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Pharmacoeconomics of pharmaceutical interventions related to dosage form in a hospital complex in southern Brazil

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Abstract

Objective: To identify and quantify the pharmacist interventions (PhIs) related to adequate pharmaceutical dosage form and to measure the actual and potential avoidable expenses. **Methods:** A cross-sectional study with a quantitative approach and retrospective data collection for 2021 was conducted in a tertiary hospital from Porto Alegre with 1,089 hospital beds. The study included the PhI for adequacy of the pharmaceutical dosage form to the prescribed dose and evaluated the drugs involved, acceptability by the medical team, and the financial impact. The data were exported from NoHarm.ai® and compiled into a Microsoft Office Excel® structured spreadsheet. The study was approved by the Ethics Committee of the institution under opinion No. 37227020.6.0000.5335. **Results:** During the study period, 634,547 prescriptions were written, of which 142,177 (22.41%) were evaluated by clinical pharmacists. From this evaluation, 4,918 PhIs were made, of which 432 (8.78%) referred to the pharmaceutical dosage form. After applying the selection criteria, 79 (18.29%) PhIs were excluded, resulting in 353 (81.71%). The PhIs analyzed were grouped into three outcomes: accepted 191 (54.11%), not accepted 151 (42.78%), and not applicable 11 (3.11%). Among the 191 accepted interventions, 135 (70.68%) resulted in changing the pharmaceutical dosage form of the prescribed drug, generating US$ 6,553.97 in savings per year for the institution, and 56 (29.32%) resulted in a reevaluation of the treatment leading to drug discontinuation. For the 151 interventions that were not accepted, potential savings of US$ 3,575.13 per year were estimated if the intervention was accepted. The drugs with the highest number of interventions were enoxaparin (24.93%), ondansetron (21.37%) and methadone (11.24%). From another perspective, the drugs that presented the greatest financial impact from the accepted interventions were epoetin-alpha (51.76%), morphine (19.08%) and enoxaparin (10.49%). **Conclusion:** Clinical pharmacists adjust drug dosage form during a prescription review. Over one year, these adjustments accounted for approximately 9% of the interventions and generated cost savings of $ 6,500, showing the clinical and economic importance of prescription evaluation by clinical pharmacists.

Key words: hospital pharmaceutical service; drug prescriptions; pharmacoeconomics, clinical pharmacist.

Farmacoeconomia das intervenções farmacêuticas relacionadas à apresentação de medicamento em complexo hospitalar do sul do Brasil

Resumo

Objetivo: Identificar e quantificar as Intervenções Farmacêuticas (IF) relacionadas à adequação de apresentação de medicamentos e mensurar os gastos evitáveis reais e potenciais. **Método:** Estudo transversal de abordagem quantitativa com coleta de dados retrospectiva referente ao ano de 2021, realizado em hospitalar terciário com cerca de 1000 leitos localizado no município de Porto Alegre. Foram incluídas no estudo as IF de adequação da apresentação do medicamento para a dose prescrita e avaliadas quanto aos medicamentos envolvidos, a aceitabilidade pela equipe médica e os valores monetários economizados reais e potenciais. Os dados foram exportados do sistema NoHarm.ai® e compilados em planilha estruturada de Microsoft Office Excel®. O estudo foi aprovado pelo Comitê de Ética da instituição sob parecer nº 37227020.6.0000.5335. Resultados: No período do estudo, foram realizadas 634.547 prescrições médicas, das quais 22,41% foram avaliadas pelos farmacêuticos clínicos. A partir desta avaliação foram realizadas 4.918 IF, sendo 432 (8,78%) referentes à apresentação do medicamento. Após a aplicação dos critérios de exclusão foram analisadas 353 (81,71%) intervenções. As IF analisadas foram agrupadas em: aceitas (54,11%), não aceitas (42,78%) e não se aplica (3,11%). Dentre as intervenções aceitas (n=191), 135 (70,68%) resultaram em substituição da apresentação do medicamento prescrito, gerando economia anual de US$6,553.97 para a instituição e 56 (29,32%) resultaram em reavaliação do tratamento acarretando em suspensão do medicamento. Para as intervenções não aceitas (n=151) foi estimado um potencial de economia anual em caso de aceite da IF de US$3,575.13. Os fármacos com maior número de intervenções foram: enoxaparina (24,93%), ondansetrona (21,37%) e metadona (11,24%). Os fármacos que apresentaram maior impacto financeiro a partir das intervenções aceitas foram: alfaepoetina humana (51,76%), morfina (19,08%) e enoxaparina (10,49%). **Conclusões:** A adequação de apresentação de medicamentos pelo farmacêutico clínico durante a análise da prescrição no período de um ano representou cerca de 9% das intervenções e gerou uma economia de 6,5 mil dólares, demonstrando a importância clínica e econômica da avaliação da prescrição pelo farmacêutico clínico.

