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INSTITUTO NACIONAL DE INFECTOLOGIA EVANDRO CHAGAS
DOUTORADO EM PESQUISA CLÍNICA EM DOENÇAS INFECCIOSAS

EDUARDO CORSINO FREIRE

FREQUÊNCIA E CLASSIFICAÇÃO DE INCIDENTES RELACIONADOS COM MEDICAMENTOS PREVENÍVEIS PELA ATUAÇÃO DO FARMACÊUTICO CLÍNICO EM INFECTOLOGIA

Rio de Janeiro
2023

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Tese apresentada ao Programa de pós-Graduação em Pesquisa Clínica (INI) para obtenção do grau de Doutor em Pesquisa Clínica em Doenças Infecciosas.

Orientador: Prof. Dr. Pedro Emmanuel Alvarenga Americano do Brasil

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“Adoramos a perfeição,
porque não a podemos ter;
repugna-la-íamos, se a
tivéssemos. O perfeito é
desumano, porque o humano é
imperfeito”.

Fernando Pessoa

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Resumo

Introdução: Monitorar a ocorrência de Incidentes Preveníveis Relacionados a Medicamentos (IPRM) é essencial para garantir a segurança do uso de medicamentos e priorizar as intervenções clínicas do farmacêutico. Intervenções em farmácia clínica reduzem o risco de danos com medicamentos durante a hospitalização. No entanto, existem dados escassos e heterogêneos sobre as IPRM hospitalares. **Objetivo:** Este estudo teve como objetivo estimar a taxa de incidência de IPRM, bem como avaliar a magnitude e os tipos de IPRM em um hospital especializado em doenças infecciosas. **Métodos:** Trata-se de um estudo observacional prospectivo. Pacientes com 18 anos ou mais, internados na enfermaria clínica do Instituto Nacional de Infectologia Evandro Chagas de 13/06/2019 a 13/03/2020, foram incluídos consecutivamente e acompanhados até alta ou transferência para a unidade de terapia intensiva. A cada sete dias de acompanhamento, a equipe do projeto verificou a ocorrência do desfecho de interesse, definido como incidentes relacionados a medicamentos de danos de gravidade média a muito alta (ou dano potencial) que podem ser evitados pelos farmacêuticos clínicos. A gravidade do IPRM foi classificada de acordo com os critérios do Código de Avaliação da Gravidade e da ferramenta de triagem para notificação de eventos adversos. Os dados foram analisados com o software R-project e Microsoft Excel. As estimativas de incidência foram realizadas como número de eventos dividido por pessoa-ano com intervalos de confiança de Poisson de 95%. **Resultados e discussão:** A proporção de pacientes com IPRM foi de 79% (168/212). A taxa de incidência foi ligeiramente maior nas mulheres e menor entre os participantes mais jovens (18 a 39 anos). Pacientes com Paracoccidioidomicose apresentaram menor incidência de IPRM quando comparados aos pacientes com doença de Chagas, HIV/AIDS ou Tuberculose. O número de eventos aumenta quanto maior o tempo de internação hospitalar. Foram observados 494 incidentes, com uma frequência de 1,7 incidentes por prescrição. Os incidentes mais frequentes foram interações medicamentosas, erro de aprazamento, Reações Adversas com Medicamento, duplicidade e erro de dose. **Conclusão:** O serviço de saúde especializado em doenças infecciosas possui características específicas de IPRM quando comparado com outras especialidades. A frequência de IPRM que

requerem intervenções do farmacêutico clínico entre pacientes com doenças infecciosas é muito alta. Como a taxa de incidentes é bastante alta e os tipos de incidentes variam, o trabalho dos farmacêuticos clínicos deve ser bastante extenso. É necessário que os cuidados farmacêuticos sejam racionalizados, por exemplo, por meio do desenvolvimento de instrumentos de predição de IPRM, uma vez que essa alta demanda não é acompanhada por um aumento no número de farmacêuticos clínicos.

Palavras-Chave: Serviço de Farmácia Clínica, Efeitos Colaterais e Reações Adversas Relacionados a Medicamentos, Taxas de Incidência, Doenças Infecciosas.

Abstract

Introduction: Monitoring the occurrence of Preventable Drug-Related Incidents (PDRI) is essential to ensure the safety of medication use and prioritize the pharmacist's clinical interventions. Interventions in clinical pharmacy reduce the risk of drug damage during hospitalization. However, there are scarce and heterogeneous data on hospital IPRM. **Objective:** This study aimed to estimate the incidence rate of PDRI, as well as to evaluate the magnitude and types of PDRI in a hospital specialized in infectious diseases. **Methods:** This is a prospective observational study. Patients aged 18 years or older, admitted to the clinical ward of the Instituto Nacional de Infectologia Evandro Chagas from 06/13/2019 to 03/13/2020, were consecutively included and followed up until discharge or transfer to the intensive care unit. Every seven days of follow-up, the project team verified the occurrence of the outcome of interest, defined as drug-related incidents of medium to very high harm severity (or potential harm) that can be avoided by clinical pharmacists. The severity of PDRI was classified according to the criteria of the Severity Assessment Code and the triage tool for reporting adverse events. Data were analyzed using R-project software and Microsoft Excel. Incidence estimates were performed as number of events divided by person-years with 95% Poisson confidence intervals. **Results and Discussion:** The proportion of patients with PDRI was 79% (168/212). The incidence rate was slightly higher in women and lower among younger participants (18 to 39 years old). Patients with Paracoccidioidomycosis had a lower incidence of PDRI when compared to patients with Chagas disease, HIV/AIDS or Tuberculosis. The number of events increases the longer the length of hospital stay. A total of 494 incidents were observed, with a frequency of 1.7 incidents per prescription. The most frequent incidents were drug interactions, scheduling errors, Adverse Drug Reactions, duplication and dose errors. Conclusion: The health service specialized in infectious diseases has specific characteristics of PDRI when compared to other specialties. The frequency of PDRI requiring clinical pharmacist interventions among patients with infectious diseases is very high. As the incident rate is quite high and the types of incidents vary, the work of clinical pharmacists must be quite extensive. Pharmaceutical care needs to be rationalized, for

example through the development of PDRI prediction instruments, since this high demand is not accompanied by an increase in the number of clinical pharmacists.

Keywords: Clinical pharmacy service, Drug-related side effects and Adverse reactions, Incidence rates, Infectious diseases.

Sumário

LISTA DE ABREVIATURAS

Adverse Drugs Events - ADE

Adverse Drug Reactions - ADR

Adverse Events - AE

Assembléia Mundial da Saúde - AMS

Drug-Related Incidents - DRI

Incidentes Preveníveis Relacionados com Medicamentos - IPRM

Instituto Nacional de Infectologia Evandro Chagas - INI

Intensive Care Unit - ICU

Eventos Adversos Relacionados com Medicamentos - EAM

Núcleo de Segurança do Paciente - NSP

Medical Dictionary for Regulatory Activities - MedDRA

Medication Errors - ME

Organização Mundial de Saúde - OMS

Preventable Drug-Related Incidents - PDRI

Problemas Relacionados com Medicamentos - PRM

reação adversa a medicamento - RAM

Severity Assessment Code - SAC

Tecnologia da Informação - TI

Unidade de Terapia Intensiva - UTI

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1 REFERENCIAL TEÓRICO

No fim década de 1990, o American Institute of Medicine publicou um relatório intitulado "Errar é humano". Este relatório estimou que cerca de 44.000 a 98.000 pacientes morriam devido a erros evitáveis nos hospitais americanos a cada ano, o que elevou a segurança dos pacientes aos olhos do público (LARK; KIRKPATRICK; CHUNG, 2018).

Confrontada com a evidência de danos substanciais à saúde pública devido à segurança inadequada do paciente, a 55ª Assembléia Mundial da Saúde (AMS) em 2002 aprovou uma resolução instando os países a fortalecer a segurança dos sistemas de atenção e monitoramento da saúde. A resolução também solicitou que a Organização Mundial de Saúde (OMS) liderasse o estabelecimento de normas e padrões globais e apoiasse os esforços dos países na preparação de políticas e práticas de segurança do paciente (ANVISA, 2015). Em maio de 2004, a AMS aprovou a criação de uma aliança internacional para melhorar a segurança do paciente globalmente, sendo a Política de Segurança do Paciente da OMS lançada no mês de outubro do mesmo ano (WHO, 2009)

A segurança do paciente é um constructo que implica um comportamento destinado a minimizar o risco de eventos adversos aos pacientes, através de atividades concebidas para evitar danos (ALBRECHT, 2015), sendo os eventos adversos definidos como incidente que resulta em dano ao paciente. Incidente, por sua vez, é definido como evento ou circunstância que poderia ter resultado, ou resultou, em dano desnecessário ao paciente, compreendendo, portanto, os eventos adversos e os quase erros, ou seja, não necessariamente atinge o paciente (BRASIL A, 2013).

Apesar do progresso nos últimos anos, a falta de segurança para o paciente continua a ser um importante problema de saúde pública. A literatura revela que essa questão é mais complexa do que inicialmente percebida e é pertinente a todos os contextos de saúde (LARK; KIRKPATRICK; CHUNG, 2018).

Propor ações que estimulem segurança é trabalhar com minimização de riscos de modo a reduzir a ocorrência de eventos adversos relacionados à assistência à saúde a níveis aceitáveis. Sob este ponto de vista, observa-se a relevância de identificar as características e estabelecer os parâmetros dos riscos envolvidos com a permanência

do paciente no hospital para reduzir falhas e eventos adversos evitáveis (RODRIGUES, 2017).

Indivíduos hospitalizados recebem assistência complexa, que por sua vez, segundo a “Teoria da Normalidade dos Acidentes” descrita por Charles Perrow (Normal Accidents, 1999), apresenta alto risco para eventos adversos. Entre estes, os eventos adversos relacionados com medicamentos (EAM) são os que ocorrem com maior frequência, tornando-se uma grande preocupação para os gestores da saúde (BOHOMOL; RAMOS, 2007).

A farmacoterapia é amplamente utilizada para fins curativos, paliativos e diagnósticos nos pacientes, sendo os mais vulneráveis à ocorrência de EAM os que utilizam múltiplos medicamentos (OLIVEIRA et al., 2014). Estes indivíduos estão mais susceptíveis a reação adversa a medicamento (RAM), que pode ser entendida como qualquer resposta prejudicial ou indesejável e não intencional que ocorre com medicamentos em doses normalmente utilizadas. Não são considerados como RAM os efeitos que ocorrem depois do uso acidental ou intencional de doses maiores que as habituais (toxicidez absoluta) (BRASIL, 2011). Todavia, são considerados EAM, por estarem em uma categoria mais ampla que as RAM.

Um estudo conduzido na África do Sul avaliou a mortalidade associada ao desenvolvimento de RAM em pacientes hospitalizados com vírus da imunodeficiência humana (HIV/AIDS). O estudo constatou que, dos 356 óbitos, 56 (16%) estavam relacionados com RAM e, destes, 43% eram evitáveis. Os medicamentos mais relacionados com óbito foram tenofovir, rifampicina e sulfametoxazol/trimetoprima (MOUTON et al., 2015).

No Brasil, ainda não se sabe a dimensão real dos EAM, embora seja o quinto país no mundo e o primeiro da América Latina em consumo de medicamentos (CASSIANI, 2005). A segurança do paciente e o uso seguro de medicamentos são questões prioritárias na medicina moderna. Esforços atuais em todo o mundo estão sendo desenvolvidos para reduzir a morbidade e a mortalidade relacionadas ao consumo de medicamentos e aos problemas a eles relacionados (OPAS; WHO, 2015).

Os problemas relacionados com medicamentos (PRM) são falhas com resultados clínicos negativos, derivados da farmacoterapia que, produzidos por diversas

causas, conduzem ao não alcance dos objetivos terapêuticos ou ao surgimento de efeitos não desejados (SANTOS et al., 2003). Entende-se, portanto, que os PRM são a categoria mais ampla e engloba todos os incidentes relacionados a medicamento, incluindo os quase erros, EAM e as RAM; de forma que, PRM > EAM > RAM.

A complexidade que envolve o uso de medicamentos se correlaciona com a força de acoplamento de interações de falhas ou “cascata de eventos” (PERROW, 1999), demandando, assim, que as falhas na medicação sejam vistas como com sequências multicausal e de abordagem multidisciplinar, para que se possa identificar e corrigir fatores que contribuam para suas ocorrências (CASSIANI, 2005).

A multidisciplinaridade no uso dos medicamentos favorece a atuação do farmacêutico clínico nos serviços de saúde, e estabelece uma barreira de segurança para minimizar EAM, que estão normalmente presentes na politerapia (RODRIGUES, 2017).

O estudo de Jacobi (JACOBI, 2016) demonstra que pacientes com intervenções clínicas do farmacêuticas tiveram um risco 34% menor de qualquer EAM ou erro de medicação, com razão de risco igual a 0,66, em comparação com pacientes controle tratados nas mesmas clínicas. Sendo o erro de medicação entendido como qualquer evento evitável que, de fato ou potencialmente, pode levar ao uso inadequado de medicamento (FERRACINI; FILHO, 2010).

Outro exemplo é do American College of Cardiology, que executou uma estratégia de atuação incluindo farmacêuticos clínicos em equipes de tratamento médico de pacientes agudos e demonstraram a redução de eventos adversos evitáveis em 78% (JACOBI, 2016).

