Prevalence of errors in the preparation and administration of intravenous drugs in

adults: Meta-analysis with meta-regression

Prevalência de erros no preparo e administração de medicamentos intravenosos em adultos:

Metanálise com meta-regressão

Prevalencia de errores en la preparación y administración de medicamentos intravenosos en

adultos: Metaanálisis con metarregresión

Received: 01/10/2024 | Revised: 01/24/2024 | Accepted: 01/25/2024 | Published: 01/29/2024

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Abstract

Objective: To evaluate the average prevalence of errors in the preparation and administration of intravenous medications in a hospital by means of a meta-analysis. Method: Systematic review through meta-analysis with meta-regression, registered in PROSPERO (CRD42022324431), with a search in the seven databases, using the Rayyan QCRY®. The methodological quality of the selected studies was assessed using the Newcastle-Ottawa Scale. The meta-analysis was calculated using the random-effect model and adjusted by the inverse of the variance, and analyses were carried out to investigate heterogeneity. Results: 34 primary studies were included. The estimated prevalence of errors in the preparation and administration of intravenous drugs was 41,23% (IC95% 30,51-51,96; I2 = 100,00%). Conclusion: The results reflect the lack of health systems official data on the reporting of errors in institutions, the basis for the effective strategies that ensure for patient safety in the process medicated.

Keywords: Medication errors; Infusions, intravenous; Administration, intravenous; Nurse Practitioners; Patient safety; Hospital care.

Resumo

Objetivo: Avaliar a prevalência média de erros no preparo e administração de medicamentos intravenosos em um hospital por meio de metanálise. Método: Revisão sistemática por meio de meta-análise com meta-regressão, registrada no PROSPERO (CRD42022324431), com busca nas sete bases de dados, utilizando o Rayyan QCRY®. A qualidade metodológica dos estudos selecionados foi avaliada pela Escala Newcastle-Ottawa. A metanálise foi calculada pelo modelo de efeito aleatório e ajustada pelo inverso da variância, e análises foram realizadas para investigar a heterogeneidade. Resultados: foram incluídos 34 estudos primários. A prevalência estimada de erros no preparo e administração de medicamentos intravenosos foi de 41,23% (IC95% 30,51-51,96; I2 = 100,00%). Conclusão: Os resultados refletem a falta de dados oficiais dos sistemas de saúde sobre a notificação de erros nas instituições, base para estratégias eficazes que garantam a segurança do paciente no processo medicamentoso.

Palavras-chave: Erros de medicação; Infusões intravenosas; Administração intravenosa; Profissionais de enfermagem; Segurança do paciente; Assistência hospitalar.

Resumen

Objetivo: Evaluar la prevalencia promedio de errores en la preparación y administración de medicamentos intravenosos en un hospital mediante un metanálisis. Método: Revisión sistemática mediante metanálisis con

metarregresión, registrado en PROSPERO (CRD42022324431), con búsqueda en las siete bases de datos, utilizando el Rayyan QCRY®. La calidad metodológica de los estudios seleccionados se evaluó mediante la Escala de Newcastle-Ottawa. El metanálisis se calculó utilizando el modelo de efectos aleatorios y se ajustó por la inversa de la varianza, y se realizaron análisis para investigar la heterogeneidad. Resultados: Se incluyeron 34 estudios primarios. La prevalencia estimada de errores en la preparación y administración de medicamentos intravenosos fue del 41,23% (IC95% 30,51-51,96; I2 = 100,00%). Conclusión: Los resultados reflejan la falta de datos oficiales de los sistemas de salud sobre el reporte de errores en las instituciones, base para estrategias efectivas que garanticen la seguridad del paciente en el proceso de medicación.

Palabras clave: Errores de medicación; Infusiones intravenosas; Administración intravenosa; Enfermeras practicantes; Seguridad del paciente; Atención hospitalaria.

1. Introduction

The issue of patient safety has gained notoriety in global discussion spaces since the Institute of Medicine (IOM): *To Err is Human* (1999) (Kohn et al. 2000; WHO, 2017; Serafim et al. 2017) which estimated 180,000 patient deaths per year (13.6%) and 6.5% permanent dysfunction, caused by care errors in the United States of America (USA), from which the World Health Organization (WHO) has been consolidating goals in order to reduce serious harm caused by the inadvertent use of intravenous drugs in the world (WHO, 2017; ISMP, 2018) and in Brazil, since 2013, with the implementation of the National Patient Safety Program (PNSP) (Brazil, 2013).