Palavras-chave: serviço de farmácia hospitalar; prescrição de medicamentos; farmacoeconomia, farmacêutico clínico.

Introduction

Clinical pharmacy is characterized by a set of health actions centered on the patient's needs and aimed at promoting rational medication use to optimize pharmacotherapy and minimize the risks inherent to such use[1]. Among these actions is the technical evaluation of prescriptions that enables identifying drug-related problems (DRPs) that can result in harms to the patients' health and in economic consequences to the institutions[2,3]. After identifying a DRP, a pharmacist intervention (PhI) is carried out with the patient or health professionals to solve or prevent the risk situation encountered[4,5].

The "pharmaceutical dosage form" intervention is among the most frequent PhIs in the hospital environment[6]. This intervention refers to unavailability or inadequacy of the drug presentation for the prescribed dose or for the patient's clinical particularities[7].

Inadequate pharmaceutical dosage form for the prescribed dose occurs when the drug has more than one standardized formulation in the institution and the most appropriate one was not selected at the time of prescription. As a result, there may be: increased handling of the drug by the nursing team, increased patient discomfort when administering the drug, increased healthcare-related waste, and increased costs to the institution[8].

A positive correlation was shown between pharmacist interventions and the reduction of unnecessary health-related costs[9,10]. A study conducted in a reference cardiology hospital from Santa Catarina revealed that 41.8% of the PhIs generate cost reductions for the institution[5]. A systematic review of the economic evaluation of clinical pharmacy services conducted in China noticed that 80% of the articles included in the study demonstrated economic benefits to hospitals[11].

Pharmacoeconomic evaluation makes it possible to identify, calculate and compare the clinical and economic benefits of drug therapy to offer the patient the best treatment at the lowest cost possible. Cost minimization analysis (CMA) is one of the recommended analyses for the pharmacoeconomic evaluation; it consists in comparing costs between two or more treatment alternatives that present equivalent efficiency and effectiveness[12].

Considering the need to optimize health care expenses and the scarcity of studies related to the topic in the country, this study aimed at identifying the PhIs related to the most appropriate pharmaceutical dosage form for the prescribed dose that were performed during the prescription analysis process by the Clinical Pharmacy team in a tertiary hospital from southern Brazil, as well as at verifying the economic impact given the cost minimization analysis.

Methods

This is a cross-sectional study with a qualitative approach and retrospective data collection, referring to the period from January 1st to December 21st, 2021.

The sample consisted of the PhIs related to pharmaceutical dosage form that were performed during this period and from the process of analyzing the drug prescriptions by a team of four clinical pharmacists and four resident pharmacists from the Multiprofessional Integrated Residency in Health program with an emphasis on Intensive Care in a tertiary hospital center with 7 hospitals and nearly 1,000 beds, which provides care to adult and pediatric patients, located in Porto Alegre/RS.

