pharmacotherapy (Table 1). A total of 50 DRPs were identified, which represents a rate of 131.6 DRPs/100 patients. Seventeen patients presented at least 1 DRP, corresponding to 42% of total. Among the types of DRP found, non-quantitative drug ineffectiveness was the most frequent type (34%), followed by non-quantitative drug insecurity (32%), quantitative ineffectiveness (18%) and, finally, quantitative drug insecurity (14%). The DRP related to non-use of the medication required was identified only once (2%) and the problem corresponding to the use of unnecessary medications according to their comorbidity was not identified in any of the 38 patients analyzed (Table 2).

Table 2. Distribution of the drug-related problems classified by type (Rio de Janeiro, 2020).

Type of DRP	% (n = 50)
Type 3 - Non-quantitative ineffectiveness	34 (17)
Type 5 - Non-quantitative insecurity	32 (16)
Type 4 - Quantitative ineffectiveness	18 (9)
Type 6 - Quantitative insecurity	14 (7)
Type 1 – The patients do not using the drugs they need	2 (1)
Type 2 - The patients using drugs they do not need	0 (0)

Most of the patients who presented some DRP were male (13; 59.1%), with predominance of the age group from 0 (zero) to 4 (four) years old (12; 48.0%) and main diagnosis of *osteogenesis imperfecta* (3; 60%). Nearly 13 patients (86.7%) had at least one drug interaction in their prescriptions. The subgroup with some DRP showed the following medians: age, 2.2 years old (IQR: 1.3 – 4.5); number of drugs, 5 (five) (IQR: 5.0 – 6.0); and number of drug interactions, 1 (IQR: 1.0 – 2.0). Significant differences (p-value < 0.05) were found for the "number of drugs in using" and "number of drug interactions" variables (Table 3).

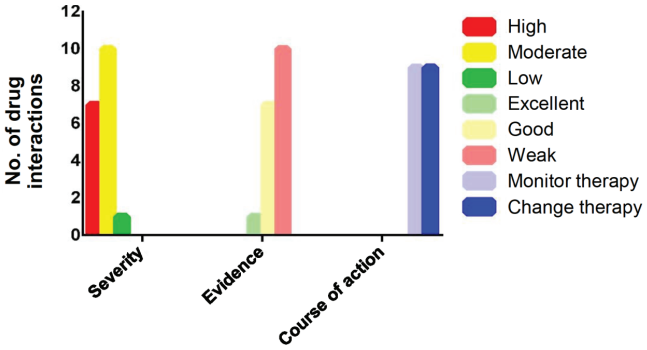
Table 3. Characteristics of the study population, according to presence of DRPs (Rio de Janeiro, 2020).

Variables	Median (IQR)[1]		p-value[2]
	With DRPs	Without DRPs	
Patient's age (years old)	2.2 (1.3 – 4.5)	3.6 (1.5 – 6.2)	0.42
Nº of drugs in using	5 (5.0 – 6.0)	2 (1.0 – 3.0)	<0.01
Nº of drug interactions	1 (1.0 – 2.0)	0 (0 – 0)	<0.01

[1] IQR: Interquartile Range; [2] Wilcoxon Signed Rank Test

A total of 18 drug interactions involving 16 different drugs were found in 15 of the 38 patients evaluated in the institution's Pediatrics ward. The percentage of patients that had at least one drug interaction was 39.5%, and some patients had more than one interaction. Most of the interactions involved drugs acting on the Central Nervous System, such as phenobarbital (six interactions), clonazepam (five interactions), baclofen (four interactions) and morphine (three interactions). Among 18 interactions, seven were classified as high severity, ten as moderate severity, and only one interaction was classified as low severity. As for the clinical evidence, seven were classified according to *UpToDate*® as having a good level of clinical evidence, while ten had a weak level and one was classified with an excellent level of evidence (Figure 1).

Figure 1. Characteristics of the drug interactions identified and course of action suggested (Rio de Janeiro, 2020).