Porém, a existência de número suficiente de farmacêuticos para atender à carga de trabalho cada vez mais elevada com a qualidade e segurança é um desafio (RODRIGUES, 2017). A racionalização dos cuidados farmacêuticos e a seleção de pacientes com maior risco de EAM são necessárias (MARTINBIANCHO J.K. et al., 2011). Modelos de previsão podem ser ferramentas valiosas para essa finalidade. Eles podem estimar as probabilidades individuais e ajudar na identificação de pessoas com alto risco de sofrerem eventos adversos (WELTEN et al., 2018).

A literatura aponta diversas formas para a detecção de falhas ocorridas na medicação dos pacientes, como notificações, relatórios anônimos, revisão de prescrição, entre outros, todos com vantagens e desvantagens; todavia a literatura também aponta que devem ser ajustados às necessidades de cada instituição (BOHOMOL; RAMOS, 2007). Diferentes indicadores de risco de morbidade relacionados aos medicamentos têm sido pesquisados nos Estados Unidos da América, Canadá e Europa, porém todos em farmácias comunitárias. Entretanto, pouco se observa, na área hospitalar, publicações de um instrumento farmacêutico de avaliação de pacientes internados.

2 JUSTIFICATIVA

Em um estudo realizado pelo Serviço de Farmácia do Hospital das Clínicas de Porto Alegre em 2011, pesquisadores propuseram um escore de risco para paciente com necessidades de acompanhamento pelo farmacêutico clínico. Esse instrumento seleciona o nível de prioridade de monitoramento da farmacoterapia, sendo o alto risco o que exige prioridade de monitoramento; o risco moderado o que necessita de monitoramento, mas não em caráter de emergência; e baixo risco o que recomenda que pacientes que devem ser apenas observados (MARTINBIANCHO J.K. et al., 2011).

O estudo de Martimbiancho (MARTINBIANCHO J.K. et al., 2011) acompanhou pacientes transplantados, pacientes internados em Unidade de Terapia Intensiva (UTI) adulto, pediátrico e neonatal, além de pacientes da pediatria, oncologia pediátrica e pacientes da psiquiatria. Não foi observada no estudo a descrição de sua aplicação na área da infectologia. Os preditores de risco utilizados neste estudo, dentre outros, foram: idade, medicamentos intravenosos, medicamentos potencialmente perigosos, disfunções renais, cardíacas, pulmonares, imunossupressão e imunocomprometimento. Esse escore, uma vez aplicado aos pacientes internados do Instituto Nacional de Infectologia Evandro Chagas (INI) pelo Núcleo de Segurança do Paciente (NSP), apontou todos os pacientes avaliados como de moderado e alto risco (dados não publicados).

Como a maioria dos pacientes atendidos no INI apresentam doenças como tuberculose, HIV/AIDS e doença de Chagas, a utilização do escore de risco elaborado pelo estudo de Martinbiancho e colaboradores (2011) faria com que todos os pacientes fossem atendidos pela farmácia clínica, se contrapondo como a necessidade de racionamento dos serviços clínicos farmacêuticos apontada pelo mesmo estudo. A característica da população atendida pelo INI se mostra muito diferente da população avaliada pela equipe de Martinbiancho (2011), de modo que é possível que o escore proposto por ela de fato não seja aplicável à população de pacientes do INI, não somente por não ter discriminado pacientes de baixo risco, mas também pelo fato de os preditores em si poderem ser diferentes.

O INI contava, no período do estudo, com a atuação de apenas um farmacêutico clínico restrito a UTI, que é sempre um ambiente de alto risco para EAM, tanto pelo grande número de itens na prescrição quanto pela frequência elevada de disfunções orgânicas. A atuação do farmacêutico clínico neste setor tem sido capaz de evitar EAM potencialmente graves, através de auxílio no aprazamento da prescrição com a enfermagem, ajustando doses, tempo de infusão e volume de diluição.

O farmacêutico clínico avalia todos os itens da prescrição, suas interações com potencial para EAM e ao mesmo tempo acompanha a evolução dos exames laboratoriais dos pacientes, o que consome muito tempo do profissional e corrobora com a necessidade de racionalização das atividades farmacêuticas apontadas pelo estudo de Martinbiancho (2011).

Na tentativa de conseguir racionalizar os serviços farmacêuticos clínicos, a Gerência de Risco do NSP e a Farmácia Clínica desenvolveram uma matriz de risco, de forma empírica, para seleção de pacientes com maior risco de EAM na enfermaria do INI. Todavia, não há evidência científica que comprove a sua eficácia.

Em virtude da necessidade de racionalização dos serviços do farmacêuticos clínicos ser observada em todos os hospitais, e principalmente nos públicos, incluindo o INI, bem como das especificidades da população atendida nesse serviço de saúde, por não ter sido verificado na literatura um instrumento de predição de Incidentes Preveníveis Relacionados com Medicamentos (IPRM) para pacientes internados em unidades de infectologia e também pela reemergência de doenças infecciosas e parasitárias, elevando o número de procura por serviços de infectologia e consequentemente a utilização de medicamentos pela população acometida por estas doenças, se justifica a pesquisa dos IPRM em uma unidade de infectologia; assim como a avaliação da sua frequência e classificação de risco para subsidiar decisões gerenciais quanto a necessidade e/ou racionalização dos serviços clínicos realizados por farmacêuticos.

3 OBJETIVO GERAL

Auxiliar a decisão do farmacêutico clínico disponibilizando informações sobre incidentes relacionados com a prescrição de medicamentos em pacientes portadores de doenças infecciosas.

3.1 Objetivos Específicos

- Descrever a incidência de IPRM nos pacientes internados na enfermaria do INI;
- Classificar os IPRM nos pacientes internados na enfermaria do INI.

4 METODOLOGIA

4.1 Delineamento:

Trata-se de um estudo de segmento observacional com seleção sequencial dos participantes. Aprovado pelo CEP, com numeração CAAE 04870918.8.0000.5262.

4.2 Participantes:

Foram incluídos consecutivamente pacientes com doenças infecciosas internados na enfermaria do Instituto Nacional de Infectologia (INI) Evandro Chagas no período de 13/06/2019 a 13/08/2020. O INI está localizado no Rio de Janeiro/Brasil e caracteriza-se como um hospital público e terciário federal de alta complexidade, especializado no atendimento de pacientes com doenças infecciosas. Durante o período do estudo, possuía 22 leitos de enfermaria e 4 leitos de unidade de terapia intensiva (UTI), com uma taxa média anual de internação de aproximadamente 575 pacientes/ano.

Os critérios de inclusão foram: estar internado na enfermaria durante o período de inclusão, ter idade igual ou superior a 18 anos, não ter recebido atendimento do farmacêutico clínico.

Os critérios de exclusão foram: tempo de internação <24 horas; ausência de uso de medicamentos nas primeiras 48 horas de internação; pacientes que foram admitidos diretamente na UTI e pacientes transferidos da UTI para a enfermaria.

Os pacientes que foram admitidos na enfermaria e depois transferidos para a UTI foram descontinuados do estudo no momento da transferência.

4.3 Desfecho

O desfecho deste estudo foram os incidentes relacionados com medicamentos, com potencial de média a muito alta gravidade, compreendendo incidentes clinicamente significativos relacionados à prescrição de medicamentos e RAM evitáveis.

Os seguintes incidentes foram incluídos como erros de prescrição: prescrição de medicamentos com interações (interação maior ou moderada, de acordo com drugs.com), erro de dose, erro de posologia, erro de diluição, erro de via de administração, erro de concentração, erro de infusão, erro de tempo de tratamento, erro de aprazamento, indicação, falta de prescrição de medicamentos, erro de tempo de infusão, erro de veículo, além de duplicação de prescrição, incluindo aqueles identificados (corrigidos ou não) pelo profissional de farmácia do hospital.

A análise de risco dos IPRM consistiu na avaliação da gravidade, que foi estabelecida por meio da definição dos efeitos dos incidentes sobre os pacientes (Tabela 1) e da avaliação da probabilidade de ocorrência de cada incidente (Tabela 2). Uma matriz de risco (Quadro 1) combinando a gravidade e a probabilidade do IPRM permitiu que as categorias para os níveis de risco fossem estabelecidas. Uma matriz de gravidade versus probabilidade é um meio de combinar classificações qualitativas ou semiquantitativas de consequências e probabilidades para produzir um nível de risco ou escore de risco.

O nível de risco foi então estabelecido em função da matriz. O produto de multiplicação obtido entre os valores de probabilidade e gravidade definiu o nível de risco inerente, que é o nível de risco sem considerar as barreiras que reduzem ou podem reduzir a probabilidade de sua ocorrência ou sua gravidade. O nível de risco definido pela matriz está associado a uma regra de decisão, que determina como tratar ou não o risco (BRASIL, 2018; ASSOCIAÇÃO BRASILEIRA DE NORMAS TÉCNICAS, 2012). É por meio da análise desse valor que o Núcleo de Segurança do Paciente (NSP), do serviço de saúde onde a pesquisa ocorreu, prioriza ações corretivas para os incidentes identificados.

Tabela 1: Classificação de Eventos Adversos de Assistência de acordo com a gravidade (adaptada da ferramenta de classificação e triagem do Código de Avaliação de Gravidade (SAC) para notificação de eventos adversos)

CATEGORIA	Valor	DEFINIÇÃO
Grave	5	Morte ou perda permanente ou grave de função que está relacionada ao processo de cuidado em saúde e difere do desfecho esperado
Principal	4	Perda temporária grave de função que está relacionada ao processo de cuidado em saúde e difere do resultado esperado
Moderado	3	Perda maior Perda permanente temporária ou moderada de função que está relacionada ao processo de cuidados de saúde e difere do resultado esperado
Menor	2	Perda temporária moderada ou perda permanente menor de função que está relacionada ao processo de cuidados de saúde e difere do resultado esperado
Mínimo	1	Pequena perda temporária de função que está relacionada ao processo de cuidado em saúde e difere do resultado esperado

Fonte: NEW ZEALAND, 2017.

Tabela 2: Classificação de Eventos Adversos de Assistência de acordo com a Probabilidade (adaptada da ferramenta de classificação e triagem do Código de Avaliação de Gravidade (SAC) para notificação de eventos adversos)

CATEGORIA	Valor	DEFINIÇÃO
Muito alto	5	Quase certo de que ocorra pelo menos uma vez nos próximos três meses, mais de 95% de chance
Alto	4	Provavelmente ocorrerá pelo menos uma vez nos próximos quatro a 12 meses, 66 a 95%
Moderado	3	Espera-se que ocorra dentro dos próximos um a dois anos, entre 26 – 65% de chance
Baixo	2	Evento pode ocorrer em algum momento nos próximos dois a cinco anos, entre 5 – 25% de chance
Muito baixo	1	Improvável de recorrência – pode ocorrer apenas em circunstâncias excepcionais, *i. e.* >cinco anos, menos de 5% de chance

Fonte: NEW ZEALAND, 2017.

Quadro 1: Matriz de Risco gravidade x probabilidade, adaptada.

		Probabilidade				
		Muito baixo	Baixo	Moderado	Alto	Muito alto
Severidade	Mínimo	1	2	3	4	5
	Menor	2	4	6	8	10
	Moderado	3	6	9	12	15
	Principal	4	8	12	16	20
	Grave	5	10	15	20	25

Escore de Nível de Risco: 1 -5 baixo ou muito baixo; 6 – 9 médio; 10 – 15 alto e 16 – 25 muito alto.
Fonte: ASSOCIAÇÃO BRASILEIRA DE NORMAS TÉCNICAS, 2012.

O Algoritmo de Naranjo (Tabela 3) foi utilizado como ferramenta de classificação causal para suspeitas de eventos de RAM (NARANJO et al., 1981).

Tabela 3: Questionário de Causalidade de Naranjo.

Questões	**Sim**	**Não**	**Desconhecido**
1. Existem notificações conclusivas sobre essa reação?	**+1**	**0**	**0**
2. A reação apareceu após a administração do medicamento?	**+2**	**-1**	**0**
3. A reação melhorou quando o medicamento foi suspenso?	**+1**	**0**	**0**
4. A reação reapareceu quando foi readministrado?	**+2**	**-1**	**0**
5. Existem causas alternativas (mesmo outro medicamento)?	**-1**	**+2**	**0**
6. A reação reaparece com a introdução de um placebo?	**-1**	**+1**	**0**
7. A concentração plasmática está em um nível tóxico?	**+1**	**0**	**0**
8. A reação aumentou com uma dose mais elevada ou foi reduzida com uma dose mais baixa?	**1**	**0**	**0**
9. O paciente já experimentou tal reação anteriormente com o medicamento do mesmo fármaco?	**+1**	**0**	**0**
10. A reação foi confirmada por alguma prova objetiva?	**+1**	**0**	**0**
			Total =

Fonte: NARANJO et al., 1981.

Após a utilização do questionário Naranjo, onde cada questão recebe uma pontuação e ao final é obtida a soma dos pontos, as suspeitas de RAM foram classificadas de acordo com o escore geral do questionário. As RAM suspeitas que receberam escore zero ou negativo foram classificadas como duvidosas, as que receberam de 1 a 4 pontos foram classificadas como possíveis, as que receberam q 5 a 8 pontos foram classificadas como prováveis e as que receberam 9 ou mais pontos foram classificadas como definitivas.

O Medical Dictionary for Regulatory Activities (MedDRA) foi utilizado neste trabalho para tornar a identificação uniforme das RAM (BROWN; MADEIRA; MADEIRA, 1999). O MedDRA é baseado na terminologia de propriedade da Agência Reguladora de Medicamentos e Produtos de Saúde do Reino Unido (MHRA) e foi desenvolvido para atender à necessidade de terminologia médica padronizada.

