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Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde

Original Paper

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Mapping of drug-related problems involving the prescription of opioid drugs in a teaching hospital in Curitiba

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Submitted: 17-01-2023 Resubmitted: 17-05-2023 Accepted: 24-05-2023

Double blind peer review

Abstract

Introduction: Drug-Related Problems (DRPs) are unwanted events presented in pharmacotherapy that negatively affect the treatment of a disease and the actions of Clinical Pharmacy in pharmacovigilance of prescriptions aims on the minimization of these problems. Considering that referral hospitals for trauma often use opioid drugs in trauma patients' management, it is necessary to carry out an investigation into DRPs involving the prescription of opioids in these hospitals. **Objective:** To map the DRPs identified in the prescription of opioid drugs in the management of patients in the ward of a teaching hospital in Curitiba. **Methods:** The research was retrospective and observational. Prescription data was collected from February 2019 to April 2021. From the 14.014 prescriptions analyzed in the period, it was calculated through the DOT (Days of Therapy) that 6.996 of them contained opioids. Of the prescriptions evaluated, 9.075 had DRPs, 1.550 of which were related to opioids. **Results:** The main problem involving the prescription of opioids in the wards is cost-effectiveness (73,61%); the main cause of DRP is the prescription of the inappropriate drug form for the patient in question (73,23%). In 87,74% of the cases, an intervention was proposed to the prescriber; however, in only 35,61% of the cases the proposed intervention was accepted and fully implemented, so that the problem was fully resolved in only 36,6% of the cases. In 29,55% of the cases, the problem was not resolved due to lack of cooperation on the part of the prescribing physician. Also, a steady decrease in the incidence rate of DRPs was observed over time, as consequence of pharmacovigilance of prescriptions and prescribers. **Conclusion:** The research was not only fruitful in designing a complete mapping of opioid-related DRPs in the hospital, but also highlighted the effectiveness of the educational action of pharmacists on prescribers.

Keywords: Drug Prescriptions; Medication Errors; Pharmacovigilance; Hospital Care; Analgesics, opioids.

Mapeamento de problemas relacionados a medicamentos envolvendo a prescrição de fármacos opioides em um hospital universitário de Curitiba

Resumo

Introdução: Problemas Relacionados a Medicamentos (PRMs) são eventos indesejados presentes na farmacoterapia que afetam negativamente o tratamento de uma doença, e a Farmácia Clínica Hospitalar atua na farmacovigilância das prescrições, visando minimizar esses problemas. Tendo em vista que centros hospitalares de referência em trauma frequentemente fazem uso de fármacos opioides no manejo de pacientes traumatizados, faz-se necessário que haja uma investigação acerca dos PRMs envolvendo a prescrição de opioides nesses hospitais. **Objetivo:** Realizar o mapeamento dos PRMs identificados na prescrição de fármacos opioides na enfermaria de um hospital universitário em Curitiba. **Métodos:** Pesquisa retrospectiva e observacional. Os dados das prescrições foram coletados no período de fevereiro de 2019 até abril 2021. A partir das 14.014 prescrições analisadas, calculou-se pela relação de DOT (*Days of Therapy*) que 6.996 delas continham opioides. Das prescrições avaliadas, 9.075 possuíam PRMs, dos quais 1.550 eram relacionados a opioides. **Resultados:** Constatou-se que o principal problema envolvendo a prescrição de opioides nas enfermarias é o de custo-efetividade (73,61%); já a principal causa de PRM é a prescrição da forma inapropriada de droga para o paciente em questão (73,23%). Em 87,74% dos casos, uma intervenção era proposta ao prescritor, contudo, em apenas 35,61% dos casos a intervenção proposta era aceita e totalmente implementada, de modo que o problema era totalmente resolvido em apenas 36,46% dos casos, e, ainda, em 29,55% dos casos, o problema não foi resolvido por falta de colaboração por parte do médico prescritor. Também, foi observado um decréscimo constante na taxa de incidência de PRMs com o tempo, consequência da farmacovigilância das prescrições e dos prescritores. **Conclusão:** A pesquisa foi frutífera no delineamento de um mapeamento completo dos PRMs relacionados a opioides no hospital, e também evidenciou a eficácia da ação educativa dos farmacêuticos junto aos prescritores.