Errors in the medication process occur through dysfunctions that involve three dimensions in the context of services: the handling of products, such as medicines, solutions and diluents; procedures, represented by protocols and standards; and systems, which involve several interdependent stages and actions (WHO, 2017). Errors in the preparation stage include the mishandling of supplies in relation to a drug prescription, which is influenced by previous stages (INS, 2016; NCC MERP, 2018), such as manufacturing, transportation and storage failures (WHO, 2017; Westbrook et al., 2011) or during the process of selecting and handling the supplies, such as inappropriate reconstitution/dilution (Mendes et al., 2018; Herting et al., 2018; Nguyen et al., 2015), physical-chemical incompatibility, lack of aseptic technique (Abbasinazari et al., 2013; Mendes et al., 2018; Herting et al. 2018), among others.

Errors in drug administration are preventable events that can lead to the inappropriate use of drugs, with or without adverse events for the patient (Billstein-Leber et al., 2018). The damage caused by errors in the preparation and administration of intravenous drugs has a negative impact on the quality of care and can have serious clinical consequences for patients. A retrospective study carried out in a hospital in Brazil in 2017, using 262 adverse event notification reports, showed that 19.4% of the injuries were mild, 4.2% of the injuries were moderate and 1.5% of the injuries caused the patient's clinical condition to become severe (Lima Neto et al., 2018).

Errors in the medication process also cause damage to health institutions and the dynamics of care. The increase in hospitalization time and the additional use of technologies and medicines (Couto et al., 2018; Paulino et al., 2021), are responsible for the unnecessary increase in the cost of care.

In 2016, the additional cost of errors in the medication process in a Brazilian hospital amounted to R\$96,877.90 (Paulino et al., 2021), and in the same year, around 1.3 million people were affected by adverse events in Brazil, causing 170,000 deaths (Couto et al., 2018).

In the medication use system, composed of multisectoral and multiprofessional stages (ASHP, 2018), errors in the preparation and administration of medications are specialized during nursing care (Siman et al., 2021). However, the predisposing factors for medication errors are related to service structures, whether physical or organizational, which interfere with the care dimension (Siman et al., 2021; Reason, 2000).

In this context, the cause of errors in health institutions is strongly linked to systemic factors, which through latent failures compromise patient safety, determined by dysfunctions in the organization of the work process, the lack of implementation of clinical guidelines and the absence of a patient safety culture, making it necessary to know the frequency

and weaknesses that predispose to unsafe care at a strategic level, in order to address the root cause of errors in institutions (Reason, 2000).

The aim is to evaluate the average prevalence of errors in the preparation and administration of intravenous drugs in a hospital environment in national and international studies by means of a meta-analysis.

2. Methodology

Type of study

This is a systematic review using meta-analysis with meta-regression, carried out in accordance with the following guidelines *Preferred Reporting Items for Systematic reviews and Meta-Analyses* (PRISMA) (McKenzie et al., 2020). The study was registered at *International Prospective Register of Systematic Reviews* (PROSPERO), n° CRD42022324431. The guiding question was elaborated according to the acromion PIO (Santos, Pimenta, Nobre, 2007): Population (hospitalized adults); Intervention (exposure to factors related to errors in the preparation and administration of intravenous medications) and Outcomes (errors in the preparation and administration of intravenous medications in a hospital environment).

Error definition

This study defined errors in the medication process as the occurrence of a preventable event that causes inappropriate use of medication or harm to the patient, related to professional practice, the inputs used, procedures and systems, at any stage of the medication use system (NCC MERP, 2018).

Eligibility criteria

Observational studies were included carried out with the adult population, in a hospital environment, without limits on the period of publication and language; classified as original. The following were excluded from the study: case reports, conference abstracts, systematic reviews or meta-analyses, and articles not made available in full by the authors.

All the studies that presented the frequency of errors related to the preparation and administration of intravenous drugs for hospitalized adults, carried out by nursing professionals, with the same unit of analysis in common, were considered.