When necessary, pharmaceutical interventions were performed for the drug interactions found by the main researcher. Among the 18 interactions, six did not need intervention due to the fact scheduling of the medication time by the Nursing team was spaced sufficiently enough for no interactions to occur and/or due to their clinical relevance. Therefore, a total of 12 interventions were found. In relation to the course of action for the interactions found, nine considered to changing the therapy; where eight of them did not have the pharmaceutical interventions accepted and one did not need any intervention due to spacing in the medications' schedule. The remaining nine interactions, which considered monitoring of the therapy, three did have the interventions refused, five did not need any intervention and one was accepted (Table 4).

Table 4. Drug interactions between the drugs involved in the DRPs and results of the pharmaceutical interventions performed (Rio de Janeiro, 2020).[1] (Continued)

Medications	Result of the drug interaction	Severity	Evidence	Course of action	Pharmaceutical intervention	Response to the pharmaceutical intervention
Risperidone Fluoxetine	Fluoxetine can increase risperidone serum concentration.	Moderate	Good	Monitor therapy	N/A[2]	Patient dependent on prescribed drugs and schedule spaced sufficiently enough to avoid any interactions (e.g. 02:00 p.m. 10:00 p.m. and 06:00 a.m. for medication A and Noon, 08:00 p.m. and 04:00 a.m. for medication B)
Phenobarbital Phenytoin	Phenobarbital can reduce phenytoin serum concentration, which in turn can increase phenobarbital serum concentration.	Moderate	Good	Monitor therapy	N/A	Patient dependent on prescribed drugs and schedule spaced sufficiently enough to avoid any interactions (e.g. 02:00 p.m. 10:00 p.m. and 06:00 a.m. for medication A and Noon, 08:00 p.m. and 04:00 a.m. for medication B)
Carbamazepine Clonazepam	Carbamazepine can increase metabolism of clonazepam, which can reduce its serum concentration.	High	Weak	Change therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, for being a neurological patient dependent on drugs acting on the CNS.
Cholecalciferol Cholestyramine	Cholestyramine can reduce Vitamin D (Cholecalciferol) absorption, which can reduce its serum concentration.	Moderate	Weak	Change therapy	Refused	The patient's clinical condition requires administration of cholestyramine every 3 hours, which precludes changing the schedule.

Table 4. Drug interactions between the drugs involved in the DRPs and results of the pharmaceutical interventions performed (Rio de Janeiro, 2020). (Concluded)

Medications	Result of the drug interaction	Severity	Evidence	Course of action	Pharmaceutical intervention	Response to the pharmaceutical intervention
Clonazepam Phenobarbital	Phenobarbital can increase metabolism of clonazepam, which can reduce its serum concentration.	High	Weak	Change therapy	Refused	Intervention refused for being a neurological patient dependent on drugs acting on the CNS.
Levetiracetam Phenobarbital	Levetiracetam can reduce phenobarbital serum concentration.	Moderate	Weak	Monitor therapy	Accepted	The Nursing team changed the scheduling of the medication administration time, and levetiracetam was then suspended.
Ferrous sulfate Omeprazole	Omeprazole can reduce absorption of formulations that contain iron.	Moderate	Good	Monitor therapy	N/A	Patient dependent on prescribed drugs and schedule spaced sufficiently enough to avoid any interactions (e.g. 02:00 p.m. 10:00 p.m. and 06:00 a.m. for medication A and Noon, 08:00 p.m. and 04:00 a.m. for medication B)
Cholecalciferol Calcium Carbonate	Calcium carbonate can increase the possible toxic effects of Vitamin D analogues.	Moderate	Weak	Monitor therapy	N/A	Patient dependent on prescribed drugs and schedule spaced sufficiently enough to avoid any interactions (e.g. 02:00 p.m. 10:00 p.m. and 06:00 a.m. for medication A and Noon, 08:00 p.m. and 04:00 a.m. for medication B)
Cholestyramine Levothyroxine	Cholestyramine can reduce levothyroxine serum concentration.	Moderate	Good	Change therapy	N/A	Patient dependent on prescribed drugs and schedule spaced sufficiently enough to avoid any interactions (e.g. 02:00 p.m. 10:00 p.m. and 06:00 a.m. for medication A and Noon, 08:00 p.m. and 04:00 a.m. for medication B)
Phenobarbital Carbamazepine	Phenobarbital can reduce carbamazepine serum concentration.	Moderate	Good	Monitor therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, for being a neurological patient dependent on drugs acting on the CNS.
Fluoxetine Omeprazole	Fluoxetine can increase omeprazole serum concentration.	Low	Excellent	Monitor therapy	N/A	Patient dependent on prescribed drugs and schedule spaced sufficiently enough to avoid any interactions (e.g. 02:00 p.m. 10:00 p.m. and 06:00 a.m. for medication A and Noon, 08:00 p.m. and 04:00 a.m. for medication B)
Methadone Clonazepam	Clonazepam can increase the depressant effect of methadone on the Central Nervous System.	High	Weak	Change therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, for being a neurological patient dependent on drugs acting on the CNS. In addition to that, the patient was undergoing opioid (methadone) weaning.
Methadone Baclofen	Baclofen can enhance the depressant effect of methadone on the Central Nervous System.	High	Weak	Change therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, as the patient was undergoing opioid (methadone) weaning.
Baclofen Morphine	Baclofen can enhance the depressant effect of morphine on the Central Nervous System.	High	Weak	Change therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, as the patient was undergoing opioid (morphine) weaning.
Clonazepam Morphine	Clonazepam can enhance the depressant effect of morphine on the Central Nervous System.	High	Weak	Change therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, as the patient was undergoing opioid (morphine) weaning.
Clonazepam Baclofen	Clonazepam can increase possible toxic effects of baclofen.	Moderate	Good	Monitor therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, for being a neurological patient dependent on drugs acting on the CNS.
Phenobarbital Morphine	Phenobarbital can enhance the depressant effect of morphine on the Central Nervous System.	High	Weak	Change therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, as the patient was undergoing opioid (morphine) weaning.
Phenobarbital Baclofen	Phenobarbital can increase possible toxic effects of baclofen.	Moderate	Good	Monitor therapy	Refused	Intervention refused due to the recommendation of the sector's Neurology team, for being a neurological patient dependent on drugs acting on the CNS.