Palavras-Chave: Prescrições de Medicamentos; Erros de Medicação; Farmacovigilância; Assistência Hospitalar; Analgésicos Opioides.

Introduction

Drug prescriptions by medical professionals must follow the logic of rational medications use – that is, the prescription of a medication should be consistent with the symptoms presented by the patient; progress with absence of factors that disrupt the pharmacodynamics of this drug, such as drug interactions; and meet other technical safety factors, such as dose, administration route, treatment time, cost and adherence[1]. However, it is common for medical prescriptions to be accompanied by Drug-Related Problems (DRPs) – surveys carried out by the World Health Organization (WHO) in a 2006 study found that more than 50% of the prescriptions, administrations and sales of medications are made inappropriately[2]; and a number of systematic reviews have shown that the DRP prevalence rates fluctuate from 7% to 10% of all medical prescriptions[3,4].

Drug-Related Problems were defined by the Third Consensus of Granada in 2007 as negative results derived from pharmacotherapy that, for various reasons, lead to failure to achieve the therapeutic objective or to the onset of unwanted effects[5]. The *Pharmaceutical Care Network Europe Foundation* (PCNE) 8.02 classification, in turn, defines DRPs as "events or circumstances involving drug therapy that actually or potentially interfere with the desired health outcomes"[6].

The Clinical Pharmacy service at the hospitals is responsible for dispensing medications upon medical prescription, in cases of hospitalized patients and, in the context of pharmaceutical care, it generally performs a DRP verification and analysis[7,8]. In order not only to prevent diseases but also to promote health and through a process of monitoring a therapeutic plan, pharmacists prevent, identify and solve DRPs in order to achieve concrete results that improve the patients' quality of life[9,10].

A number of studies have shown that this work of screening, detection, categorization, intervention and monitoring DRPs in drug prescriptions administered within hospitals by pharmacists has exerted a positive impact on the in-hospital environment[1,7,8]. Namely, pharmaceutical care leads to a considerable increase in quality of life and to a decrease in mortality among the patients involved, a reduction in the incidence of new and recurrent DRPs, a drop in the patients' hospitalization time and lower hospital expenses[11,12,13].

In turn, opioid drugs are medications prescribed for the treatment of average and severe pain, either acute or chronic, in post-surgical, oncological, polytraumatized or burned patients, among other specific situations[14,15]. Physicians who work in the emergency room or first aid sectors of hospitals commonly use these medications in the treatment of traumatized individuals due to their analgesic capacity[14,16,17], enabling the occurrence of DRPs involving the prescription and management of opioid drugs in patients hospitalized in hospitals that are a reference in trauma. A retrospective review from 2017 revealed significant potential for accidental overdose caused by the prescription of opioids for patients who suffered recent traumas, both in those treated with these medications exclusively during hospitalization and in those who had their pharmacological therapies extended to the home environment[18]. In agreement with a 2019 review[19], this study points out that indiscriminate and improper use of this class of medication not only causes safety-related problems but also related to effectiveness, as an inadequate dose does not have the desired effect on pain control.

Thus, the research is justified by the need to map DRPs related to opioid drugs in hospitals that are a reference in trauma care due to the important link between these variables; in other words, between the prescription of opioids and trauma patients, as well as the high recurrence of DRPs in medical prescriptions, added to the lack of scientific production with this focus. This analysis also aims at generating improvements in the care of hospitalized patients treated with opioids, as it sheds light on DRPs that occur recurrently without being given attention, which can generate a significant improvement in the quality of life of patients treated in reference hospitals; as lack of these data limits the creation of policies, protocols and improvements in the ability to handle these drugs by the hospitals' clinical staff.