A adoção dessa terminologia única facilita a comunicação e a compreensão entre diferentes atores, incluindo organizações de pesquisa. As interações medicamentosas foram classificadas de acordo com o banco de dados do Drugs.com. Neste trabalho, foram utilizados apenas as consideradas major.

4.5 Coleta de dados e Inspeções dos dados:

Os dados dos pacientes foram coletados a partir de prescrições e do prontuário eletrônico do paciente. Seguindo a mesma lógica de farmacovigilância de verificação e captação de dados incompletos nos prontuários referentes ao evento de interesse, a equipe multiprofissional e o próprio paciente também foram consultados. Registros e relatos da equipe foram considerados fontes de dados referentes aos eventos de interesse do participante.

Os dados foram coletados por um grupo de quatro farmacêuticos juniores. A coleta teve início no primeiro dia de internação ou no primeiro dia útil após a admissão,

com a assinatura do termo de consentimento livre e esclarecido, seguido da coleta de informações como dados pessoais e dados da primeira prescrição.

As coletas subsequentes ocorreram a cada sete dias corridos após a internação, por meio da verificação dos prontuários dos pacientes (prescrições, exames laboratoriais e laudos multidisciplinares de evolução clínica) para identificação do IPRM ocorrido nesse período.

Esse procedimento foi repetido a cada sete dias até que o paciente recebesse alta ou transferência. Se o paciente recebeu alta ou foi transferido antes de completar um dos períodos de sete dias, também foram analisados os dias entre a última coleta e a saída do paciente da enfermaria.

Todos os dados coletados foram digitados e armazenados no programa RedCap (HARRIS et al., 2009). Após a inserção dos dados no RedCap, um farmacêutico sênior verificou, confirmou ou ajustou os dados e atribuiu classificações, a investigação foi eminentemente observacional, e não houve proposta de intervenção sistematizada por parte da assistência para evitar esses incidentes.

4.6 Plano de gestão e análise:

O gerenciamento dos dados foi realizado através do programa RedCap hospedado no INI/Fiocruz. Este software atende a todas as exigências da RDC 17/2010 da ANVISA e CFR 21 parte 11 do Food and Drug Administration que rezam sobre segurança, hierarquização e acesso aos dados.

Os dados coletados do participante se tornaram anônimos e codificados, ou seja, não houve como ligar o dado coletado ao nome ou identificador do participante, salvo pelo código da pesquisa, que foi armazenado em separado. A estrutura de rede de Tecnologia da Informação (TI) e servidores no INI, tem como rotina a cópia de segurança de todos os dados da rede a cada 24h.

Adicionalmente, os dados da pesquisa foram copiados, também para fins de segurança, semanalmente para um disco rígido externo, o que permitiria, no caso de catástrofe, a recuperação com facilidade dos dados para dentro da mesma estrutura de gerenciamento com uma perda de no máximo uma semana de trabalho.

Ao fim do processo de divulgação de relatório de pesquisa em formato científico, a equipe pode verificar a pertinência de disponibilização dos dados brutos anonimizados ou de sua parte, de tal forma a não prejudicar o andamento ou desenvolvimento de projetos/relatórios posteriores que utilizem pelo menos parte destes dados e simultaneamente atendam às boas práticas de transparência de geração de conhecimento.

O plano de análise consistiu nas seguintes etapas principais: inspeção dos dados; estudo de padrões de dados ausentes necessidade de imputação e codificação.

Os dados foram analisados com o software R-project e Microsoft Excel. As estimativas de incidência de IPRM foram realizadas como número de eventos dividido por pessoa-ano com intervalos de confiança de Poisson de 95%, estratificados em grupos de acordo com idade, sexo, diagnóstico, escore de comorbidades de Charlson (QUAN et al., 2011) e tipos de incidentes.

5 RESULTADOS E DISCUSSÃO

5.1 Artigo 1

INCIDENCE OF PREVENTABLE DRUG-RELATED INCIDENTS IN AN INFECTIOUS DISEASES HOSPITAL

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Data availability statement

The data used and/or analyzed during the study are available from the corresponding author on reasonable request.

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Conflict of interest disclosure

The authors declare no conflict of interests.

Ethics approval statement

All measures of protection and confidentiality of the participants were taken, based on the good clinical practice standards from Document of the Americas, and National Health Council regulatory standards for research with human beings contained in the Resolution No. 466/ December 2012. The project was approved in the ethics national system for research with human beings (https://plataformabrasil.saude.gov.br/login.jsf) with the number CAEE: 04870918.8.0000.5262.

Patient consent statement

Not applicable.

Permission to reproduce material from other sources

Not applicable.

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Abstract

What is known and Objective: Monitoring the occurrence of Preventable Drug-Related Incidents (PDRI) is essential to ensure the safety of medication use and prioritize clinical pharmacy interventions. However, there are scarce and heterogeneous data regarding hospital PDRIs. This study aimed to estimate the incidence rate of PDRI in a hospital specialized in infectious diseases. **Methods:** This is an observational prospective study. Patients 18 years old or older, admitted to the clinical ward of the Evandro Chagas National Institute of Infectious Diseases from 2019/06/13 to 2020/03/13, were consecutively included, and followed until discharge or transfer to the intensive care unit. Every seven days of follow-up, the project team verified the occurrence of the outcome of interest, defined as drug-related incidents of medium to very high severity harm (or potential harm) that can be prevented by the clinical pharmacists (PDRI). The severity of PDRI was classified according to the criteria of the Severity Assessment Code and triage tool for reporting adverse events (NEW ZEALAND, 2017). Data were analyzed with R-project software. Incidence estimates of PDRI were performed as number of events divided by person-year with 95% Poisson confidence intervals. **Results and discussion:** The proportion of patients with PDRI was 79% (168 / 212). The incidence rate was slightly higher in women, and was lower among younger participants (18 to 39 years old). Patients with Paracoccidioidomycosis presented a lower incidence of PDRI when compared to patients with Chagas disease, HIV/AIDS or Tuberculosis. The number of events increases the longer the hospital length of stay. Drug interactions, timing and dose errors, and adverse reactions were the most frequent PDRI in the sample. **What is new and Conclusion:** The health service specialized in infectious diseases has PDRI peculiarities when compared with other specialties. As the incident rate is quite high and the types of incidents vary in origin, the work of clinical pharmacists must be quite extensive.

Keywords: Clinical pharmacy service, Drug-related side effects and adverse reactions, Incidence Rates, Infectious Disease.

What is known and Objective

Since 1999, with the publication of the report “To Err Is Human: Building a Safer Health System” by the U.S. Institute of Medicine, the “Patient Safety” movement has been gaining increasing attention and support. According to that report, about 44,000 to 98,000 patients died due to avoidable errors in U.S. hospitals each year (LARK; KIRKPATRICK; CHUNG, 2018).

Patient Safety is described as "reduction, to an acceptable minimum, of the risk of unnecessary harm associated with health care” (ANVISA, 2015). In Brazil, several health surveillance practices emerged based on regulations, such as policies and technical standards, inspections and monitoring, in order to improve the patient safety. Nevertheless, only after the Federal Government launched the National Program for Patient Safety, in 2013, specific and remarkable action directed to patient safety took place (BRASIL B, 2013). This program created hospital sectors or departments responsible for patient safety management, aiming to improve the quality of health services in Brazil (BRASIL B, 2013).

Health services incidents are defined by Brazilian legislation as an event or circumstance causing unnecessary real or potential harm to the patient. These incidents include adverse events (AE) and near misses. AEs are defined as an unintentional damage to the patient due to a clinical intervention, and not to the disease itself (DE VRIES et al., 2008). Near miss is an unplanned event that did not result in injury, illness, or damage - but had the potential to do so (BRASIL B, 2013).

AE are responsible for economic and social impacts, and can lead to disability and death. Few studies have shown that AEs occur in 14-25% of hospitalized patients, reaching 33% of patients over 65 years of age (GIARDINA et al., 2018); 40% to 70% of these AEs are preventable (“avoidable incidents”) (FRAGATA, 2011; RAFTER et al., 2017; VINCENT, 2001). Avoidable incidents are those that would not occur if health care had taken place according to the recommendations of good operating practices (BRASIL B, 2013) for the patient's health needs (MICHEL, 2004).

The incidents in health services can be related to medicines, therefore there is a conceptual correlation with Drug-Related Problems (DRP). DRP are either

pharmacotherapy negative clinical results due to non-achievement of therapeutic goals or to the emergence of unwanted effects (SANTOS et al., 2003).

Therefore, DRPs are a broad category and encompasses all drug-related incidents (DRI), including near misses, Medication Errors (ME), Adverse Drugs Events (ADE) and Adverse Drug Reactions (ADR). MEs are preventable incidents that may lead to or are leading to inappropriate medication use (FERRACINI; FILHO, 2010); ADE is any undesirable clinical occurrence that occurs during drug treatment, but which may not have a causal relationship with the treatment, while ADR is a “drug response that is undesirable and unintended, that occurs in treatment at commonly used doses (WHO, 2002). Medicines are widely used by the population and are essential in the therapeutic strategy in health services. However, its use is inherently associated with the risk of DRI (CANO; ROZENFELD, 2009). To ensure the safety of medications use, it is imperative to monitor the occurrence of DRI (BOTELHO et al., 2020). DRI monitoring is crucial for reducing its risks to acceptable levels, as well as for prioritizing clinical pharmacy interventions (SOUZA et al., 2018). However, data regarding hospital DRI are scarce and heterogeneous, which jeopardize the understanding of preventable incidents and their frequency (DE VRIES et al., 2008). Thus, recommendations focused on medication use aiming to improve Patient Safety are based on limited information (RAFTER et al., 2017). Evidence shows that clinical pharmacists are the main professionals who can prevent, identify and correct avoidable DRI, possibly reducing its incidence by 80% (KHALILI et al., 2013). Nevertheless, clinical pharmacy services usually have several challenges, such as low funding, reduced number of pharmacists, as well as an increasing working load (ALSHAKRAH; STEINKE; LEWIS, 2019).

However, not all preventable DRIs are susceptible to clinical pharmacists’ interventions (e.g. medication administration errors). Identifying the incidence of avoidable DRI in health services has educational and planning value, and can help health managers in formulating measures to avoid and correct the potential DRI (SAAVEDRA et al., 2016). This study aimed to estimate the incidence rate of DRI that are preventable by clinical pharmacists (preventable DRI - PDRI) in a hospital specialized in infectious diseases.

Methods

This is an observational follow-up study. Patients with infectious diseases admitted to the ward of the Evandro Chagas National Institute of Infectious Diseases (INI) from 2019/06/13 to 2020/08/13 were consecutively included. INI is located in Rio de Janeiro/Brazil, and is characterized as a high-complexity, federal public and tertiary hospital, specialized in the care of patients with infectious diseases. During the study period, it had 22 ward beds and 4 intensive care unit (ICU) beds, with an average annual hospitalization rate of approximately 575 patients/year.

The inclusion criteria were: to be hospitalized in the ward during the inclusion period, to be 18 years of age or older, not to have received care from the clinical pharmacist and to consent participation. Exclusion criteria were: hospital length of stay <24 hours; absence of medication use during the first 48 hours of hospitalization; patients who were admitted directly to the ICU and patients transferred from the ICU to the ward, since in the ICU patients received care from clinical pharmacists on a regular basis. Patients who were admitted to the ward and then transferred to the ICU were discontinued from the study at the time of transfer.

Outcomes were defined as clinically relevant drug-related incidents that could be prevented by the clinical pharmacists. Therefore, ADEs of medium to very high severity harm and incidents that affect the patient with the potential of medium to very high severity harm related to medication prescription were considered as outcomes. The severity of PDRI was classified according to the criteria of the Severity Assessment Code (SAC) and triage tool for reporting adverse events (NEW ZEALAND, 2017). As for the intensity, they were classified according to the recommendations by ANVISA, as described in the Qualifying Intensity Gradation for Health Conditions (ANVISA, 2016).

Therefore, outcome are the ADRs, drug interactions, administration of drugs that led to real damage or with potential severity of medium to very high harm, as long as they are preventable by the clinical pharmacist, and the prescription errors. Prescription errors are errors of unintentional decision or wording that may reduce the likelihood of treatment

being effective or increase the risk of patient injury when compared with established and accepted clinical practices (DEAN, 2000).

The following were included as prescription errors: prescription of drugs with interactions, dose error, dosage error, dilution error, administration route error, concentration error, infusion error, treatment time error, scheduling error, indication error, lack of medication prescription, infusion time error, vehicle error, in addition to prescription duplication, including those identified (corrected or not) by the hospital pharmacy professional.

Patient data were collected from prescriptions and electronic medical records and, in case of incomplete data, the multiprofessional team and the patient were consulted for clarification. All data collected were typed and stored in the RedCap software (HARRIS et al., 2009)).