Study identification strategy

The studies were selected through an electronic search in the Virtual Health Library (VHL) and the following databases: Excerpta Medica dataBASE (Embase), *National Library of Medicine (PubMed), Science Direct, Scopus, Web of Science*TM, Specialized Nursing Database (BDENF), *Scientific Electronic Library Online* (SciELO), through a comprehensive and independent search was carried out by two researchers between January 2023 and July 2023. These databases were selected considering the number of articles indexed in order to access the substantial scientific production worldwide on the topic.

In order to carry out a comprehensive search of the literature, the reviews and reference lists of the included studies were analyzed to add pertinent studies that were not found indexed in the databases.

The main descriptors used in the searches were: "medication error", "intravenous infusions", "patient safety", "nursing professionals", "hospital care/hospitals" and their respective MESHs, combined using Boolean operators "*and*" e "*or*". A manual search was also carried out for the references cited in the selected articles and published systematic review articles. The articles were managed using the *Rayyan* QCRY® program.

The following search strategy was used in Pubmed and served as the basis for other searches, undergoing adaptations according to the criteria of each database: PubMed: *Medication error AND (infusions intravenous OR infusion, intravenous OR infusion, intravenous OR infusion) Medication error and infusion, intravenous OR Medication error and*

intravenous infusion OR Medication error and infusions intravenous and hospital care)). Science Direct: (Medication error OR (errors, medication; error, medication; error medication) AND (infusions intravenous OR infusion, intravenous OR infusion intravenous OR infusion) Medication error and infusion, intravenous OR Medication error and infusion intravenous OR Medication error and infusions intravenous and hospital care)). Scopus: (medication AND error AND (infusions AND intravenous OR infusion, AND intravenous OR infusion AND intravenous OR infusion) medication AND error AND infusion, AND intravenous OR medication AND error AND infusion OR medication error and infusion intravenous OR infusion, and intravenous OR medication error and infusion, intravenous OR infusion, and intravenous OR medication error and infusion intravenous OR infusion, and infusion oR medication error AND infusion, and intravenous AND hospital AND care). Web of Science: Medication error and infusion, intravenous OR infusion intravenous OR infusion) Medication error and infusion, intravenous OR infusion intravenous OR infusion OR Medication error and infusions intravenous OR Medication error and infusions intravenous oR infusion) AND intravenous oR infusion, intravenous OR infusion, AND intravenous OR infusion, intravenous OR infusion error and infusions on the intravenous oR infusion error and infusions intravenous oR infusion error and infusions intravenous oR infusion error and intravenous OR infusion, AND intravenous OR infusion) AND error AND infusion AND error AND infusion AND error AND infusion, AND intravenous OR medication) AND error AND intravenous OR medication) AND error AND infusion, AND intravenous OR medication, AND error AND infusion, AND intravenous OR medication) AND error AND infusions AND intravenous AND hospital AND care. Scielo: Medication error e BDENF: Medication error.

Study selection

The studies were selected by two independent reviewers by analyzing the titles and abstracts of the publications identified, excluding duplicates and reviewing the full text, which, in the event of divergent opinions, was evaluated by a third reviewer.

Data extraction

To extract the data, a pre-defined form was used with the following information: authors, location of the study, sample, prevalence (%), stage of the process and quality score.

Evaluation of methodological quality

An adaptation of the Ottawa Hospital Research Institute's Newcastle-Ottawa (NOS) Quality Assessment Scale for Case-Control and Cohort Studies (Wells et al., 2021), do Ottawa Hospital Research Institute, was used to assess the quality of the longitudinal study included in this review.

Statistical analysis

The primary outcome was the prevalence of errors in the preparation and administration of intravenous drugs, with a 95% confidence interval (95%CI) and was based on an estimate of the total number of doses of intravenous drugs prepared and administered.

The meta-analysis was calculated using the random effect model and adjusted by the inverse of the variance. The degree of heterogeneity of the studies was identified using the chi-squared test (significance p<0.05), the I-squared statistic (I²) of *Higgins* e *Thompson* (2003) random effects analysis was performed after confirming heterogeneity between studies and subgroup analysis by study continent and type of medication error. In addition, meta-regression analyses were performed to explore potential sources of heterogeneity for the outcome, including the year of study (< 2017; \geq 2017), ICU (no; yes), doses assessed (< 1000; \geq 1000) and methodological quality (high; moderate; low). In all analyses, a p-value <0.05 was considered statistically significant.