In this sense, the main objective of the current study is to analyze and characterize the incidence of Drug-Related Problems (DRPs) regarding the prescription of opioid drugs in a University Hospital from Curitiba, using the DRP PCNE 8.02 international qualification system[6].

Methods

The Cajuru University Hospital is located in the city of Curitiba, capital of the state of Paraná, and is a reference in the care of clinical and surgical emergencies exclusively aimed at patients from the public health network (SUS). This hospital has a Clinical Pharmacy staff made up of two clinical pharmacists and two resident pharmacists in Hospital Pharmacy, a group that is responsible for analyzing medical prescriptions prior to dispensing medications. This prospective audit of medical prescriptions is an important service performed by the Clinical Pharmacy and is carried out by comparing the medical prescriptions with the diverse information obtained in the clinic and from the laboratory tests of the patients, so that each auditor promotes a critical analysis of the actual indication of a given drug for each patient.

Thus, if an analyst identifies any inconsistency between the prescribed medication and the patient analyzed, the prescription is selected as with a DRP and changes in pharmacotherapy are suggested to the prescribers, according to the indications inherent to each case. This non-compliant prescription is then cataloged in a table that aims at unraveling the particularities of the DRP through the classification of DRPs by the *Pharmaceutical Care Network Europe Foundation*, version 8.02 of 2017[6].

In this context, through a retrospective observational design, the current research aimed at mapping the main causes, consequences and outcomes of the DRPs found by clinical pharmacists during the review of medical prescriptions, in order to then draw a complete profile, with all the available information, of the DRPs involving the prescription of opioids to patients hospitalized in ward beds at the health institution in question. The project was approved by the Ethics Committee of the Cajuru University Hospital on October 23rd, 2020, and by the Research Ethics Committee of the Pontifical Catholic University of Paraná on November 1st, 2020, with CAAE No. 40021320.0.0000.0020, and consubstantiated CEP opinion No. 4,458,243.

The first study stage consisted in the direct acquisition of data of interest from the DRP spreadsheet. Initially, the number of Drug-Related Problems (DRPs) found in the hospitalized patients, detected by the hospital's Clinical Pharmacy in the 27-month

period between February 2019 and April 2021 and present in the table fed by the pharmaceutical analysts, was surveyed. Among the pool of cataloged DRPs, only problems related to codeine, tramadol, morphine and methadone prescribed to patients hospitalized in the wards were filtered; therefore, prescriptions made in environments of Intensive Care Units, Surgical Centers and Emergency Room were excluded, given that the Clinical Pharmacy staff does not review prescriptions made in these scenarios. The described survey showed that 14,014 prescriptions were analyzed during this period, presenting a total of 9,075 DRPs, of which a total of 1,550 contained DRPs specifically related to opioids, accounting for a monthly mean of 57.40 opioid-related DRPs found in the period.

The total number of medical prescription in the Cajuru Hospital was also surveyed, extracted from the hospital management system. It turns out that, due to a change in the hospital management system, only information after December 2019 was available for analysis; the number of prescriptions for the 17 months between December 2019 and April 2021 was surveyed. For the prescription data, the following were filtered: narcotic analgesic medications (codeine, methadone, morphine and tramadol); prescriptions referring to the ward beds, medications prescribed at the time, and duplicate prescriptions were excluded; and, after this filter, 30,492 prescriptions containing opioids were reached in the 17-month period. Of these 30,492 prescriptions, tramadol represents 18,886 prescriptions (61.93%), morphine accounts for 5,026 (16.48%), codeine is found in 4,197 prescriptions (13.76%) and methadone represents 2,383 prescriptions (7.81%).

At this moment, is was necessary to calculate how many of the prescriptions actually made in the hospital were evaluated by the Clinical Pharmacy. As can be seen in Table 1, it is known that, in 27 months, the pharmacy analyzed 14,014 prescriptions, which might contain DRPs or not. Given that the prescriptions that did not contain DRPs were not cataloged as to their content, there is no exact number of prescriptions involving opioids that did not contain DRPs to be used as a reference for calculations, for later analysis.