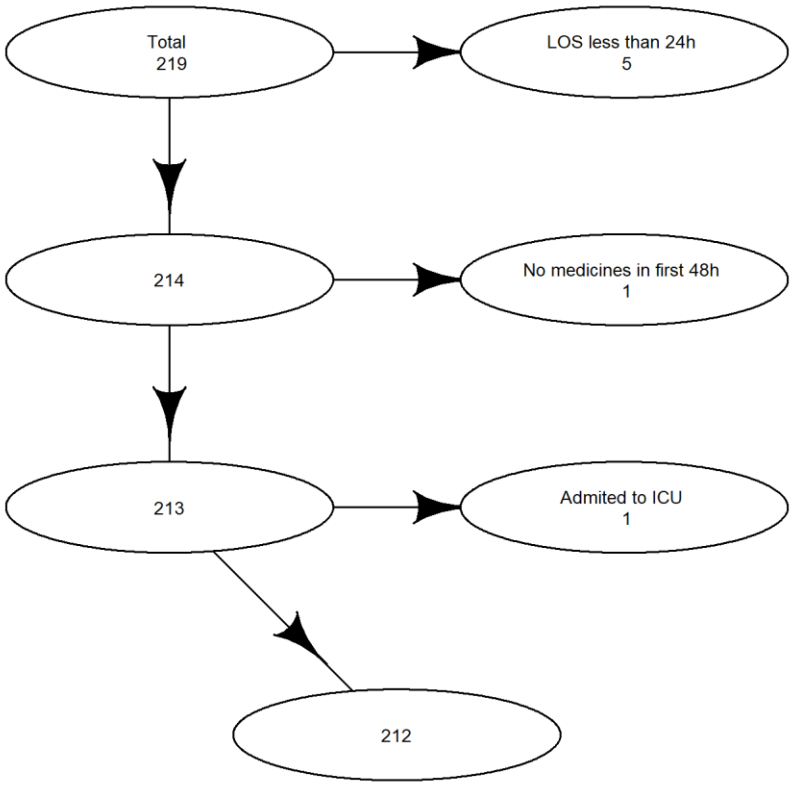
The first patient's hospitalization in the inclusion period was considered as the observation unit. Subsequent hospitalizations of the same participant in the inclusion period were ignored. At each seven-day period of hospitalization, the project team verified the occurrence the outcome of interest. Data were analyzed with R-project software. Incidence estimates of PDRI were performed as number of events divided by person-year with 95% Poisson confidence intervals, stratified into groups according to age, sex, diagnosis, Charlson's score of comorbidities (QUAN et al., 2011) and types of incidents.

Results and discussion

Results

During a period of nine months of data collection, 219 patients were screened. Seven patients were excluded or discontinued from the research. Therefore, 212 participants were analyzed. (Figure 1)

Figure 1 - Inclusion and exclusion flow diagram.



The incidence of patients with any type of PDRI was 79% (168 / 212). The groups with higher PDRI incidence were non-elderly adults (median age 45.5 years), male, mixed-race and with comorbidities. Patients were also stratified by number of hospitalizations in the last year and it was observed that most patients had no recent hospitalizations and had none or one hospitalization in the previous 12 months. However, there is no differences of PDRI incidence among previous hospitalizations groups. (Table 1)

Table 1: Sample description by presence or absence of any preventable drug related incident during hospital admission.

	Preventable Drug Related Incident		
	No	Yes	Total
Total	44	168	212
Age			
median (IQR)	38.50 (30.25 - 58.50)	45.50 (35.00 - 58.00)	44.00 (33.00 - 58.00)
Age			
[18,39]	22 (50.00)	59 (35.12)	81 (38.21)
(39,60]	11 (25.00)	70 (41.67)	81 (38.21)
(60,80]	9 (20.45)	38 (22.62)	47 (22.17)
(80,1e+02]	2 (4.55)	1 (0.60)	3 (1.42)
Sex			
Female	12 (27.27)	69 (41.07)	81 (38.21)
Male	32 (72.73)	99 (58.93)	131 (61.79)
Ethnicity			
Black	12 (27.27)	35 (20.83)	47 (22.17)
Brown	14 (31.82)	85 (50.60)	99 (46.70)
White	18 (40.91)	48 (28.57)	66 (31.13)
Education			
Ignored	2 (4.55)	3 (1.80)	5 (2.37)
≤5 years	11 (25.00)	53 (31.74)	64 (30.33)
6-8 years	9 (20.45)	39 (23.35)	48 (22.75)
9-11 years	15 (34.09)	52 (31.14)	67 (31.75)
>11 years	7 (15.91)	20 (11.98)	27 (12.80)
Number of admissions in the last year			
0	27 (61.36)	100 (59.52)	127 (59.91)
1	13 (29.55)	52 (30.95)	65 (30.66)
2	2 (4.55)	10 (5.95)	12 (5.66)
3	1 (2.27)	4 (2.38)	5 (2.36)
4	0 (0.00)	2 (1.19)	2 (0.94)
≥5	1 (2.27)	0 (0.00)	1 (0.47)
There was hospitalization in the last 30 days?			
No	38 (86.36)	152 (90.48)	190 (89.62)
Yes	6 (13.64)	16 (9.52)	22 (10.38)
Illegal drugs?			
No	39 (88.64)	144 (85.71)	183 (86.32)
Yes	5 (11.36)	24 (14.29)	29 (13.68)
Intravenous illicit drugs?			
No	44 (100.00)	166 (98.81)	210 (99.06)
Yes	0 (0.00)	2 (1.19)	2 (0.94)

Tobacco use?			
No	32 (72.73)	135 (80.36)	167 (78.77)
Yes	12 (27.27)	31 (18.45)	43 (20.28)
Ignored	0 (0.00)	2 (1.19)	2 (0.94)
Alcohol use?			
No	29 (65.91)	121 (72.02)	150 (70.75)
Yes	15 (34.09)	44 (26.19)	59 (27.83)
Ignored	0 (0.00)	3 (1.79)	3 (1.42)
Comorbidities?			
No	16 (36.36)	24 (14.29)	40 (18.87)
Yes	28 (63.64)	144 (85.71)	172 (81.13)
Chagas disease			
No	44 (100.00)	143 (85.12)	187 (88.21)
Yes	0 (0.00)	25 (14.88)	25 (11.79)
Leishmaniasis			
No	43 (97.73)	167 (99.40)	210 (99.06)
Yes	1 (2.27)	1 (0.60)	2 (0.94)
Paracoccidioidomycosis			
No	44 (100.00)	165 (98.21)	209 (98.58)
Yes	0 (0.00)	3 (1.79)	3 (1.42)
HTLV			
No	41 (93.18)	165 (98.21)	206 (97.17)
Yes	3 (6.82)	3 (1.79)	6 (2.83)
Sporotrichosis			
No	44 (100.00)	164 (97.62)	208 (98.11)
Yes	0 (0.00)	4 (2.38)	4 (1.89)
Tuberculosis			
No	38 (86.36)	143 (85.12)	181 (85.38)
Yes	6 (13.64)	25 (14.88)	31 (14.62)
HIV/AIDS			
No	22 (50.00)	69 (41.07)	91 (42.92)
Yes	22 (50.00)	99 (58.93)	121 (57.08)
Hospitalization outcome			
Death	0 (0.00)	5 (2.98)	5 (2.36)
Discharge	41 (93.18)	138 (82.14)	179 (84.43)
Extended leave	0 (0.00)	2 (1.19)	2 (0.94)
Transfer to another unit	0 (0.00)	13 (7.74)	13 (6.13)
Transfer to ICU	3 (6.82)	10 (5.95)	13 (6.13)
Length of stay (days)			
[0,7]	25 (56.82)	61 (36.75)	86 (40.95)
(7,14]	12 (27.27)	60 (36.14)	72 (34.29)
(14,21]	5 (11.36)	18 (10.84)	23 (10.95)
(21,28]	1 (2.27)	13 (7.83)	14 (6.67)
(28,35]	0 (0.00)	7 (4.22)	7 (3.33)

(35,42]	1 (2.27)	5 (3.01)	6 (2.86)
(42,49]	0 (0.00)	2 (1.20)	2 (0.95)
Length of stay (days) median (IQR)	5.50 (3.00 - 12.25)	10.00 (6.00 - 16.00)	9.00 (5.00 - 15.00)

Most patients had only one incident (45.99%). The incidence PDRI according to week since hospital admission increases the longer the patients' length of stay. The PDRI type with the highest frequency was drug interaction (53.58%), followed by ADR, dose error and dosage error, respectively. The distribution of PDRI was not homogeneous over time, since dilution errors were observed only in the first week, dosage errors decreased over time, while ADR and drugs with duplicated prescription increased over time. For those who had two incidents, the rate was 13.23% and for those who had three incidents, the rate was 6.07%, and in these two cases the incidences also increased with the length of hospital stay. (Table 2)

Table 2: Types of preventable drug related incidents by length of stay.

	Days since hospitalization			
	<7	7 to 14	≥14	Total
Total	94	157	210	461
ADR				
No	91 (96.81)	144 (91.72)	191 (90.95)	426 (92.41)
Yes	3 (3.19)	13 (8.28)	19 (9.05)	35 (7.59)
Drug prescription with interactions?				
No	41 (43.62)	80 (50.96)	93 (44.29)	214 (46.42)
Yes	53 (56.38)	77 (49.04)	117 (55.71)	247 (53.58)
Dose error?				
No	90 (95.74)	142 (90.45)	199 (94.76)	431 (93.49)
Yes	4 (4.26)	15 (9.55)	11 (5.24)	30 (6.51)
Dosage error?				
No	87 (92.55)	148 (94.27)	202 (96.19)	437 (94.79)
Yes	7 (7.45)	9 (5.73)	8 (3.81)	24 (5.21)
Dilution error?				
No	90 (95.74)	157 (100.00)	210 (100.00)	457 (99.13)
Yes	4 (4.26)	0 (0.00)	0 (0.00)	4 (0.87)
Administration route error?				
No	92 (97.87)	156 (99.36)	204 (97.14)	452 (98.05)
Yes	2 (2.13)	1 (0.64)	6 (2.86)	9 (1.95)
Concentration error?				
No	93 (100.00)	156 (99.36)	209 (99.52)	458 (99.57)
Yes	0 (0.00)	1 (0.64)	1 (0.48)	2 (0.43)
Infusion error?				
No	93 (98.94)	157 (100.00)	210 (100.00)	460 (99.78)
Yes	1 (1.06)	0 (0.00)	0 (0.00)	1 (0.22)
Treatment time error?				
No	93 (98.94)	157 (100.00)	209 (100.00)	459 (99.78)
Yes	1 (1.06)	0 (0.00)	0 (0.00)	1 (0.22)
Scheduling error?				
No	83 (88.30)	144 (91.72)	183 (87.14)	410 (88.94)
Yes	11 (11.70)	13 (8.28)	27 (12.86)	51 (11.06)
Indication error?				
No	94 (100.00)	157 (100.00)	208 (99.05)	459 (99.57)
Yes	0 (0.00)	0 (0.00)	2 (0.95)	2 (0.43)

Lack of prescription for any medication?				
No	92 (97.87)	157 (100.00)	209 (100.00)	458 (99.57)
Yes	2 (2.13)	0 (0.00)	0 (0.00)	2 (0.43)
Unnecessary drug prescribed?				
No	92 (97.87)	154 (98.09)	209 (99.52)	455 (98.70)
Yes	2 (2.13)	3 (1.91)	1 (0.48)	6 (1.30)
Infusion time error?				
No	94 (100.00)	157 (100.00)	210 (100.00)	461 (100.00)
Yes	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Vehicle error?				
No	94 (100.00)	157 (100.00)	210 (100.00)	461 (100.00)
Yes	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Drug prescribed in duplicate?				
No	93 (98.94)	151 (96.18)	199 (94.76)	443 (96.10)
Yes	1 (1.06)	6 (3.82)	11 (5.24)	18 (3.90)

The incidence rate in women was only slightly higher than in men. Additionally, the incidence rate was lower among younger participants (18 to 39 years old). When dividing patients by type of infection, we observed a lower PDRI rate in patients with Paracoccidioidomycosis when compared to Chagas disease, HIV/AIDS or Tuberculosis. When the occurrences are separated by type, the highest rate is observed in the group of drug interaction, scheduling error, ADR e dose error, respectively.

Table 3: Incidence rates, overall and by groups of interest, by 100 Person-year.

Variables	Categories	Events	PT	Rate	lower	upper
General		444	8.8	5027	4570.2	5517.1
Sex	Female	182	2.7	6748.8	5803.9	7803.7
	Male	262	4.9	5352.1	4723.6	6041
Age	[18,39]	156	3.4	4621.2	3924.5	5405.9
	(39,60]	194	2.8	7015.7	6063.1	8075.4
	(60,80]	93	1.4	6570.3	5303	8049
	(80, or +]	1	0	2809.6	71.1	15654.2
Comorbidities	No	69	1.2	5727.8	4456.6	7248.9
	Yes	375	6.2	6074	5474.7	6721
Hospitalization in the last 30 days	No	393	6.6	5963.6	5388.5	6583.3
	Yes	51	0.8	6468	4815.8	8504.2
Main infection	Chagas disease	263	4.7	5588.2	4933.2	6306
	Leishmaniasis	35	0.7	5052.9	3519.5	7027.3
	Paracoccidioidomycosis	30	1	3002.1	2025.5	4285.6
	HTLV	59	1.4	4112.5	3130.7	5304.9
	Sporotrichosis	78	1.3	5935.3	4691.6	7407.5
	Tuberculosis	274	4.7	5828.7	5158.9	6561.3
	HIV/AIDS	421	7.8	5372.8	4871.8	5911.4
Types of preventable drug-related incidents	ADR	35	8.8	396.3	276	551.1
	Drug prescription with interactions	253	8.8	2864.5	2522.4	3240.1
	Dose error?	31	8.8	351	238.5	498.2
	Dosage error?	24	8.8	271.7	174.1	404.3
	Dilution error?	4	8.8	45.3	12.3	116
	Administration route error?	9	8.8	101.9	46.6	193.4
	Concentration rate?	3	8.8	34	7	99.3
	Treatment time error?	1	8.8	11.3	0.3	63.1
	Scheduling error?	51	8.8	577.4	429.9	759.2
	Indication error?	2	8.8	22.6	2.7	81.8
	Lack of prescription for any medication?	2	8.8	22.6	2.7	81.8
	Unnecessary drug prescribed?	6	8.8	67.9	24.9	147.9
	Infusion time error?	0	8.8	0	0	41.8
	Vehicle error?	0	8.8	0	0	41.8
	Drug prescribed in duplicate?	22	8.8	249.1	156.1	377.1

Discussion

The main results to be discussed are: (a) The amount of PDRI in infectious disease inpatients is comparable with PDRI in studies with older populations; (b) the PDRI amount appears to be similar in patients who have had recent hospitalizations; (c) the PDRI incidence is similar in groups with or without comorbidities; (d) the number of events increases the longer the hospital stay; (e) Drug interactions, timing and dose errors and adverse reactions were the most frequent PDRI in the sample.