The PhIs included in the study were all those related to "pharmaceutical dosage form". The PhIs related to inappropriate pharmaceutical dosage form for the administration route, pharmaceutical dosage form out of stock in the market, pharmaceutical dosage form not standardized in the institution, pharmaceutical dosage form provided by the Ministry of Health, inadequate pharmaceutical dosage form for the patient's clinical condition, and pharmaceutical dosage form undergoing an acquisition flow change were excluded from the sample. This latter was related to the pandemic period, when it was necessary to reevaluate the acquisition of some drugs due to high prices and/or market shortages.

The prescription analysis was performed daily by the Clinical Pharmacy team using the *NoHarm.ai®* Artificial Intelligence tool for this purpose; patients in Intensive Care Unit (ICU) beds were prioritized, followed by those in the Inpatient Unit (IU). *NoHarm.ai®* has a prescription prioritization score to be evaluated by the pharmacy according to patient and prescription risk stratification considering factors such as the following: number of altered tests, number of alerts in the prescription, number of high surveillance drugs, and number of different items from the previous prescription.

During the prescription analysis, the following aspects are observed: dose, frequency, schedule, administration route, pharmaceutical dosage form, drug indication, treatment duration, allergies, duplicity, and need for dose and/or frequency adjustment due to renal and/or hepatic function.

The data were collected by means of PhI reports generated in NoHarm.ai® and compiled in a Microsoft Office Excel® structured spreadsheet. The following data were analyzed: The PhI related to adequate pharmaceutical dosage form for the prescribed dose, drugs involved, acceptability of the PhI and financial impact.

The financial impact assessment was performed by means of a cost minimization analysis, as effectiveness of the treatment alternatives is the same. The treatment cost before and after the PhI was calculated by multiplying the unit value of the drug pharmaceutical dosage form by the number of units required to complete the dose, daily frequency and treatment time. The unit value for each drug was obtained by calculating the arithmetic mean of the purchase value during the period in 2021. The amounts in Brazilian Reais (BRL) were converted to US Dollars (USD) based on the exchange rate stipulated by the Central Bank of Brazil (BRL 1.00 = USD 5.58 on December 31st, 2021)[13].

Daily frequency was used in all situations, regardless of the medications having been prescribed "If Necessary" (IN) or "According to Medical Criterion" (AMC). Treatment time was expressed in days and considered until medication use discontinuation or until the date of the subsequent intervention. The interventions could be performed more than once for the same patient and prescription. This might take place randomly by means of the Artificial Intelligence system, as it elaborates the prescription prioritization score to be evaluated by clinical pharmacists according to patient and prescription risk stratification.

The costs saved from the accepted PhIs and the one that could have potentially been avoided from the PhIs that were not accepted were calculated by the difference between the estimated treatment cost before the PhI and the estimated value of the treatment after the PhI. It is noted that all the PhIs were included in the estimation related to the PhIs that were not accepted, even those that might have had plausible reasons for non-acceptance. On the other hand, the amount saved from the accepted interventions that resulted in drug discontinuation was not calculated because it would not be possible to estimate treatment time and dosage.

All the "pharmaceutical dosage form" PhIs were confirmed in the NoHarm.ai® system and evaluated regarding their outcomes as accepted, not accepted and not applicable. The interventions in the not applicable situation are related to hospital discharge or death before the next prescription or within 24 hours, not making it possible to verify the outcome as accepted or not accepted.

The study was approved by the Research Ethics Committee of the institution under study with Certificate of Presentation for Ethical Appraisal No. 37227020.6.0000.5335.