With the objective of statistically estimating this value, the DOT ("Days of Therapy") formula calculation was chosen. The Days of Therapy (DOT) calculation is considered the most appropriate measure to assess the impact of management programs on the medication use, especially antimicrobials, and can be used in this context. DOT represents the number of days that a patient receives drug therapy, regardless of the drug dose[20,21].

Thus, during the research period, a mean of 1,793.65 monthly prescriptions were made, a value taken as "prescriptions-day". The number of daily doses in the institution's hospitalization units during this period was also surveyed, reaching a mean of 3,601.24 per month, a value taken as "patients-day". The aforementioned values are then applied to the DOT formula, described below, in order to analyze density of the medications prescribed in the pool of hospitalization units.

Equation 1

$$DOT = \frac{(\text{OPIOID PRESCRIPTIONS x DAY IN THE WARDS})}{(\text{PATIENTS x DAY IN THE WARDS})} \text{X100}$$

Considering that each month in the research period had different numbers of ward vacancies and different amounts of prescriptions for opioids, so that each month had a different DOT, the mean of the DOTs for the months was calculated, resulting in 49.91%; which means that, on average, from December 2019 to April 2021, 49.91% of the hospital ward beds had some opioid prescription attached. However, taking into account that the DOT reported a mean of 49.91% of the prescriptions contain opioids, it was possible to estimate how many of the prescriptions analyzed actually contained opioids, using the following formula:

Equation 2

$$OPIOID\ PRESCRIPTIONS\ x\ DAY\ EVALUATED\ BY\ CPh = \frac{DOT}{100}\ x\ TOTAL\ ANALYSES\ BY\ CPh$$

$$OPIOID\ PRESCRIPTIONS\ x\ DAY\ EVALUATED\ BY\ CPh = \frac{49.91}{100}\ x\ 14.014 = 6.994$$

Thus, it is estimated that the Clinical Pharmacy evaluated 6,994 prescriptions including opioids during the research. The next step was to determine the estimated rate of opioid-related DRPs. Considering that the Clinical Pharmacy found 1,550 opioid-related DRPs, nearly 22.16% of the opioid prescriptions evaluated contained DRPs, as shown in the formula below.

Equation 3

$$OPIOID\ DRP\ RATE = \frac{OPIOID\ DRPs}{OPIOID\ PRESCRIPTIONS\ x\ DAY\ EVALUATED\ BY\ CPh}$$

$$OPIOID\ DRP\ RATE = \frac{1{,}550}{6{,}994} = 22.16\%$$

The calculated rate of opioid-related DRPs, which represents the estimated rate of opioid-related DRPs in all prescriptions made in the hospital environment, within the limits imposed by the inclusion and exclusion criteria, is close to the mean of the opioid-related DRP rates for the period: 25%.

After the statistical data determination through the methodology described above, it was not necessary to resort to statistical validation tests to verify consistency of all the information obtained. The data collected from the database and those calculated based on the diverse information included in this database were compiled in tables by using *Microsoft Excel*® 2010. Subsequently, a descriptive data analysis was performed, shown in absolute and percentage values for all calculations and preparation of tables and graphs, using the same program. The main data described are compiled in Table 1 below:

Results

The 1,550 medical prescriptions containing opioid-related DRPs analyzed by the Clinical Pharmacy of the Cajuru University Hospital from February 2019 to April 2021 were tabulated according to the DRP-PCNE 8.2. international reference, which classifies each DRP according to five main criteria: problem, cause, intervention, implementation and outcome.

Table 1. Relationship between prescriptions analyzed and DRPs found for calculating the estimated number of prescriptions containing opioids analyzed, and the opioid-related DRP rate per prescription.