(a) The amount of PDRI in inpatients is comparable with older populations.

The literature points out that incidents occurs in 1 of each 10 inpatients (O'HARA et al., 2018), and the most frequent incidents are drug-related or prescription incidents (BOHOMOL; RAMOS, 2007). In our study, where we only observed drug-related incidents, we observed the incidence in almost 8 out of 10 patients. The literature describes heterogeneous incidence rates of drug incidents, mainly due to the differences in the definitions of incidents and in the methodologies used in the different studies (ROZENFELD; GIORDANI; COELHO, 2013). This makes it difficult to compare results among different studies. Therefore, we sought to compare with studies where the population studied, the type of hospital and location of the study were similar.

A study that analyzed occurrence of ADE in hospitalized patients in federal public hospitals in Rio de Janeiro found a cumulative incidence of 15.6% (ROZENFELD; GIORDANI; COELHO, 2013). In our study, we identified that the incidence rate of PDRI is comparable to those presented in the literature for elderly patients, and when we cut out our studied population for only the elderly, this incidence is even higher. Another interesting finding of our study was that the incidence rate is slightly higher among females, but with no statistically significant difference. This is also a controversial finding in the literature, where we found studies pointing to a higher incidence for males (JOSE; RAO; JIMMY, 2008;

SHAMNA et al., 2014; SOUZA et al., 2018; SUTHAR, J.V.; DESAI, S.V., 2011), and some studies show a higher incidence for females (HUSSAIN et al., 2010; STAVREVA et al., 2008).

To date, we have not observed any other work that specifically assessed PDRI as defined in this study, nor performed in a hospital specialized in infectious diseases. Therefore, it can be difficult to make comparisons regarding the incidence of PDRI with other studies.

(b) The PDRI amount appears to be similar in patients who have had recent hospitalizations.

We would expect patients with a history of recent illness to be more vulnerable to drug incidents due to convalescence, especially ADRs. However, in this study, the incidence of PDRI was similar for those who were not hospitalized in the previous 12 months prior to the patient's participation in the research. Most ADRs are considered preventable, as they are mostly previously known and reported incidents. Unfortunately, there are few studies that correlate ADRs with readmissions. There is little evidence linking ADRs in the first hospitalization with readmissions (DORMANN et al., 2004).

Even with little evidence, we identified a study that hospitalized patients with a diagnosis of pneumonia and who suffered ADR have a higher risk of readmission. Furthermore, when there is a 1-point increase in the readmission rate, the risk of ADR increases by 15% (WANG et al., 2022).

Even with the information from this study, we cannot say that patients admitted to hospitals with high readmission rates have a higher risk of ADE. Information of this type would be interesting, as it would help clinical pharmacists to improve drug safety, prioritizing their intervention in patients who undergo early readmission.

In our study, 40.48% of patients who had PDRI had one or more hospitalizations in the 12 months prior to participating in the research. It is not possible to state that readmissions are related to the incidence of PDRI. Mainly, when we observe readmissions in the 30 days prior to readmission, in which we had 10.38% of patients with readmissions, and among them 9.52% presenting PDRI.

The readmission rate in Brazil, which measures readmissions in the last 30 days, is considered an indicator of hospital quality. That said, the concepts of safety and quality in health services are often confused. To avoid this, we must understand that the quality of a health service has several dimensions such as safe, effective, efficient, patient-focused, timely and equitable care. Thus, it is understood that safety is one of the dimensions of quality (LEE et al., 2019). With this, we can reflect on the proportion of 9.52% of patients with rehospitalization and PDRI in relation to the 79.24% of total patients with PDRI. Our data suggest that even in a hospital with a readmission rate considered satisfactory, and therefore with quality, the action of clinical pharmacists is necessary to reduce PDRI. For these can present themselves in large proportions. Furthermore, our study also suggests, unlike Wang et al (2022)), that the incidence of PDRI is higher in patients who have not had recent previous hospitalizations.

(c) The PDRI incidence is similar in groups with comorbidities.

Individuals with comorbidities have greater frailty in their organ systems. Additionally, the drugs needed to treat the cause of hospitalization are added to the drugs already in use to treat the underlying diseases. We found in the literature studies that attribute multiple comorbidities to the incidence of ADE (SAEDDER et al., 2015; TOSCANO GUZMÁN et al., 2021). This information is not corroborated in this research, which identified similar PDRI incidence among patients with or without comorbidities.

Studies associating comorbidity with patient age, additionally age and comorbidities are also related to higher risk of PDRI in hospitalized patients (PONT et al., 2014). Therefore, age and comorbidities are possible effect modifiers on PDRI incidence rates. This type of note is certainly due to the fact that older patients often have multiple comorbidities, leading to probable drug polytherapy, increasing the chances of PDRI (PARAMESWARAN NAIR et al., 2016).

Another plausible explanation for a higher incidence of PDRI in patients with comorbidities is the possibility of drug-disease interactions, as there may be drug effects on a certain organ system, further harming the organs affected by the comorbidities.

In addition, organic alterations such as cardiac, hepatic and renal dysfunctions can alter the pharmacokinetics of drugs, and even exacerbate their effects. Some studies indicate that such a situation can increase ADR rates, as well as other PDRIs (ONDER et al., 2010).

In this study, the patients who presented HIV/AIDS were the group with the highest of PDRI incidence, followed by patients with tuberculosis and Chagas disease. Additionally, when considering the incidence rates, Sporotrichosis and Leishmaniasis have similar PDRI rates. Therefore, analyzing rates beyond the counts are important to give reasonable interpretations.

Although the literature demonstrate a correlation between comorbidities and drug incidents, some studies do not guarantee this relationship. There examples corroborating similar rates among those with and without comorbidities or with a higher incidence of ADE in individuals without any comorbidity(HOONHOUT et al., 2010).

(d) The number of events increases the longer the hospital stay.

The length of hospital stay has been pointed out as a possible predictor for the incidence of PDRI by some authors (TANGIISURAN et al., 2012). The increased length of hospital stay favors greater use of medications, either due to more doses administered of the same medication, or due to the need to add more medications to their therapy, increasing the probability of an incident occurring.

Establishing a causal correlation between them is not always a possible task, because this correlation is not pointed out in all studies (DORMANN et al., 2004). However, our work identified a considerable increase of PDRI incidence over time of hospitalization.

The longer the hospital stay, the greater the global incidence rate of PDRI, but this fenomena is not homogeneous along different incident types. Drug interactions, ADRs and drugs prescribed in duplicate increase as the length of stay increases. However, this trend is not observed in the other groups of incidents, such as dose error, which was the third type of incident with the highest incidence, and dilution error.

Some studies estimate that a drug incident can add up to 4 more days to hospital stay (SÁNCHEZ MUÑOZ-TORRERO et al., 2010; TANGIISURAN et al., 2012). Other studies have already correlated a stay longer than 12 or 14 days in the hospital as a major risk factor for ADR (CARBONIN; BERNABEI; SGADARI, 1991). What we have in fact is that studies show that there is a correlation between length of stay and PDRI, however, we still lack information on who is the cause of the other.

(e) Drug interactions, scheduling error, adverse reactions and dose error were the most frequent PDRI.

Drug interactions are often preventable, as they are interactions between two or more drugs or drug-food that can lead to harmful effects to patients (ZHENG et al., 2018). Patients using drug polytherapy, often due to comorbidities, are at greater risk of drug interactions (ESPINOSA-BOSCH et al., 2012).

Some studies indicate that between 15 and 45% of hospitalized patients have drug interactions in their prescriptions during hospitalization, and in general this value is around 33% (ESPINOSA-BOSCH et al., 2012; ZHENG et al., 2018). In our study, we observed 53.58% of patients with drug interactions considered serious, and this proportion could be even higher if we considered all interactions in prescriptions.

The value found in our study compares with studies carried out in ICU, which presented higher values, ranging from 46.3% to 90.3% (ZHENG et al., 2018). The rate per 100 patients/year in our study was 2864.5, well above the data in the literature, which indicates between 37 and 106 depending on the analyzed study (ESPINOSA-BOSCH et al., 2012).

Although we make a comparison with the literature, it should be noted that large discrepancies are observed in studies on the subject, since the definitions, as well as the methodologies of the studies, vary greatly. In addition, there are no studies that include health services that exclusively care for patients with infectious diseases for a comparison with our study.

Drug interactions can be considered prescribing errors because, being preventable, they should not be prescribed (ALSHAKRAH; STEINKE; LEWIS,

2019; TULLY, 2012). These errors are considered a subtype of medication error and may be present in 50% of hospital admissions in adults, reaching between 68% and 75% in children (ALANAZI; TULLY; LEWIS, 2016).

Dose errors are among the most common prescription errors (ANZAN et al., 2021; LEWIS et al., 2009; PATEL et al., 2016; SLIGHT et al., 2019), with incidence between 17.4% and 47.3% (PATEL et al., 2016).

Although the literature points to dose error as the most common error, we observed that it was the fourth most frequent PDRI. This difference can probably be explained by the wide variety of definitions and methods used by researchers in the area.

We also found divergent results in the literature regarding the frequency of dose errors during the hospitalization period. The study by Sligth et al (2019) reports that this type of PDRI decreases with length of hospital stay, which was not observed in our study.

Another result that also drew attention was errors in the scheduling of prescription drugs. This type of PDRI was the second most frequent one, with a rate of 577.4 incidents per 100 person-years.

Scheduling error means that one or more doses are being given at the wrong time or not being given. In addition, as drugs can interact when administered at the same time, physicochemical interactions can occur if administered at the same time by the same route. This can often be explained by the standardization of appointment times in health institutions (PALMA SOBRINHO; CAMPOS; SILVA, 2020).

Although we find in the literature notes correlating scheduling error with drug interactions, there are still few studies that can better elucidate how much this actually happens and what impact it has on patients (PEREIRA et al., 2018).

However, as drug interactions and scheduling errors were the PDRIs that most affected patients in our research, it is possible that these two incidents have some sort of correlation. However, as this perspective was not the focus of this work, further studies are necessary to investigate this hypothesis.

An important subgroup of PDRI is preventable ADRs, and some studies point to ADRs as the fifth most common cause of hospital death in Europe (MONTANÉ; CASTELLS, 2021). Recent studies indicate that ADRs can occur between 1.6%

and 41.4% of hospitalized patients (BOUVY; DE BRUIN; KOOPMANSCHAP, 2015).

In our study, we identified that ADRs were the third PDRI that most affected patients admitted to the ward. We observed a rate of 396.3 incidents per 100 patients/year, representing 7.59%. Our study also identified that ADRs increased considerably the longer the hospital stay was.

A 2018 Brazilian study identified AE incidence of 16.2% in hospitalized patients (RIBEIRO et al., 2018). Recent studies point to an incidence ranging from 11% to 31% only for serious ADR (KHALILI et al., 2011). However, none of these studies showed the incidence in health services specialized in infectious diseases.

AE rates were generally quite high. Among the characteristics of the population studied were the presence of comorbidities, indicating the use of more medications; as well as the age group most affected was that of non-elderly adults, with a higher proportion of patients seen, suggesting that the work of the clinical pharmacist can be quite arduous.

With a high incidence of PDRI, clinical pharmacists will need more interventions to ensure greater safety of drug therapy. Our results show that the most common types of incidents come from medical prescriptions such as interactions and dose errors, from medication scheduling performed by nurses.

The greater the number of incidents, the greater the work of clinical pharmacists. However, it is necessary to evaluate the characteristics of these incidents, whether potential or real, as well as their severity and degree of risk for patients, which was not the objective of this study, in order to better interpret how much this high incidence of PDRI can influence the workload of clinical pharmacists.

What is new and Conclusion

Health service specialized in infectious diseases has peculiarities in relation to PDRI, when compared with studies carried out in hospitals that serve other specialties. We found that the incidence rate was 79.24%, similar to the rates of older populations.

The main types of PDRI are drug interactions, scheduling errors, ADR and dose errors, the length of hospital stay increases the incidence of PDRI and that previous hospitalizations do not seem to influence the incidence of PDRI subsequent hospitalizations.

As the incident rate is quite high and the types of incidents vary in origin, as well as incidents occurring in the older age group of patients, the work of clinical pharmacists must be quite extensive.

As we believe that the incidence of PDRI influences the amount of work performed by clinical pharmacists, and as the various studies in this area demonstrate that, in general, there are few pharmacists for the amount of clinical services, it is necessary that new studies be carried out, in an attempt to elucidate the characteristics of these incidents, as well as whether there is a need to develop a tool for prioritizing patient care by clinical pharmacists according to the risk of PDRI.