Publication bias analysis was not carried out as this measure is inappropriate for meta-analysis of proportions (Hunter et al., 2014). All the analyses were carried out in the R software, version 4.2.10 (R: A Language and Environment for Statistical Computing, Vienna, Austria), using the 'Meta' package, version 5.2-0.

3. Results and Discussion

Figure 1 describes the study selection process. Of the 4.599 studies found in scientific databases. After analysis by two independent reviewers, 34 studies were eligible for inclusion in the meta-analysis.

	Identification, selection and inclusion of studies
I D E N T I F I C A T	Number of studies found (n=4.599) PUBMED (n=605) WEB OF SCIENCE (n=439) SCOPUS (n=258) SCIENCE DIRECT (n=2.817) EMBASE (n=94) SCIELO (n=228) BDENF (n=158)
I O N S O R T I N G	Number of studies (n=248) EMBASE (n=85) PUBMED (n=21) WEB OF SCIENCE (n=68) BDENF (n=09) SCOPUS (n=33) SCIELO (n=15) SCIENCE DIRECT (n=17)
I N C L U S I O	34 studies included in the systematic review

Figure 1 - Flowchart of identification, selection and inclusion of studies.

Source: Prepared by the authors (2023).

Study characteristics

The studies were published between 2003 and 2022. All the studies were described as observational, prospective and carried out in five continents and thirteen countries, with 14 studies carried out in America, seven studies in Europe, seven studies in Asia, three studies in Oceania, two studies in Africa, and a study was carried out in the United States of America and England.

The preparation and/or administration of 36,178 doses of intravenous medications were analyzed. The information for identifying the studies selected for this meta-analysis can be found in Table 1.

There were studies in which the errors were related to the administration stage, the preparation process or the preparation and administration of intravenous drugs, with studies showing the frequency of errors for each stage and one study also detailed errors in the pre-preparation stage.

In terms of methodological quality, the studies presented a low risk of bias and therefore high methodological quality and moderate risk of bias.

Authors	Year	Country	Local	Sample (Dose)	Frequency (%)	Process Step	Quality
Abbasinazari et al.	2013	Iran	SU, orthopedics and gastroenterology	357	35,6%	3	Moderate
Alomi et al.	2019	Saudi Arabia	ICU, SU, MU e Specialized Units	805	15,1%	2	Moderate
Anselmi, Peduzzi e dos Santos	2007	Brazil	Hospital	807	6,7	2	Moderate
Berdot et al.	2012	France	Specialized Units, Cardiovascular Surgery	131	31,0%	2	Moderate
Blandford <i>et al</i> .	2019	USA e England	ICU, SU e MU	3172	71,0%	2	High
Burger e Degnan	2016	USA	ICU	216	51,0%	1	Moderate
Cousins et al.	2005	United Kingdom	SU e MU	273	49,0%	3	High
Ding et al	2015	China	SU	589	12,8%	2	Moderate
Fahimi et al.	2008	Iran	ICU	524	9,4%	3	High
Fekadu et al.	2017	Ethiopia	SU e MU e gynecological	384	46,1%	2	High
Felek; Mulatu; Yesmaw	2015	Ethiopia	MU	323	61,0%	2	High
Han; Coombes; Green	2005	Australia	UC	687	18,0%	3	Moderate
Helmons et al.	2009	USA	ICU	374	18,5%	2	Moderate
Hertig et al.	2018	USA	Hospital	329	10,4%	1	High
Hoefel; Lautert	2006	Brazil	ICU, SU e MU	99	80,0%	3	Moderate
Husch et al.	2005	USA	MU	426	66,9%	3	High
Jessurun et al.	2022	Holland	SU e MU	614	59,8%	2	High
Lyons et al.	2018	England	UM, SU e ICU	2008	53,0%	2	High
Mendes et al.	2018	Brazil	Emergency	303	17,8%	3	High
Nguyen et al.	2015	Vietnam	Clinical ward	2342	73,2%	3	Moderate
Ong; Subasyini	2013	Malaysia	Hospital	349	97,7%	3	High
Owens et al.	2020	USA	Emergency	676	2,96%	2	High
Rodriguez-Gonzalez et al.	2012	Spain	Gastroenterology	402	17,4%	2	Moderate
Romero et al.	2013	Chile	ICU	194	56,2%	3	High
Schnock et al.	2017	USA	ICU, SU e MU	1164	60,0%	2	High
Silva; Camerini	2012	Brazil	ICU, SU e MU	367	98,0%	2	High
Skog et al.	2022	USA	ICU, SU e MU, orthopedics e Emergency	350	32,7%	2	High
Taxis; Barber	2003	United Kingdom	ICU, SU, MU e oncology	1042	49,0%	3	High
Volpe et al.	2014	Brazil	MU	241	68,0%	3	Moderate
Westbrook et al.	2011	Australia	Clinical ward	568	69,7%	3	Moderate
Wirtz; Taxis; Barber	2003	United Kingdom	Hospital	140	24,3%	3	Moderate
Wiseman <i>et al</i> .	2018	Australia	ICU e MU	2599	86,0%	2	Moderate
Wright et al.	2019	USA	Hospital	1530	1,44%	1	High
Yousef et al.	2022	Jordan	MU	1012	35,0%	2	High