Results

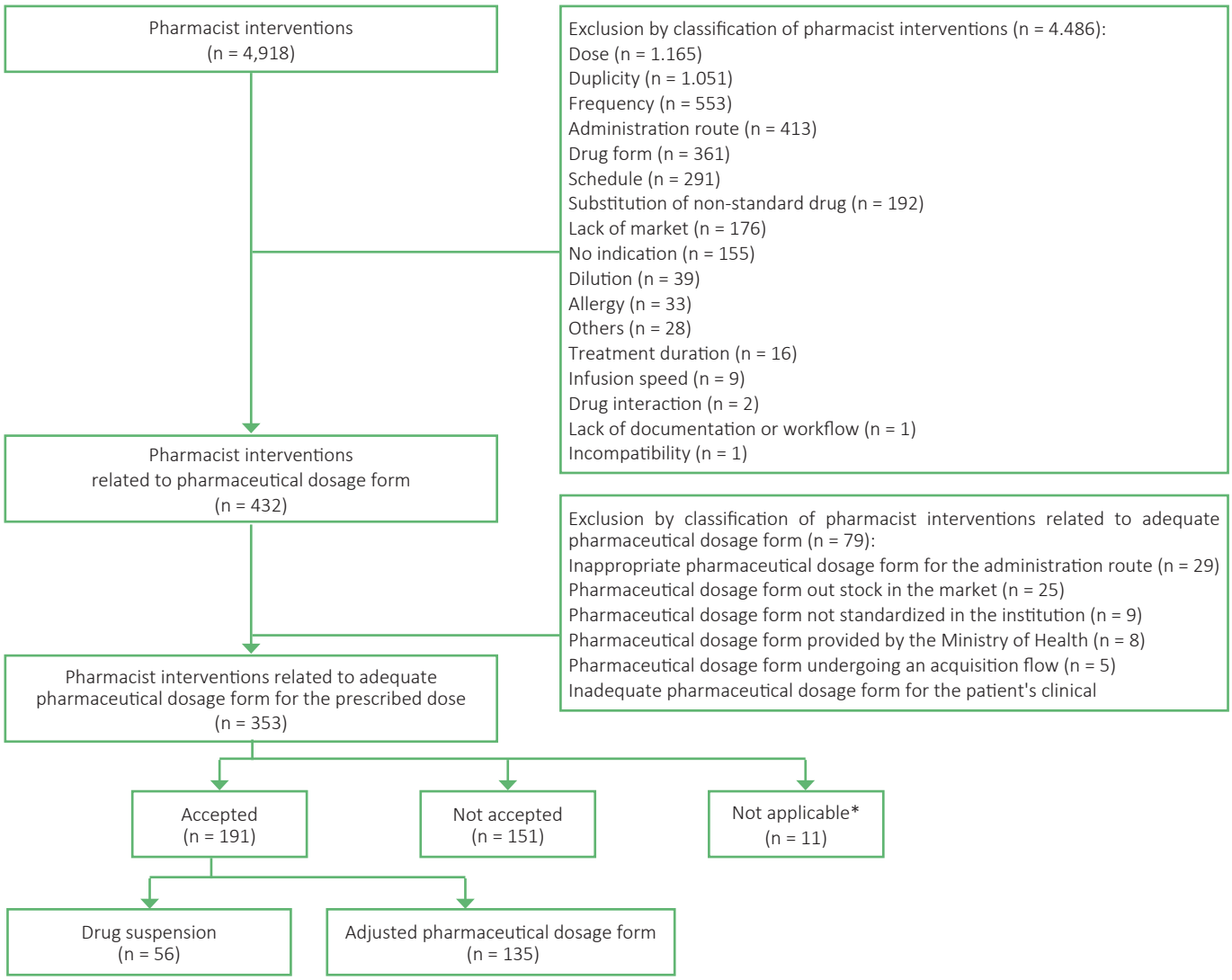
During a one-year period, in a hospital with more than a thousand beds, 634,547 prescriptions were generated, of which 22.41% were evaluated by the clinical pharmacists and resulted in 4,918 pharmacist interventions, of which 2,884 (58.64%) were accepted by the medical team.

A total of 432 PhIs related to pharmaceutical dosage form adequacy were performed, of which 79 (18.29%) were excluded considering the exclusion criteria. Of all 353 (81.71%) PhIs included in the study, 191 (54.11%) were accepted, 151 (42.78%) were not accepted and 11 (3.11%) were categorized in the "Not applicable" criterion, as shown in Figure 1.