Month	Prescriptions analyzed	Total DRPs found	Opioid-related DRPs found	Prescriptions containing opioids (calculated)	Opioid-related prescription/ prescription rate (%)
Feb-19	55	112	10	27	36.4
Mar-19	97	130	12	48	24.8
Apr-19	155	184	19	77	24.6
May-19	189	179	18	94	19.1
Jun-19	363	353	73	181	40.3
Jul-19	481	338	72	240	30
Aug-19	361	218	45	180	25
Sep-19	719	353	40	359	11.1
Oct-19	654	292	33	326	10.1
Nov-19	497	251	16	248	6.5
Dec-19	70	95	21	35	60.1
Jan-20	314	314	67	157	42.8
Feb-20	307	270	74	153	48.3
Mar-20	415	319	74	207	35.7
Apr-20	463	362	82	231	35.5
May-20	545	367	73	272	26.8
Jun-20	790	492	99	394	25.1
Jul-20	907	532	113	454	25
Aug-20	1026	649	135	513	26.4
Sep-20	695	382	64	347	18.5
Oct-20	838	531	106	418	25.3
Nov-20	723	397	50	361	13.9
Dec-20	742	389	69	370	18.6
Jan-21	520	367	50	260	19.3
Feb-21	904	438	74	451	16.4
Mar-21	675	438	50	337	14.8
Apr-21	509	323	11	254	4.3
Total	14, 014	9,075	1,550	6,994	0.25

The Problem criterion defines a DRP in terms of safety, effectiveness and need to use the medication for the patient in question. Analyzing the data collected and described in the "Type of Problem" section in Table 2, it is verified that the main problem involving the prescription of opioids in the wards is cost-effectiveness (P3.1), in 73.61% of the situations. The second most prevalent problem, employing an unnecessary drug (P3.2), corresponds to 10.39%, and is more than seven times less frequent than the main problem.

The Cause criterion analyzes whether the direct cause of the DRP is in the prescription (that is, in choice of the drug, pharmaceutical form, treatment duration or dose), if it is in the structure of the prescription (that is, in cases of important information missing in the prescription, or in case of missing drug prescription), or if it is in dispensing of the drug (that is, if the error is in administration of the drug, or in the patient's acceptance of the treatment). As evidenced in the "Cause of the Problem" section in Table 2, the main cause of DRPs is the prescription of an inappropriate form of drug for the patient in question (C2.1), in 73.23% of the cases.

The Intervention criterion analyses the measure adopted by the pharmacist that detected some DRP. As the "Intervention" section in Table 2 points out, in 87.74% of the cases, an intervention was proposed to the prescriber (I1.3), and only in 4.65% of the times there was no need for intervention by the pharmaceutical analyst (I0.1), as the prescription did not need to be adjusted. The Implementation criterion analyzes the prescriber's response to the intervention proposed by the pharmaceutical analyst, that is, whether the pharmacist's intervention was rejected, partially accepted or completely accepted. As pointed out in the "Implementation" section from Table 2, only in 35.61% of the cases was an intervention proposed to the prescriber accepted or fully implemented (A1.1). It is worth noting that only in 4.45% of the cases there were no proposals by the pharmacist who detected the DRP (A3.2). In turn, the Outcome analyses the DRP outcome after the intervention and implementation stages: if the DRP was not solved, was partially resolved, or fully resolved. As evidenced in the "Outcomes" section from Table 2, only in 36.46% of the cases was the problem totally solved (O1.1).

Finally, Figure 1 shows the evolution of the process of analyzing prescriptions and finding DRPs by clinical pharmacists over the 27 months of analysis, data already presented in Table 1. In this graph, the bars represent the absolute number of opioid-related DRPs found, and the dashed line represents the rate of opioid-related DRPs, that is, the percentage of prescriptions analyzed that had DRPs. It is noted that, at the beginning of the research, although relatively few prescriptions containing opioids were analyzed (nearly 27 of the 55 prescriptions analyzed in the month), the percentage of errors found was high: 36.4%; in other words, 10 of them contained DRPs. Although there are two peaks in the DRP rates, in June 2019 and December 2019, which are explained in depth in the Discussion, the trend is for the DRP rates to drop over time, associated or not with the increase in the number of analyses.