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5.2 Artigo 2

Frequency and classification of drug-related incidents in an infectious disease ward of a high-complexity hospital

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Data availability statement

The data used and/or analyzed during the study are available from the corresponding author on reasonable request.

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Conflict of interest disclosure

The authors declare no conflict of interests.

Ethics approval statement

All measures of protection and confidentiality of the participants were taken, based on the good clinical practice standards from Document of the Americas, and National Health Council regulatory standards for research with human beings contained in the Resolution No. 466/ December 2012. The project was approved in the ethics national system for research with human beings (https://plataformabrasil.saude.gov.br/login.jsf) with the number.

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Patient consent statement
Not applicable.

Permission to reproduce material from other sources
Not applicable.

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Abstract

Introduction: Patient safety is defined by Brazilian legislation as the reduction of risks of unnecessary harm. Interventions in clinical pharmacy reduce the risk of drug harm during hospitalization. Thus, assessing the magnitude and types of drug-related incidents preventable by clinical pharmacy intervention (PDRI) is a good strategy to quantify the need for time and personnel to carry out pharmaceutical care. **Method:** This is an observational follow-up study, in which patients with infectious diseases admitted to the ward of the Instituto Nacional de Infectologia Evandro Chagas were consecutively included. PDRIs with a potential of medium to very high severity (i.e., clinically significant prescription errors and avoidable adverse drug reactions (ADR) were the outcome. The PDRI were classified according to severity and probability, receiving a numerical gradation for each of these variables. Subsequently, they were classified according to the risk level, through the multiplication product between the severity value and the probability value. Thus, a risk score was obtained for each PDRI. **Results and Discussion:** Were included 212 patients, among which 168 presented PDRI. Were observed 494 incidents, with a frequency of 1.7 incidents per prescription. The most frequent incidents were drug interactions, scheduling error, ADR, duplicity and dose error. **Conclusion:** The frequency of PDRI requiring clinical pharmacist interventions among patients with infectious diseases is very high. It is necessary that pharmaceutical services are rationalized, e.g., through the development of instruments to predict PDRI, since this high demand is not accompanied by an increase in the number of clinical pharmacists.

Keywords: Clinical pharmacy service, Drug-related side effects and adverse reactions, Incidence Rates, Infectious Disease.

Introduction

Patient safety is the reduction of the risks of unnecessary harm associated with health care to acceptable minimum (BRAZIL, 2013). The perspective of “minimum acceptable” corresponds to what is possible, regarding the knowledge and resources available compared to the risk of an alternative treatment or even no treatment (WORLD HEALTH ORGANIZATION; SAFETY, 2010).

Incidents in health services are defined by Brazilian legislation as an event or circumstance causing unnecessary actual or potential damage to the patient. Therefore, they include Adverse Events (AE), which are incidents that affect patients and cause harm; and “near misses”, which are circumstances with potential harm to patients (BRASIL B, 2013). Usually, the scientific literature defines AE as a complication or damage to the patient, unintentionally caused by a clinical intervention and not by the progress of a disease. (DE VRIES et al., 2008). When incidents result from failures, they are considered preventable (POSSOLI et al., 2021). Preventable incidents are those that would not occur if health care had taken place in accordance with the recommendations of good operational practices (BRASIL B, 2013) for the patient's health needs (MICHEL, 2004).

In the literature, were observed different definitions for different types of incidents. Therefore, drug-related problems (DRPs) are a broad category and encompass all drug-related incidents (DRIs), including near misses; Medication Errors (ME), - as any preventable event that, in fact or potentially, may lead to inappropriate medication use when compared to established and accepted clinical practices (DEAN, 2000; FERRACINI; FILHO, 2010) - Adverse Drug Events (ADE) - any undesirable clinical occurrence that occurs during drug treatment, but which may not have a causal relationship with the treatment - and Adverse Drug Reaction (ADRs) - an “undesirable and unintentional drug response that occurs on treatment at commonly used doses (WHO, 2002). It is estimated that more than half of prescribed drugs have some inadequacy, which can lead to incidents and harm to patients (WORLD HEALTH ORGANIZATION, 2009).

It is essential to ensure good outcomes during health care, but this becomes increasingly challenging with increasing complexity in hospital care (POSSOLI et al., 2021). One good example is pharmacotherapy, one of the most common

health interventions, often difficult to manage (KRÄHENBÜHL-MELCHER et al., 2007). Drug incidents are important preventable factors that jeopardize patient's safety (WHO, 2017). Therefore, for pharmacotherapy to be safe in hospitals, the care process needs to be well planned and with initiatives for safe medication practices (SCHEPEL et al., 2019).

Clinical pharmacy is an area of pharmaceutical activity, started in the 1960s in the United States of America, that follows the philosophy of pharmaceutical care, concerned with the appropriate use of medicines (KORAYEM et al., 2021; SCHEPEL et al., 2019).

In this area, pharmacists assume responsibility for managing safe medication practices (SCHEPEL et al., 2019), improving results through practices of identification, prevention and resolution of drug-related problems (DRP) (VAN DER LINDEN et al., 2020)

Clinical pharmacist services complement multiprofessional health teams and optimize drug therapy (MORGAN et al., 2018), as they act as specialists in medicines and evidence-based care in healthcare teams (TALON et al., 2020). To ensure the appropriate use of medications, promoting patient safety, clinical pharmacists have a strategic position and have been shown to improve prescribing practices, preventing adverse drug events, reducing medication errors, costs, length of stay, and reducing mortality (PENM et al., 2015).

A very wide variety of drug-related incidents preventable by clinical pharmacy interventions (PDRI) can occur in hospitalized patients with infectious diseases due to the variety of drugs used for these patients, as well as the increasing number of people affected by these diseases, the emergence of new diseases and the presence of several comorbidities. The consequences of these PDRI can be pronounced in the reduction of quality of life, increased length of hospital stay, increased health costs and even increased morbidity and mortality of patients (PENM et al., 2015).

There are more deaths caused by inadequate drug therapy than caused by breast cancer, acquired immunodeficiency syndrome and traffic accidents (INSTITUTE OF MEDICINE, 2000). Incidents with medication occur frequently and their probability increases according to the complexity of the treatment (GRAF et al., 2005).

Identification of PDRI and pharmaceutical intervention are essential to reduce their consequences on patients' lives (AYALEW; MEGERSA; MENGISTU, 2015). In an ideal model, each hospital should have the necessary resources to provide clinical pharmaceutical services to each patient, based on their needs (LEWIS, 2017; SUGGETT; MARRIOTT, 2016). However, clinical pharmaceutical intervention not available to all seem to be an universal issue (ALSHAKRAH; STEINKE; LEWIS, 2019; NHS ENGLAND, 2013)

The literature points out that clinical pharmaceutical services incorporate a wide range of activities (PENM et al., 2015) and that lack of time and staff are barriers to making them available to all hospitalized patients (AWAD; AL-EBRAHIM, 2006). Patients with infectious diseases have specificities, especially those with chronic conditions, that make the use of multiple medications a common practice. Therefore, assessing the magnitude and types and outcomes of PDRI is a good strategy to rationalize clinical pharmaceutical care. This research aims to quantify, describe and classify PDRI in hospitalized patients in an infectious disease ward, since these data are scarce in the literature, so that it is possible to subsidize the discussion of the need to rationalize pharmaceutical clinical care.

Methods

This is an observational follow-up study. Patients with infectious diseases admitted to the ward of the Evandro Chagas National Institute of Infectious Diseases (INI) from 06/13/2019 to 08/13/2020 were consecutively included. INI is located at Rio de Janeiro/Brazil, and is characterized as a high-complexity, federal public and tertiary hospital, specialized in the care of patients with infectious diseases. During the study period, it had 22 ward beds and 4 intensive care unit (ICU) beds, with an average annual hospitalization rate of approximately 575 patients.

To be included in the study, the participant had to be hospitalized in the ward during the inclusion period, be 18 years of age or older, could not have received care from the clinical pharmacist and consent to participate. Exclusion criteria were: length of stay less than 24 hours; prescription without medication in the first 48 hours of hospitalization; admission directly to the ICU; patients transferred

from the ICU to the ward. Patients who were admitted to the ward and then transferred to the ICU were discontinued from the study.

The outcome of this study was PDRI with potential of medium to very high severity, comprising clinically significant incidents related to the prescription of medications and avoidable ADR.

The following incidents were included as prescription errors: prescription of drugs with interactions (either major or moderate interaction, according to drugs.com), dose error, dosage error, dilution error, administration route error, concentration error, infusion error, treatment time error, scheduling error, indication, lack of medication prescription, infusion time error, vehicle error, in addition to prescription duplication, including those identified (corrected or not) by the hospital pharmacy professional.

Risk analysis of PDRIs consisted of assessing severity, which was established by defining the effects of incidents on patients (Table 1) and assessing the probability of occurrence of each incident (Table 2). A risk matrix (Chart 1) combining the severity and probability of PDRI allowed categories for risk levels to be established. A severity versus probability matrix is a means of combining qualitative or semi-quantitative rankings of consequences and probabilities to produce a risk level or risk score. The risk level is then established as a function of the matrix. The multiplication product obtained between the probability and severity values defined the level of inherent risk, which is the level of risk without considering the barriers that reduce or may reduce the probability of its occurrence or its severity. The risk level (Chart 2) defined by the matrix is associated with a decision rule, which determines how to treat or not treat the risk (BRAZIL, 2018; BRAZILIAN ASSOCIATION OF TECHNICAL STANDARDS, 2012). It is through the analysis of this value that the Patient Safety Center (NSP – Núcleo de Segurança do Paciente), of the health service where the research took place, prioritizes corrective actions for the identified incidents.

CATEGORY	Value	DEFINITION
Severe	5	Death or permanent or severe loss of function that is related to the health care process and differs from the expected outcome
Major	4	Severe temporary loss of function that is related to the health care process and differs from the expected outcome
Moderate	3	Major loss Temporary or moderate permanent loss of function that is related to the health care process and differs from the expected outcome
Minor	2	Moderate temporary loss or minor permanent loss of function that is related to the health care process and differs from the expected outcome
Minimal	1	Small temporary loss of function that is related to the health care process and differs from the expected outcome

Table 0 1: Classification of Assistance Adverse Events according to severity (adapted from Severity Assessment Code (SAC) rating and triage tool for adverse event reporting) (NEW ZEALAND, 2017).

CATEGORY	Value	DEFINITION
Very high	5	Almost certain to occur at least once in next three months, greater than 95% chance
High	4	Will probably occur at least once in the next four-12 months, 66 – 95%
Moderate	3	Is expected to occur within the next one to two Years, between 26 – 65% chance
Low	2	Event may occur at some time in the next two to five Years, between 5 – 25% chance
Very Low	1	Unlikely to recur – may occur only in exceptional circumstances, *i.e.* >five Years, less than 5% chance

Table 0 2: Classification of Assistance Adverse Events according to Probability (adapted from Severity Assessment Code (SAC) rating and triage tool for adverse event reporting) (NEW ZEALAND, 2017).

		Probability				
		Very Low	Low	Moderate	High	Very high
Severity	Minimal	1	2	3	4	5
	Minor	2	4	6	8	10
	Moderate	3	6	9	12	15
	Major	4	8	12	16	20
	Severe	5	10	15	20	25

Chart 1: Risk Matrix severity x probability, adapted (BRAZILIAN ASSOCIATION OF TECHNICAL STANDARDS, 2012). Risk Level Score: 1 -5 low or very low; 6 – 9 medium; 10 – 15 high and 16 – 25 very high.

The Naranjo Algorithm (Table 3) was used as a causal classification tool for suspected ADR events (NARANJO et al., 1981).

Issues	**Yes**	**No**	**Unknown**
1. Are there conclusive notifications about this reaction?	**+1**	**0**	**0**
2. Did the reaction appear after the administration of the drug?	**+2**	**-1**	**0**
3. Did the reaction improve when the drug was suspended?	**+1**	**0**	**0**
4. Did the reaction reappear when it was re-administrated?	**+2**	**-1**	**0**
5. Are there alternative causes (even another drug)?	**-1**	**+2**	**0**
6. Does the reaction reappear with the introduction of a placebo?	**-1**	**+1**	**0**
7. Is plasma concentration at a toxic level?	**+1**	**0**	**0**
8. Has the reaction increased at a higher dose or reduced with a lower dose?	**1**	**0**	**0**
9. Has the patient experienced such a reaction previously with medicine of the same drug?	**+1**	**0**	**0**
10. Has the reaction been confirmed by any objective evidence?	**+1**	**0**	**0**
			Total =

Table 0 3: Causality Questionnaire of Naranjo.

After using the Naranjo questionnaire, where each question receives a score and at the end the sum of the points is obtained, suspected ADRs were classified according to the overall score of the questionnaire. Suspected ADRs that received zero or negative scores were classified as doubtful, those that received 1 - 4 points were classified as possible, those that received that received 5 - 8 points were classified as probable and those that received 9 or more points were classified as definite.

The Medical Dictionary for Regulatory Activities (MedDRA) was used in this work to make ADRs uniform identification (BROWN; WOOD; WOOD, 1999). MedDRA is based on terminology owned by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and was developed to address the need for standardized medical terminology. The adoption of this unique terminology facilitates communication and understanding between different actors, including research organizations. Drug interactions were classified according to the Drugs.com database. In this work, only those considered major were used.