Table 1 – Identification of studies selected for meta-analysis on errors in the preparation and administration of intravenous medications in a hospital environment, sample per dose.

Legend: USA: United States of America; 1 – Preparation; 2 – Administration; 3 - Preparation and Administration; SU: Surgical Unit; MU: Medical Unit; ICU: Intensive care unit. Source: Prepared by the authors (2023).

The analysis revealed heterogeneity using the Q test (p=0.000) and the I2 statistic (I2 = 100.0%). The estimated prevalence of errors in preparing and administering doses of intravenous drugs grouped in the studies was 41.23% (95%CI 30.51-51.96; I2 = 100.00%) (Figure 2).

Figure 2 - Estimated prevalence of errors in preparing and administering doses of intravenous drugs grouped.

Study	Events	Total	Events per 100 observations	Proportion	95% CI	Weight
Abbasinazari et al. 2013	36	357	-	10.08	[7.16; 13.69]	2.9%
Alomi et al. 2019	105	694	+	15.13	[12.54; 18.02]	2.9%
Berdot et al. 2012	430	1501	+	28.65	[26.37; 31.01]	2.9%
Blandford et al. 2019	71	3172	+	2.24	[1.75; 2.82]	3.0%
Burger e Degnan 2016	110	216		50.93	[44.06; 57.77]	2.9%
Cousins et al. 2005	132	273	- 1 -	48.35	[42.29; 54.45]	2.9%
Ding et al. 2015	76	593		12.82	[10.23; 15.78]	2.9%
Fahimi et al. 2008	22	524	+	4.20	[2.65; 6.29]	2.9%
Fekadu et al. 2017	169	366	-	46.17	[40.98; 51.43]	2.9%
Felek, Mulatu e Yesmaw 2015	353	360	A.M. 100	+ 98.06	[96.03; 99.21]	2.9%
Han, Coombes e Green 2005	126	639	- + -	19.72	[16.70; 23.02]	2.9%
Helmons et al. 2009	47	374		12.57	[9.38; 16.36]	2.9%
Hertig et al. 2018	260	329		79.03	[74.22; 83.30]	2.9%
Hoefel e Lautert 2006	79	99		79.80	[70.54; 87.20]	2.9%
Husch et al. 2005	285	426		66.90	[62.21; 71.36]	2.9%
Jessurun et al. 2022	367	614		59.77	[55.77; 63.68]	2.9%
Lyons et al. 2018	240	2008	+	11.95	[10.56; 13.45]	2.9%
Mendes et al. 2018	54	303		17.82	[13.68; 22.60]	2.9%
Nguyen et al. 2015	2060	5271	+	39.08	[37.76; 40.41]	2.9%
Ong e Subasyini 2013	341	349		+ 97.71	[95.53; 99.01]	2.9%
Owens et al. 2020	20	676	+	2.96	[1.82; 4.53]	2.9%
Rodriguez-Gonzalez et al. 2012	479	2314	+	20.70	[19.07; 22.41]	2.9%
Schnock et al. 2017	699	1164		60.05	[57.17; 62.88]	2.9%
Silva e Camerini 2012	355	367		+ 96.73	[94.36; 98.30]	2.9%
Skog et al. 2022	144	350		41.14	[35.94; 46.50]	2.9%
Taxis e Barber 2003	212	430		49.30	[44.48; 54.13]	2.9%
Volpe et al. 2014	416	484		85.95	[82.53; 88.92]	2.9%
Westbrook et al. 2011	420	568		73.94	[70.13; 77.51]	2.9%
Wirtz, Taxis e Barber 2003	181	610		29.67	[26.07; 33.47]	2.9%
Wiseman et al. 2018	242	2599	+	9.31	[8.22; 10.49]	3.0%
Wright et al. 2017	22	1530	+	1.44	[0.90; 2.17]	3.0%
Yousef et al. 2022	910	1012	+	- 89.92	[87.90; 91.71]	2.9%
Romero et al. 2013	66	194		34.02	[27.39; 41.15]	2.9%
Anselmi, Peduzzi e dos Santos 2007	184	2706	+	6.80	[5.88; 7.81]	3.0%
Random effects model				41.23	[30.51; 51.96]	100.0%
Heterogeneity: $I^2 = 100\%$ [100%; 100%]], p = 0					
			20 40 60 80			