Among the 191 accepted interventions, 135 (70.68%) resulted in changing the presentation of the drug prescribed, generating US$ 6,553.97 in savings for the institution, and 56 (29.32%) resulted in reevaluation of the treatment leading to discontinuation of the drug. For the 151 interventions that were not accepted, potential savings of US$ 3,575.13 were estimated in case of accepting them.

The institution researched has a registry of 95 drugs with more than one standardized presentation for the same pharmaceutical dosage form; the presentation-related PhIs involved 35 drugs. The drugs with most "presentation adequacy for the prescribed dose" interventions are presented in Table 1.

Figure 1. Descriptive flowchart of the pharmacist interventions related to pharmaceutical dosage form performed by the Clinical Pharmacy team from January 1st to December 31st, 2021, at a tertiary hospital in southern Brazil.



* Hospital discharge or death before 24 hours.

The drugs with the highest impact in relation to the actual cost avoided as a result of the accepted PhIs related to "pharmaceutical dosage form" can be seen in Table 2.

Discussion

In a one-year period, the Clinical Pharmacy service of the hospital under study performed 432 PhIs for changing the drug pharmaceutical dosage form, which represented nearly 9% of the interventions carried out. The 191 accepted interventions generated US$ 6,553.97 in savings. In addition to that, the interventions that were not accepted might generate potential savings of US$ 3,575.13.

The most frequent PhIs in the Clinical Pharmacy service of this hospital were related to dose adjustment, duplicity of medications, administration frequency, pharmaceutical dosage form and administration route. A similar result was found in a study conducted at a hospital in Espírito Santo which verified that the most frequent PhIs were the following: dose adjustment, inadequate/unnecessary medication, frequency adjustment, more appropriate therapeutic alternative, and administration route substitution[14].

Table 1. Frequency of the medications, presentations, and number of accepted and not accepted interventions associated with the Pharmacist interventions (PhIs) related to presentation in 2021 at a tertiary hospital from southern Brazil.

Drugs	PhIs (n)	PhIs (%)	Accepted (n)		Not accepted (n)	Not applicable (n)
			Drug suspension	Adjusted pharmaceutical dosage form		
Enoxaparin	**88**	**24,93**	**19**	**41**	**28**	**0**
Solution for injection 20mg	4	1,13	3	0	1	0
Solution for injection 40mg	36	10,20	6	18	12	0
Solution for injection 60mg	28	7,93	4	15	9	0
Solution for injection 80mg	20	5,67	6	8	6	0
Ondansetron	**73**	**20,68**	**7**	**14**	**45**	**7**
Solution for injection 2mg/mL 2mL	52	14,73	3	11	33	5
Solution for injection 2mg/mL 4mL	21	5,94	4	3	12	2
Methadone	**39**	**11,05**	**3**	**17**	**19**	**0**
Pill 5mg	22	6,23	2	13	7	0
Pill 10mg	17	4,82	1	4	12	0
Methylprednisolone	**33**	**9,35**	**6**	**10**	**17**	**0**
Powder for solution for injection 125mg	1	0,28	0	0	1	0
Powder for solution for injection 500mg	32	9,07	6	10	16	0
Lactulose	**19**	**5,38**	**6**	**9**	**4**	**0**
Syrup 667mg/mL 10mL	14	3,96	4	7	3	0
Syrup 667mg/mL 20mL	5	1,42	2	2	1	0
Diazepam	**14**	**3,97**	**1**	**6**	**7**	**0**
Pill 5mg	3	0,85	0	1	2	0
Pill 10mg	11	3,12	1	5	5	0
Enalapril	**14**	**3,97**	**1**	**6**	**7**	**0**
Pill 5mg	3	0,85	0	1	2	0
Pill 10mg	11	3,12	1	5	5	0
Levothyroxine	**10**	**2,82**	**0**	**5**	**5**	**0**
Pill 25mcg	5	1,41	0	2	3	0
Pill 100mcg	5	1,41	0	3	2	0
Amikacin	**8**	**2,27**	**2**	**4**	**2**	**0**
Solution for injection 50mg/mL 2mL	8	2,27	2	4	2	0
Solution for injection 250mg/mL 2mL	0	0	0	0	0	0
Acetylsalicylic acid	**6**	**1,70**	**0**	**4**	**2**	**0**
Pill 100mg	0	0	0	0	0	0
Pill 500mg	5	1,70	0	4	2	0
Ampicillin/Sulbactam	**6**	**1,70**	**0**	**3**	**3**	**0**
Powder for solution for injection 1000mg+500mg	0	0	0	0	0	0
Powder for solution for injection 2000mg+1000mg	6	1,70	0	3	3	0
Others*	**43**	**12,18**	**11**	**16**	**12**	**4**
TOTAL	**353**	**100**	**56**	**135**	**151**	**11**