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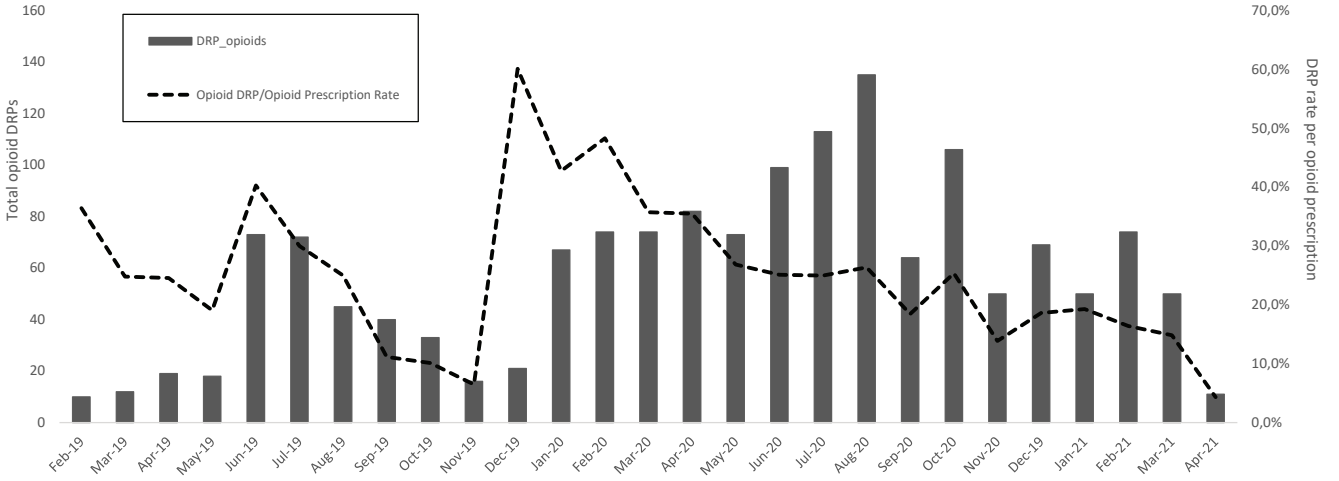
Table 2. Problems, causes, interventions, implementations and outcomes identified according to the DRP PCNE V8.02 classification in the analysis of DRPs involving all 4 options of opioid drugs available in the hospital.

Primary Domain	Secondary Domain	Frequency distribution	
		N	%
Type of Problem			
Effectiveness of Treatment P1	P1.1 Drug without effect	1	0.06
	P1.2 Suboptimal effect	124	8.0
	P1.3 Symptoms not treated	44	2.84
Safety of Treatment P2	P2.1 Problemas de segurança	77	4.97
Other P3	P3.1 Cost-effectiveness issues	1141	73.61
	P3.2 Unnecessary drug	162	10.39
	P3.3 Not clear	2	0.13
Cause of the Problem			
Drug Selection C1	C1.1 Inappropriate drug according to guidelines and protocols	90	5.81
	C1.2 Appropriate drug according to guidelines, but contraindicated	9	0.58
	C1.3 Drug without indication	54	3.48
	C1.4 Inappropriate drug combination (interaction)	3	0.19
	C1.5 Inappropriate duplication of therapeutic group or active ingredient	127	8.19
	C1.6 No medication treatment despite existing indication (omission)	66	4.26
	C1.7 Excessive drug prescribing for the same indication	3	0.19
Drug Formulation C2	C2.1 Inappropriate drug form (for this patient)	1135	73.23
Others	C3 Selected dose	47	3.03
	C4 Treatment duration	12	0.77
	C5 Dispensing	0	0
	C6 Drug usage process	3	0.19
	C7 Patient-related	0	0
	C8 Other	1	0.06
Intervention			
No intervention I0	I0.1 No intervention	72	4.65
At the prescriber level I1	I1.1 Prescriber informed only.	2	0.13
	I1.2 Prescriber requested information.	4	0.26
	I1.3 Intervention proposed to prescriber.	1360	87.74
	I1.4 Intervention discussed with prescriber.	110	7.10
Others	I2 Patient-level intervention	0	0
	I3 Drug-level intervention	1	0.06
	I4 Other interventions	1	0.06
Implementation			
Accepted intervention (by prescriber or patient) A1	A1.1 Accepted and fully implemented	552	35.61
	A1.2 Accepted and partially implemented	18	1.16
	A1.3 Accepted but not implemented	391	25.23
	A1.4 Accepted, implementation status unknow	339	21.87
Intervention not accepted (by prescriber or patient) A2	A2.1 Not accepted, unfeasible	60	3.87
	A2.2 Not accepted, lack of agreement	7	0.45
	A2.3 Not accepted, other reasons	5	0.33
	A2.4 Not accepted, reasons unknown	24	1.55
Others A3	A3.1 Proposed intervention, acceptance status unknown	85	5.48
	A3.2 Intervention not proposed	69	4.45
Outcomes			
Unknown O0	O.01 Status of the issue unknown	0	0
Resolved O1	O1.1 Issue completely resolved	564	36.46
Partially resolved O2	O2.1 Issue partially resolved	0	0
Unresolved O3	O3.1 Unresolved issue, lack of patient cooperation	1	0.06
	O3.2 Unresolved issue, lack of prescriber's cooperation	458	29.55
	O3.3 Unresolved issue, ineffective intervention	11	0.70
	O3.4 No need or possibility to resolve the issue	516	33.29
Total		1550	100