Patient data were collected from prescriptions and the patient's electronic medical record. Following the same logic of pharmaco-surveillance of verification and capture of incomplete data in the records regarding the event of interest, the multi-professional team and the patient himself were also consulted. Records and reports from the team were considered sources of data regarding the events of interest to the participant.

Data were collected by a group of four junior pharmacists. Collection began on the first day of hospitalization or on the first working day after admission, with the signing of the free and informed consent form, followed by the collection of information such as personal data and data from the first prescription. Subsequent collections took place every seven calendar days after hospitalization, by checking the patients' medical records (prescriptions, laboratory tests and multidisciplinary clinical evolution reports) to identify PDRI that occurred during this period. This procedure was repeated every seven days until the patient was discharged or transferred. If the patient was discharged or transferred before completing one of the seven-day periods, the days between the last collection and the patient's departure from the ward were also analyzed.

All data collected was typed and stored in the RedCap program. After entering the data into RedCap, a senior pharmacist checked, confirmed or adjusted the

data and assigned classifications, as the investigation was eminently observational, and there was no proposal for a systematized intervention by the assistance to avoid these incidents.

Results

This study evaluated 212 patients (Figure 1), among which 168 (79%) had PDRI. Were observed 494 incidents, with a frequency of 1.7 incidents per prescription and 3.0 incidents per patient. These prescriptions had an average of 9.0 (± 4.0) drugs.

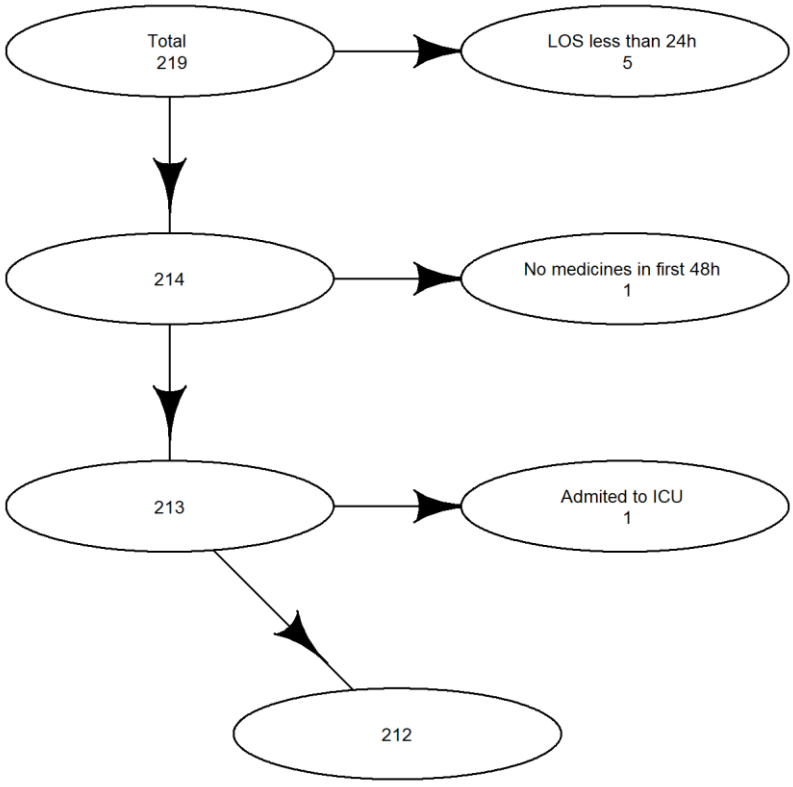

Figura 1: Inclusion and exclusion flow diagram.

There was a variety of PDRI, and more than half of them were drug interactions, followed by scheduling error, ADR and dose error (Table 4). During the PDRI period, there were no errors of infusion time and vehicle error used to dilute the medicinal product.

Frequency of types of PDRI		
PDRI	**N**	**(%)**
Duplicity	22	4.5
Scheduling error	55	11.1
Concentration error	5	1.0
Dilution error	4	0.8
Dose error	29	5.9
Indication error	6	1.2
Posology error	21	4.3
Treatment time error	2	0.4
Administration route error	10	2.0
Lack of prescription of medication	1	0.2
Drug interaction	293	59.3
ADR	46	9.3
Total	494	100

Table 0 4: Absolute counts and frequencies of PDRI types.

Regarding the severity of PDRI, the vast majority of incidents in patients with infectious diseases were severe (Table 5), with a frequency of 1.16 severe PDRI per prescription. Regarding the classification by the probability of occurrence of PDRI, more than half received the moderate classification (table 6). Regarding the classification of the degree of risk, the majority of the PDRI risk level was high, due to initial severity of classification distribution (Table 7).

Proportion of PDRI severity ratings		
Severity	**N**	**%**
Severe	340	68.8
Major	22	4.5
Moderate	132	26.7
Minor	0	0.0
Minimal	0	0.0
Total	494	100

Table 0 5: PDRI Classification for Severity.

Proportion of PDRI probability ratings		
Probability	**N**	**(%)**
Very low	71	14.4
Low	130	26.3
Moderate	293	59.3
Higth	0	0.0
Very high	0	0.0
Total	494	100

Table 0 6: PDRI Classification for Probability.

PDRI Risk Level		
RL	N	(%)
Low or very low	76	15.4
Medium	82	16.6
High	336	68.0
Very high	0	0.0
Total	494	100

Table 0 7: Incidents classification for Risk Level (severity x probability).

The ADRs were still classified by causality and distributed by the MedDRA classification. The Classification by MedDRA showed that patients have ADR of various types (Table 8), with more than half of them classified as probable caused by drug (Table 9).

MedDRA classification for ADR		
MedDRA	**N**	**%**
Fever by drug effect	6	13.04
Drug-induced kidney injury	4	8.70
Nausea	5	10.87
General disturbances and changes in the place of administration	4	8.70
Vomit	5	10.87
Neurological reaction	9	19.57
Other	13	28.26
Total	46	100

Table 0 8: Classification of PDRI for Medical Dictionary for Regulatory Activities.

ADR ratio by Naranjo classification		
Causality	**N**	**%**
Definite	0	0
Probable	26	56.5
Possible	18	39.2
Dubious	2	4.3
Total	46	100

Table 0 9: Classification of PDRI for Medical Dictionary for Regulatory Activities.

Discussion

The main results to be discussed are: (a) the frequency of PDRI in an infectious disease ward is high; (b) the classification of risk level of PDRI in an infectious disease ward was high (c) The most common prescription errors were drug interactions and drug scheduling.

This study demonstrated that patients with infectious diseases had a high number of incidents, affecting more than two thirds of the studied population. However, this study was restricted to severe or clinically relevant PDRI and therefore the number of medication incidents may have been even higher.

This study corroborates the work of Cano and Rozenfeld (2009), which states that the use of medication during hospitalization causes incidents, many of which are preventable. The high number of incidents in the serious or clinically relevant category requires reflection on the balance of strategic importance of drug therapy and on the risks inherent in its use.

When looking at the frequency of incidents per patient, this study obtained a result of 2.9 PDRI/patient. This result is practically twice that reported in a 2016 literature review, in which a variation between 1.0 and 1.5 PDRI/patient was observed (ROUGHEAD; SEMPLE; ROSENFELD, 2016). However, in the studies analyzed in this review, drug interactions were not addressed. This may explain the differences in the findings, since drug interactions ware the most frequent PDRI in this study, comprising more than half of the PDRI observed.

Another possible explanation, which corroborates the findings of this study, is that, according to the same review, manual prescriptions favor an increase in these incidents. In INI, although drug prescriptions were done in an electronic medical software, some medications were selected from a prespecified list in

software, some were typed by prescribers in an open field, and some were later added by handwriting after the prescription was printed. Therefore, there are many similarities with manual prescriptions.

Such a high frequency of serious and clinically relevant PDRI should make pharmaceutical intervention a priority area, to guarantee the quality and safety of patients in relation to pharmacotherapy. However, the frequency of these PDRI differs greatly in studies published on this topic. This is probably due to the different methodologies used, as well as the definitions they use.

Alsulami, Conroy and Choonara (2013), report that only 17.5% of the studies included in their review contained a definition of analyzed incidents that we can compare with PDRI, such as incorrect indication, dose and posology error, in addition to administration route error. However, they add inadequate instruction about the drug and error in the pharmaceutical form. The remaining reports did not even establish a clear definition for these types of incidents. The same authors also reported a wide variety of methodologies used in the evaluated studies, such as retrospective and prospective studies and the use of different questionnaires. Therefore, the results are difficult to compare.

Risk levels (probability x severity) are managed to reach acceptable levels, as determined by Brazilian legislation. In this report, were observed a high probability of occurrence of IRPD in the institution (79%), most of them being severe, thus obtaining a high to very high degree of risk, when multiplying the probability of PDRI in the institution by the values of the severities. Therefore, it is reasonable that the entity responsible for risk management in the health institution insert a safety barrier in the ward to minimize the risk of suffering some type of PDRI in the studied population. However, this classification of risk management in patient safety would make all patients in the ward studied pass through the safety barrier, such as follow-up by a clinical pharmacist. This contrasts with the need to streamline clinical pharmaceutical services.

To escape this generalization, one can try to classify the risk individually, so that each prescription has its risk score, and the clinical pharmacist can decide who to prioritize. Even if risk levels were individualized, were obtained 73.3%. of prescriptions with a very high score and 26.7% with a high score, multiplying the probability of a patient having at least one PDRI by the severity of each incident. This raises questions such as which patients or prescriptions within that score

range should be prioritized and how many practitioners are reasonable for that workload. Thus, the ideal would be to have an instrument that assesses the level of risk using the probability of occurrence of PDRI in the patient and not in the institution, so that one could better discriminate, among the population served, those with a higher degree of risk.

The characterization of PDRI in this study can help health managers to understand the magnitude of this problem in the safety of patients with infectious diseases, as well as to evaluate the possibilities of strategies to combat this type of problem.

The most frequently observed PDRIs in this study were drug interactions. It is comparable to similar studies from different countries that report this type of incident as the main one among PDRIs (ABBASINAZARI et al., 2013; KOH; KUTTY; LI, 2005). This study found that more than half of serious or clinically relevant PDRIs is moderate or major drug interactions. This type of PDRI is a permanent risk in health services and always requires investigation(SEHN et al., 2003)OBJ.

Drug interactions can occur via pharmacokinetics or pharmacodynamics. In both cases, patients may have signs or symptoms that can be mistaken for a disease or a clinical condition other than PDRI. Thus, clinical pharmacists need to be prepared to make this differentiation, with knowledge regarding pathological processes, therapeutics and pharmacology.

Many cases of serious drug interactions occur in the treatment of infectious diseases, as in cases of interactions between drugs used to treat HIV and tuberculosis. The therapy for these diseases is established by programs and protocols developed by the Ministry of Health in Brazil, and the concomitant use of many of these drugs are indicated as major or serious interactions by many computerized and online systems.

The literature points out that computerized programs for detecting drug interactions can be more efficient than clinical pharmacists for this purpose (RAVN-NIELSEN et al., 2018). However, these programs end up detecting many interactions that are irrelevant, or even unavoidable, for the treatment of patients with infectious diseases.

The simple evaluation of the prescription, without the knowledge regarding clinical protocols, can favor errors in the intervention, as there may be interactions

between drugs established in clinical protocols, which should not be changed. This study considered this type of interaction, and reinforces that the follow-up of patients in this situation should be carried out by clinical pharmacists, since these interactions can cause severe ADE.

The second class of PDRI that was most identified in this study was the scheduling error. Scheduling is an activity that is often performed automatically in electronic medical records with pre-established times. These schedules are often determined by routine or organizational culture and follow the dosage of each prescribed medication. Traditionally, nurses are responsible for this task, who is usually also responsible for organizing and avoiding failures in the planning of drug therapy (ANJOS et al., 2020). However, in either case, the scheduling of drug administration is usually set at pre-established times, with little concern with each patient specific need (AMORIM et al., 2014).

Scheduling error can lead to several problems in drug therapy. Errors such as scheduling at intervals of hours different from those recommended are quite common and may affect the plasmatic concentration of the drugs. This can lead to plasma levels outside the therapeutic window, leading to toxic doses or underdoses. Consequently, scheduling errors may lead to ADE or therapeutic failure.

Another consequence of the scheduling error is the favoring of drug interactions. Since medications with indication of intervals between equal doses can be scheduled at standardized times, medications that could not be administered at the same time end up being administered, which can also lead to severe PDRI.

It is not rare that mid-level nursing professionals are assigned to schedule drug prescriptions (SANTOS et al., 2020). This may explain the large number of scheduling errors, as this professional training does not include pharmacology discipline. It is difficult for these professionals to perceive some types of mistakes in scheduling, such as the aforementioned drug interactions.

In addition to the previous explanation, Clendon and Gibbons (2015) also associate this type of incident with the type of work shifts performed by the nursing team, not excluding fatigue, stress, combination of skills or shift practices established by the routine of the health service.

The high frequency of ADR may be linked to the high number of drugs used by patients with infectious diseases, as observed in this study, as well as the types

of drugs used, such as sulfa drugs, amphotericins, antiretrovirals, among others known causes of ADR in the literature (CHABY et al., 2018; LIN et al., 2014; NAGARAJAN; WHITAKER, 2018).

There is a very large variety of types of ADRs. However, gastric effects stand out when ADRs were analyzed by affected site or system. The vast majority of ADRs such as fevers, tremors, chills, nausea and vomiting could have been avoided, as they are known reactions related to drug administration. An example of this is the use of amphotericin B, which has great potential for adverse reactions associated with drug administration which can be prevented by means of increasing dilution and infusion time, and the use of pre- and post-infusion hydration with 500ml saline, if clinically possible.