*Others: simvastatin, fentanyl, epoetin-alpha, carvedilol, morphine, atracurium, hydralazine, immunoglobulin, metoprolol, midazolam, tacrolimus, atenolol, atorvastatin, clonazepam, dexamethasone, haloperidol, heparin, mycophenolate, pantoprazole, paracetamol, penicillin G, prednisone, propofol and terlipressin.

Table 2. Medications and number of Pharmacist interventions (PhIs) with the highest economic impact from the accepted interventions related to pharmaceutical presentation in 2021 at a tertiary hospital from southern Brazil.

Drugs	PhIs (n)	PhIs (%)	Estimated savings (US$)	Estimated savings (R$)	Percentage of the total value (%)
Epoetin-alfa	**3**	**2,22**	**3,392.58**	**18.930,60**	**51,76**
Solution for injection 40.000UI/mL 1mL	3	2,22	3,392.58	18.930,60	51,76
Morphine	**2**	**1,48**	**1,250.57**	**6.978,18**	**19,08**
Solution for injection 0,2mg/mL 1mL	2	1,48	1,250.57	6.978,18	19,08
Enoxaparin	**41**	**30,37**	**687.40**	**3.835,69**	**10,49**
Solution for injection 40mg	18	13,33	175.23	977,78	2,67
Solution for injection 60mg	15	11,11	293.50	1.637,73	4,48
Solution for injection 80mg	8	5,93	218.67	1.220,18	3,34
Immunoglobulin	**2**	**1,48**	**397.85**	**2.220,00**	**6,07**
Solution for injection 0,05g/mL 100mL (5g)	1	0,74	83.05	463,42	1,27
Solution for injection 0,01g/mL 100mL (10g)	1	0,74	314.80	1.756,58	4,80
Methylprednisolone	**10**	**7,41**	**304.81**	**1.700,84**	**4,65**
Powder for solution for injection 500mg	10	7,41	304.81	1.700,84	4,65
Others	**77**	**57,04**	**520,76**	**2.905,84**	**7,95**
TOTAL	**135**	**100**	**6,553.97**	**36.571,15**	**100**

In a study conducted at a hospital in Santa Catarina, among the PhIs that occurred at the medication level, change in formulation or presentation was the fourth most recurrent (n=107; 12.5%)[5].

The most prevalent medications associated with interventions regarding drug pharmaceutical dosage form were enoxaparin, ondansetron, methadone, methylprednisolone and lactulose. The result found corroborates the study carried out at a hospital in São Paulo which observed that the most frequent drugs for this intervention were enoxaparin, ondansetron and methylprednisolone[7].

The prevalence of enoxaparin among the pharmaceutical dosage form interventions may be justified by the inability to safely administrate smaller doses than the total dose of the dosage form, as some manufacturers do not include volume graduations on the syringes. Another aspect to be considered is the patient's discomfort in receiving multiple subcutaneous administrations to complete a single dose.