[1] Table adapted from the ***Up to Date***® database [2] N/A – Not Applicable (no pharmaceutical intervention was necessary)

Discussion

By our findings, through this research it was possible to quantify and identify characteristics related to the occurrence of DRPs in children admitted to the Pediatric ward of a reference hospital for maternal and children healthcare, obtaining a rate of 131.6 DRPs/100 patients in 42% of the sample.

A study conducted in Ethiopia in 2020, with a similar design, found a rate of 114 DRPs/100 patients and a proportion of 74% of patients who had at least one DRP[20]. There is also a study carried out in Saudi Arabia in 2019 that presented a rate of 135.7 DRPs/100 patients and a proportion of 35.9% of patients with DRPs[21]. In another study, also carried out in Ethiopia, the authors found a rate of 164.7 DRPs/100 patients and a proportion of 68.6% of patients who presented DRPs[22]; slightly higher results than those obtained in the researched institution, although with differences in sample size and study design. However, a similar study carried out in 2019 in Hungary[23], in which the authors found a rate of 105.7 DRPs/100 patients and a proportion of 8.25% of patients with DRPs, presents data below ours. According to the authors, the most frequent DRP was non-quantitative ineffectiveness (DRP type 3), whose identification was based on the presence of drug interactions that induce drug metabolism, with the possibility of increasing its elimination with a consequent reduction in plasma concentration.

In relation to the frequency of DRPs, the authors of a survey carried out in Hungary (2019) found similar data[23]. They observed higher occurrence of DRP type 3 (non-quantitative drug ineffectiveness) and DRP type 5 (non-quantitative medication insecurity): 24% and 51%, respectively. Our findings for these types of DRP were: 18% and 14%, respectively. Regarding DRP type 1 (patients do not use the drugs they need) and DRP type 2 (patients use drugs they do not need), the authors found 10% and 8.2% occurrence, respectively[23]. What the authors observed is like what was noticed in the Pediatric ward of the researched institution, where DRP type 3 and DRP type 5 corresponded to 18% and 14% of the population studied. DRP type 5 was identified by the presence of drug interactions that inhibit drug metabolism, reducing its elimination, with a consequent increase in plasma concentrations.

The main difficulty in Pediatrics is dose adjustment of the drug to be administered. The problems classified as "quantitative ineffectiveness" (Type 4 DRPs) and as "quantitative insecurity" (Type 6 DRPs) are directly related to the prescribed medication dose. Due to low availability of suitable pharmaceutical presentations for your age group, the pediatric population is considered as a therapeutic orphan.