In Brazil, many drugs distributed by the Unified Health System (SUS in its acronym in Portuguese, is one of the largest and most complex public health systems in the world, which guarantees everyone in Brazil, whether citizens or not, full, universal, and free access to all health needs in health) follow the determination of protocols of the Ministry of Health. And in the case of amphotericins, the Government authorizes the dispensation only of the deoxycholate formulation, which is the amphotericin formulation with the greatest toxicity, for patients with HIV/AIDS, which is the largest group treated with amphotericin.

In this report it was also observed a considerable frequency of medication dose errors. This is a very worrying type of PDRI, since prescription of wrong doses of medication can cause therapeutic inefficiency, when underdoses are prescribed, and may lead to serious incidents or even death, when the prescription is above the maximum allowed daily dose.

When many resident physicians assume the role of prescribing medication there more opportunities for these dose errors. Many resident physicians are newly graduated and end up adopting standard doses established by the drug literature or by the organizational culture in which they are inserted (ASHCROFT et al., 2015).

These PDRIs can be influenced by the fact that many patients use medications that require dose adjustment during hospitalization, such as antibiotics and oral anticoagulants. They may also be related to the significant number of ADRs such

as drug-induced kidney injury, which generate the need for adjustments in drug doses and this was not observed by prescribers.

Prescription duplicity is a type of PDRI that occurs frequently in hospitals, and is not only committed by newly trained prescribers, although this is generally assumed. A study by Ashcroft et al (2015) found that newly graduated physicians, especially in the first year after graduation, are twice as likely to prescribe drugs twice than senior physicians. However, the rates are similar when it comes to the duplicity of drugs capable of causing serious incidents.

The literature also informs that this type of occurrence is more frequent when several doctors attend the same patient, or when this patient changes the place of care (CHENG; CHEN, 2014). This is an opportunity for medication reconciliation by clinical pharmacists. The lack of adequate collaboration and effective communication are also identified as causing this type of PDRI (FARZI et al., 2017).

In this study, it was observed that the causes mentioned above (CHENG; CHEN, 2014; FARZI et al., 2017) were present most of the time. Many of the prescriptions were made by first-year residents and also by the medical staff responsible for his/her supervision. In addition, it was common in the hospital routine that the emergency care to patients admitted to the ward to be performed by residents on duty, who were not necessarily the ones who accompanied the patient later on. In addition, in many cases it is necessary the evaluation by a physician whose specialty is other than infectious diseases, and who only sees patients on demand. In this way, a variety of physicians could attend to the same patient during hospitalization, resulting in prescriptions with additions or even new prescriptions with duplicate medication.

As the ward did not have a clinical pharmacist, adequate interprofessional interaction to discuss the prescription was not a routine activity either. In the hospital there was also no routine or effective communication protocol to serve as a barrier in this type of incident. One of the limitations is that it cannot be attributed to the change of location or the lack of medication reconciliation, since transferred patients were not followed up by this study.

The dosage error was also a PDRI with considerable expression in this study. The frequency at which drug doses should be administered directly impact the expected result of drug therapy. Efficacy, safety and quality of treatment depends

on a good prescription of drugs, and patient safety can be compromised by flaws in the dosage of drugs.

A prescription without a correct dosage, or even without dosage specification, impacts on the activities of dispensing and administering medications. In cases of absence of the dosage of the prescribed medication, it may even make it unfeasible to dispense the medication by the pharmacy service.

The intervals between administered doses of drugs are related to pharmacokinetic and pharmacodynamic characteristics and must be strictly followed to avoid negative results related to drugs (MIASSO et al., 2006). Dosage is important data in a prescription, as it is considered a mandatory technical data for the preparation and dispensing of medicines, and in cases of unfeasibility of dispensing, both the expectations of the prescriber and the patient are frustrated (GUZATTO; BUENO, 2007).

Several situations can explain this type of PDRI, such as lack of prescription protocols, lack of knowledge/experience on the part of the prescriber, lack of adequacy of the prescribing practice and even inadequate electronic prescription systems.

A possible explanation for this percentage of dosage errors was that the electronic prescription system was undergoing changes during the research data collection period, where a part of the prescription, such as the name of the drug, presentation, was filled through a selection of pre-established items, and other information, such as dosage, had to be entered in an open field for typing. In addition, the physician resident lack of experience may have favored these errors.

The clinical pharmacist can avoid negative results associated with pharmacotherapy (MIRANDA et al., 2012), as many of these are considered preventable. The practices performed by pharmacists and their critical role in ensuring the safety and management of drug therapy have long been recognized. Since the pharmacist-physician relationship is a necessity in the care process, it improves the expected results of pharmacotherapy (ROTTA et al., 2015).

Still on the clinical care performed by pharmacists, their interventions reduce length of stay and readmissions, improve the control of biomarkers and reduce events related to diseases such as heart failure and thromboembolism (GUIGNARD et al., 2015). Wubben and Vivian (2008) describe that the actions

of clinical pharmacists are more effective when they have autonomy over actions in the prescription of medicines.

Much evidence suggests that specific actions by clinical pharmacists reduce and correct the consequences of PDRIs. Thorough evaluation of prescribed medications is essential for an assessment of drug interactions. This clinical assessment of the prescription involves evaluating the prescribed drugs and their doses, as many of the pharmacodynamic interactions are dose-dependent. In addition, the evaluation of other parameters such as dosage, scheduling, route of administration, pharmaceutical form, in addition to the site of administration and its conditions are essential for the evaluation of pharmacokinetic interactions and physicochemical interactions.

Corrective actions will be as effective as adherence to interventions carried out by pharmacists. Among these interventions are the indication of medication substitution, dose adjustment, alteration of the pharmaceutical form, change of schedule and change of administration site. These actions are often not under the governance of clinical pharmacists, and therefore need the acceptance of medical and nursing professionals to occur. Clinical pharmacists should have autonomy over scheduling, especially in the electronic medical records environment, as they can make the necessary changes, considering the specificities of each drug and patient.

Another action with robust evidence of its effectiveness on prevention of PDRIs, such as duplicity and/or absence of prescribed medication, is conciliation and reconciliation (RAVN-NIELSEN et al., 2018) In the case of known ADRs, they can be avoided by replacing the drug with another one with less potential for this type of incident. The clinical performance of the pharmacist together with the prescriber can favor these substitutions, reducing the probability of the appearance of this PDRI.

Many ADRs described in the literature are associated with drug administration, such as tremors, chills, fever, nausea, and vomiting (GALLELLI et al., 2017). Therefore, they are also subject to pharmaceutical intervention. A work of continuing education, carried out by clinical pharmacists, to the medical and nursing staff can reduce failures in the prescription and administration of medications that lead to ADR associated with medication administration.

In these cases of ADR, clinical pharmacists must evaluate and guide the medical team regarding the prescription of the most appropriate doses for each specific patient, the appropriate diluent for each medication, as well as the final concentration of the medication solution to be infused. In addition, it is also necessary to guide the nursing team regarding the programming of time and speed of drug infusion, the appropriate concentration per mL/h infused according to the type of venous access of the patient, the need to homogenize some drug solutions again, among other guidelines.

Additional actions are performed by clinical pharmacists such as evaluating the indication for treatment, analyzing prescribed doses and correlation with renal failure, weight and age of patients, identifying adverse drug events, therapeutic duplicity, evaluating time and interval between doses, drug formulation and presentation, contraindications, precautions and specific characteristics of the patient, and assessing the efficacy, safety, necessity, and quality of pharmacological therapy.

The evidence that clinical pharmacists have a fundamental role in promoting the appropriate use of medicines is unquestionable (BOSMA et al., 2007; LOURO; ROMANO-LIEBER; RIBEIRO, 2007), reaching high rates of interception of PDRI (ABDEL-QADER et al., 2010; ALJADHEY et al., 2016). However, health services have a constant increase in demand, which is not followed by an increase in the number of clinical pharmacists to meet this need (RODRIGUES, 2017).

The growing demand for clinical pharmacists to care for patients with infectious and parasitic diseases is due to the reemergence of these types of diseases, as well as the emergence of new diseases in this area, leading to greater use of drugs, which are sometimes experimental. This growing demand is not always accompanied by the allocation of pharmacists to perform clinical services.

In order to carry out clinical activities, pharmacists need to visit the wards, interview patients and the multidisciplinary health team, analyze medical records (prescriptions, administered doses or lack thereof, laboratory tests, clinical evolution, conducts and procedures performed), evaluate the general condition of the patient, evaluate the result of pharmacotherapy and even discuss these results with the other members of the health team (LIMA-JUNIOR; FREIRE, 2007).

It is imperative that strategies for the reduction of PDRIs be adopted in health services, especially those that care for infectious diseases, due to the high frequency of these incidents. And in recent years, the pharmaceutical profession has been shaping itself to meet and be part of the strategies that guarantee successful results in patient care (BOND; RAEHL; PATRY, 2004; MURRAY et al., 2009).

Despite this transformation of the profession, the demand for pharmaceutical care continues to grow, significantly increasing the workload of pharmacists, with some studies pointing to an increase of more than two thirds (CHUI; MOTT, 2012; COOKSEY et al., 2002) As a result of this increase, the literature has already been pointing out a relationship between the high workload and the low quality of pharmaceutical services, directly impacting the ability to detect PDRIs (CHEN et al., 2005; JAMES et al., 2009; MALONE et al., 2007; TULLY; BUCHAN, 2009).

This type of service performed by pharmacists requires a lot of working time, which may lead to the need to rationalize this type of activity (MARTINBIANCHO J.K. et al., 2011). One way to reduce this workload is the regulation of clinical services performed by pharmacists, stipulating a list of prescriptions or patients by pharmacists, as in Japan, Taiwan (SHAO et al., 2020) and even in Brazil, however only in intensive care units. Prioritization is essential to match the workload with the available time of clinical pharmacists, without affecting the quality of the service. However, underdeveloped skills for this prioritization are a hindrance, as it is in other health professions.

There are several prioritization tools for clinical pharmaceutical services, but many of them are not indicated for hospitalized patients, much less specific for patients with infectious diseases. Furthermore, many of them did not even have an internal and external validation process to guarantee the robustness of the tool. Thus, there is a clear need for validation, updating or even the creation of an instrument for predicting PDRIs in patients with infectious diseases that can help clinical pharmacists to rationalize their clinical care, maintaining quality and safety for patients.

Conclusion

This work identified that the frequency of serious or clinically relevant PDRI in hospitalized patients due to infectious diseases is very high. The most frequent PDRI was drug interactions. The high severity potential of these PDRIs seriously compromises patient safety. The frequency of PDRI requiring interventions by the clinical pharmacist is very high in the studied population, therefore the amount of potential work for this professional is often excessive. It is necessary to rationalize and optimize clinical pharmaceutical services to improve patients' safety, hospitalizations outcomes and health units' efficiency. One of the ways to carry out this rationalization is through instruments for predicting PDRI. However, a validated and robust instrument aimed at this type of population is not yet available. In view of this, further studies in this regard are necessary for the development of an instrument for predicting IRPD for patients hospitalized with infectious diseases.

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6 CONCLUSÃO

O INI apresenta características próprias em relação aos IPRM, quando comparados com estudos realizados em outros hospitais. Com uma taxa de incidência de 79,24%, o serviço de saúde se semelha a unidades de atendimento a populações idosas.

Os principais tipos de IPRM são interações medicamentosas, erros de aprazamento, RAM e erros de dose, e o tempo de internação aumenta a incidência de IPRM, além de que as internações prévias não parecem influenciar a incidência de IPRM subsequentes.

A frequência em que os incidentes graves ou clinicamente relevantes ocorrem em pacientes hospitalizados na enfermaria do INI é muito alta. E o alto potencial de gravidade desses incidentes compromete seriamente a segurança do paciente.

Devido a essa elevada frequência de incidentes graves as intervenções do farmacêutico clínico são extremamente necessárias na população estudada, e, portanto, a quantidade de trabalho potencial para esse profissional é muitas vezes extensa e excessiva.

Como acreditamos que esse alto potencial de ocorrência de IPRM influencia a quantidade de trabalho realizado pelos farmacêuticos clínicos, e como os diversos estudos nessa área demonstram que, em geral, há poucos farmacêuticos para a quantidade de serviços clínicos, é necessário racionalizar e otimizar a assistência clínica farmacêutica para melhorar a segurança dos pacientes, os resultados das internações e a eficiência das unidades de saúde.

Uma das formas de realizar essa racionalização é por meio de instrumentos de previsão de IPRM. No entanto, ainda não está disponível um instrumento validado e robusto voltado para esse tipo de população.

Sendo assim, faz-se necessário que novos estudos sejam realizados, na tentativa de elucidar os preditores de IPRM para esta população, bem como o desenvolvimento de uma ferramenta para priorizar os cuidados farmacêuticos ao paciente internado com doenças infecciosas de acordo com o risco de IPRM.

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Anexos

Manuscript submitted to Journal of Clinical Pharmacy and Therapeutics

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Sex, 30/12/2022 17:51
Para: Eduardo Corsino Freire <eduardo.corsino@fiocruz.br>

Dear Dr. Freire,

Congratulations, the manuscript titled "INCIDENCE OF PREVENTABLE DRUG-RELATED INCIDENTS IN AN INFECTIOUS DISEASES HOSPITAL" has been successfully submitted to Journal of Clinical Pharmacy and Therapeutics.

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