In the institution where the study was conducted, lactulose has been fractionated in an automated manner in the unit dose service since July 2020 by making sachets in standard doses of 10 mL and 20 mL that belong to the predominant prescription range. Fractionating multidose oral medications offers the benefit of minimizing waste to enhance patient safety and reduce costs related to drug waste. In this context, the clinical pharmacist contributed to maximizing the benefits cited by means of the PhIs and of the prescribers' continuing education.

The drugs involved in the pharmaceutical dosage form PhIs that represented the highest savings were human epoetin-alpha, morphine, enoxaparin, immunoglobulin and methylprednisolone. A similar study conducted in a São Paulo hospital over a 7-month period showed savings of R$ 2,390.87 for enoxaparin and of R$ 799.13 for methylprednisolone[7]. The presence of enoxaparin and methylprednisolone in this group can be related to the high frequency of interventions associated with the individual cost of these medications.

The high financial impact of the pharmaceutical dosage form interventions involving human epoetin-alpha and morphine can be explained by the significant variation in purchase value between the pharmaceutical dosage form standardized in the institution where the research was carried out, as those with high consumption allow greater bargaining power with the suppliers, enabling significantly lower prices.

No savings to the institution were observed in the presentation adequacy of acetylsalicylic acid and enalapril. The standardized pharmaceutical dosage form of acetylsalicylic acid have the same cost to the institution. In turn, the lower-dose form of enalapril had a higher cost to the institution than the higher-dose presentation. However, despite not generating savings, the PhI contributes to patient safety to avoid uncertainty of the dose administered, in addition to contributing to rationality and reduction of healthcare-related waste.

The interventions related to pharmaceutical dosage form and which are not accepted by the medical team can represent an unnecessary cost for the institution. Consequently, aiming at rationality and savings, it is suggested to consider pharmaceutical dosage form changes as an activity inherent to clinical pharmacists.

We cannot properly assert the reasons that lead to the prescriptions of pharmaceutical dosage form that worse suited for a given patient. It is necessary to conduct another study to answer this question. However, it can be stated that the hospital's prescribing system is electronic, although the clinical staff is open and different prescribing patterns are observed. In addition to that, the hospital has a large number of residents in different specialties.

This study had some limitations, such as the infeasibility of generalizing the results to other hospitals considering the standardization list of medications, the purchase flow of the drugs, and the size of the hospital. In addition, the costs in cases of treatment discontinuation or change were not estimated, and the direct costs of the medical supplies were not calculated, as well as the indirect costs related to clinical outcomes and time saved by the health professional devoted to providing care. The institution analyzed is of a large size and has the individualization system since 2020; the costs of this process were not included as it is already a service routine.

Another limitation is related to the fact that the amount saved from the accepted PhIs and the amount that could have been avoided may be underestimated considering that 22.41% of the prescriptions were evaluated by clinical pharmacists during the study period.

Finally, it should be noted that the disparate nature of the assessment and classification of the drug-related problems and PhIs across hospitals hinders comparisons, showing the importance of having a standardized Brazilian classification, nonexistent up to the present day.

Conclusion

The PhIs related to pharmaceutical dosage form accounted for 8.78% of the interventions performed by clinical pharmacists in a one-year period, constituting the fourth most frequent PhI at the institution. The results show US$ 6,553.97 in savings for the accepted pharmaceutical dosage form interventions and potential savings of US$ 10,047.56 per year when combining the accepted and not accepted pharmaceutical dosage form PhIs. Consequently, interventions performed by the clinical pharmacist reconciled the therapeutic needs with the economic outcomes for the institution.

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Collaborators

BDO contributed in research design, data collection, treatment and analysis, review and approval of the final version for publication. TDH contributed in research design, data analysis, review and approval of the final version for publication. CRB contributed in research design, data analysis, review and approval of the final version for publication.

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Declaration of conflicts of interest

The authors declare that there are is conflict of interest in relation to this article.

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