Figure 1. Relationship between prescriptions analyzed and DRPs found for calculating the estimated number of prescriptions containing opioids analyzed, and the opioid-related DRP rate per prescription.



Discussion

The current paper mapped Drug-Related Problems (DRPs) involving the prescription of opioid drugs in the ward of the Cajuru University Hospital (*Hospital Universitário de Cajuru*, HUC), Curitiba. A total of 14,014 prescriptions-days from February 2019 to April 2021 were analyzed, which presented a total of 9,075 DRPs, of which 1,550 contained DRPs specifically related to opioids. As there is no exact number of prescriptions involving opioids that did not contain DRPs to be used as a reference for calculations, the DOT formula was used, which showed that, in the period studied, 49.91% of the beds in the hospital wards had some opioid prescription attached.

Knowing, also through calculations, that around 22.16% of the prescriptions with opioids evaluated by the Clinical Pharmacy had DRPs, it was possible to apply this estimate to all opioid prescriptions performed in the hospital. Knowing that a mean of 1,793.65 opioids are prescribed per month, it is estimated that there are 397.4 opioid-related DRPs per month in the institution. Also knowing that, during the research, the pharmacists actually found a monthly mean of 57.4 opioid-related DRPs, and noting that it is estimated that there are around 397.4 DRPs per month, intense underreporting of the problem is evident: the estimate is that only one-seventh of the prescriptions with errors are effectively evaluated by the Hospital's Clinical Pharmacy. Another obstacle to a more numerous analysis is the low number of employees at the Clinical Pharmacy, only 4, for the large number of daily prescriptions corresponding to the more than 200 beds in the hospital.

Analyzing the data collected from the DRP table according to DRP PCNE V8.02, it is evident that the main Problem found is cost-effectiveness, in 73.61% of the times, and that the main Cause is the prescription of an inappropriate form of drug for the patient in question, in 73.23% of the cases (Table 2). The main Problem and Cause are directly related: this is especially due to the routine prescription of intravenous medications for patients who have no contraindications to the use of oral medications, a known less costly option for the hospital, in addition to being recommended by the *Switch* Protocol. The data obtained in the clinic and from the laboratory tests of the patients are associated with the *Switch* protocol, which proposes replacing the administration method of analgesic drugs from the intravenous to the oral route through the evaluation of treatment duration and pharmacokinetics, respecting the potency class and level and resulting in lower therapy costs[22-25].

Studies carried out in other medical units confirm the high incidence of DRPs in medical prescriptions, both in those containing opioids and other pharmacological classes. However, in these studies, other causes are pointed out as the reasons for these problems; mainly related to the dose prescribed, to unnecessary or inappropriate prescription of the medication and to the administration route. Similarly, they also emphasize the importance and benefits contributed by the review carried out by the pharmaceutical clinic and the need to increase acceptance of the interventions by the medical staff[7,23].