Nearly 47.4% of the drugs what were prescribed to the patients hospitalized in the institution's ward were involved with some type of DRP, with prevalence of the presence of drugs acting on the Central Nervous System, such as clonazepam, phenobarbital, fluoxetine, and phenytoin, and those acting on the digestive tract and metabolism (calcium carbonate, cholecalciferol, and cholestyramine). For Mechessa *et al.*, the main classes of drugs that showed some DRP were anti-infectives for systemic use (271 patients; 76.12%), followed by drugs acting on the nervous system (24 patients; 6.74%). This authors also related the number of drugs in using to the occurrence of DRPs[20].

A significant difference was found in the statistical analysis for the "number of drugs in using" and "number of drug interactions" variables in the subgroup that presented some DRP (p-value < 0.01). Other studies corroborate this result. According to Szilvay *et al.*, the more drugs a patient uses, the higher the chance for the occurrence of DRPs[24].

Other variables analyzed that obtained a statistical difference (p-value < 0.01) among the patients who presented DRPs was "number of drug interactions". A total of 18 drug interactions were found between 16 different medications, ten of them showed a moderate severity, as presented in Table 4. In relation to the recommended course of action, half of the participants stated monitoring the therapy and the other half mentioned changing the therapy. Most of the interactions were concentrated among the drugs acting on the CNS.

In order to adapt the patient's pharmacotherapy, pharmaceutical interventions were performed in the drug interaction cases in which it was deemed necessary. No intervention was necessary in some cases due to spacing in the medications' schedules and/or when one of the medications was suspended. Most of the interventions that were refused were related to patients with complex neurological conditions and dependent on antiepileptic medications and other psychotropic drugs, as justified by the assistant neuropediatrician.

A recent study showed an association between drug interactions and the occurrence of DRPs, in addition to performing pharmaceutical interventions for all the data obtained[24]. These authors found a 42% proportion of patients with drug interactions, a result like those found in the institution studied by us (39.5%).

The main limitations of this study are related to the small sample size, to the short data collection time and to the profile of the population, mostly comprised by complex patients and with rare diseases. In addition to that, the study was carried out in a single federal teaching and research institution, a reference in maternal and children healthcare, and may not be generalizable to other health units with different profiles.

The study implied mobilizing the professionals working in the institution regarding the pharmaceutical analysis of the pediatric prescriptions of oral drugs. Thus, it was possible to evidence the need for a thorough evaluation of each drug, regardless of its administration route; motivating the professionals involved in the unit's routine to intervene in the patient's oral pharmacotherapy, whenever pertinent.

Conclusion

The methodology of this research allowed identifying and quantifying drug-related problems in patients hospitalized in a pediatric ward with prescribed of oral drugs; in addition, it enabled identifying characteristics of the DRPs, as well as the main drugs involved.

Variables that showed significant differences in the patients who presented DRPs were identified, such as the number of drugs in use during hospitalization and the number of drug interactions. However, conducting studies with broader sample profiles and longer observational times involving pediatric patients may favor the determination of factors associated with the occurrence of DRPs in the pediatric population.

The studied population, made up of chronically ill children and adolescents, demands greater attention from the health team and need abundant material, technological and pharmacotherapeutic resources for their treatment. In this scenario, the pharmacist's role in the early identification of DRPs can prevent the occurrence of harms related to complexity of the pharmacotherapy, to serious drug interactions, and to the polymedication common in these patients.

This study shows the importance of reviewing the oral pharmacotherapy of the patients hospitalized in the institution's Pediatrics ward as a way to increase patient safety and improve the quality of the care provided in a public pediatric hospital.

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Collaborators

LBS and DDCG: they participated in conception of the research. LBS: data collection. LBS and SCRCC: data analysis and interpretation. LBS, SCRCC and DDCG: responsibility for all the information included in the paper, ensuring accuracy and integrity of any of its parts. LBS and SCRCC: initial and final writing of the article. SCRCC: final review of the article; final approval of the version to be published.

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Conflict of interest statement

The authors declare that there is no conflict of interest in relation to this article.

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