As also shown in Table 2, an intervention was proposed to the prescriber in 87.74% of the cases. With regard to implementation of the interventions, only in 35.61% of cases was an intervention proposed to the prescriber accepted and fully implemented; with regard to the outcome, however, the table shows the following triad: in 36.46% of the cases, the problem is completely solved; in 33.29% of the cases, there is no possibility of solving the problem (because the patient has already been discharged or because the medication has already been discontinued or replaced); and in 29.55% of the cases, the problem is not solved due to non-cooperation from the prescriber.

These data are complementary and important in concluding that, although the work of analyzing prescriptions is carried out with considerable efficiency (a mean of 28.93% of the hospital's monthly prescriptions are analyzed by the Clinical Pharmacy) and pharmacists are willing to educate the prescribers (an intervention was proposed to the prescriber 87.74% of the times), in 29.55% of the cases the problem was not solved strictly due to non-collaboration on the part of the prescriber, which can lead to an increase in morbidity and mortality among hospitalized patients.

Due to the fact that data collection took place over a 27-month period, simultaneously with proposals for interventions to prescribers in cases of errors, it was possible to graphically assess the impact of this education process through Figure 1. Namely, the inflation in June 2019 represents the moment when

the Clinical Pharmacy team began analyzing the prescriptions of patients hospitalized by the Orthopedics department, given that, until then, only prescriptions for patients hospitalized by General Surgery were analyzed. The deflation process that took place between February and May 2019 and between June and November 2019 represents the effectiveness of the educational action on the prescribers: as the pharmacists inform the prescribers about errors, these latter tend to make that specific mistake fewer times. This becomes evident when observing that, in the aforementioned periods, although the Clinical Pharmacy has analyzed more prescriptions, the percentage that present DRPs drops monthly.

The second inflation peak in the graph, which was in December 2019, was due to a change in the hospital's operating system, at which point the pharmacists turned their attention to re-registering pharmacy items, and only corrected prescriptions with more grotesque errors. After this period, it can be seen that the educational activity carried out by pharmaceutical analysts continues to generate results, reaching its peak in August 2020, when, of the 1,026 prescriptions analyzed, 649 had DRPs, of which only 135 were related to opioids, corresponding to 26.4% of the total number of DRPs.

Finally, it is worth mentioning the important role played by the Hospital's Clinical Pharmacy staff, which, through intense and effective work of educating the medical team, managed to detect a positive correlation with the incidence of opioid-related DRPs in the period. Such improvements do not only have repercussions on financial savings for the hospital but also on reducing the risk for the patients undergoing treatment.

In view of all that has been discussed, it is observed that the current research found satisfactory results that contribute to clarifying the circumstances of the DRPs found in the medical prescriptions of opioid drugs at the Cajuru University Hospital. However, the analyses were limited by the absence of some important information for developing the study, so that it was necessary to apply the DOT tool as a methodology to find such values.

Conclusion

Understanding the cause of the problems related to the prescription of opioid drugs is a way of seeking to improve the quality of life of the patients treated at reference hospitals, through the creation of effective policies and protocols in drug management and administration. In this context, the prevalence of the cost-effectiveness ratio problem (73.61%) stands out, caused by inadequate drug prescriptions (73.23%). It is also pointed out that, although very prevalent, the incessant education work carried out by the Clinical Pharmacy staff is also very limited by non-collaboration of the prescribing physicians.

Collaborators

All the authors contributed equally to the content included in the current manuscript and approved the final version.

Acknowledgments

The authors would like to thank the Clinical Pharmacy Unit at the Cajuru University Hospital for the scientific support. We also thank the pharmacists and Pharmacy residents who assisted in data collection.

Funding sources

This study did not receive financial support from any Institution.

Declaration of conflict of interests

The authors declare no conflicts of interest.

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