Source: Prepared by the authors (2023).

Subgroup analysis shows a high degree of heterogeneity on all continents, with an average prevalence of 72.18% (95%CI 21.33-100.00%) in Africa; 53.51% (95%CI 22.57-84.44%) in South America; 38.43% (95%CI 9.20-67.66%) in Asia; 35.18% (95%CI 15.02-55.35%) in North America; 35.37% (95%CI 22.52-48.22%) in Europe; and 34.30% (95%CI 0.00-73.55%) in Oceania (Figure 3 - A).

Figure 3 - Subgroup analysis by continentes and by type of errors in preparing and administering doses of intravenous drugs.

Α	-	Subgroup	analysis	by	continentes,	B-Subgroup
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А

analysis by type of error

		Evente per 100				_	011	Etu	T -1-1	Events per 100	D	054/ 01	W-!-L4
Study	Events Total	observations	Proportion	95% CI	Weight	В	Study	Events	Iotal	observations	Proportion	95% CI	weight
d a fa		4					Administration and Preparation						
Asia	00 057 1		40.00 5	7 40 40 001	0.00		Abbasinazari et al. 2013	36	357 +	1	10.08	[7.16; 13.69]	2.8%
Abbuasinazan et al. 2015	30 337 M		10.00 [2 54 40.03	2.9%		Alomi et al. 2019	105	694 +		15.13	[12.54; 18.02]	2.8%
Alomi et al. 2019 Diagrat al. 2015	76 502		13.13 [1.	Z.34, 10.0Z	2.9%		Cousins et al. 2005	132	273		48.35	[42.29: 54.45]	2.8%
Dilig et al. 2013 Fabirei et al. 2009	70 095		12.02 [1	0.25, 10.70	2.970		Ding et al. 2015	76	503 +	- Marcan	12.82	[10 23: 15 78]	2.8%
Fanimi et al. 2006	22 324		4.20 [7.76 40.441	2.9%		Eshimi et al 2008	22	524 +		1 20	[265: 6.20]	2.8%
Ope o Subactini 2012	2000 3271		07.71 10	5.52: 00.011	2.9/0		Hortin et al. 2000	280	320		70.03	[7.4 22: 83:30]	2.010
Voucof et al. 2022	010 1012	10	80.02 [8]	7 00: 01 711	2.9%		Namen at al. 2015	2080	5271	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	30.08	[17.22, 00.00]	2.0.10
Random effects model	310 1012		38.43 [0	9 20 - 67 661	20.6%		Nguyen et al. 2013 Ond o Subscuipi 2012	2000	240	1	07.71	[01.10, 40.41]	2.0 %
Heteroneneity / ² = 100% 100% 1004	Nin=0		00.40 I.	strof or loof	2010-10		Tavia a Dade a 2002	041	349	10	1 97.71	[90.00, 99.01]	2.0%
the second s	all to our o						Vales stal 2005	212	404	100	49.50	[44.40, 04.10]	2.0%
Europe							Voipe et al. 2014	410	404	100	00.90	[02.03, 00.92]	2.0%
Berdot et al. 2012	430 1501	H	28.65 [2	6.37; 31.01]	2.9%		Romero et al. 2013	00	194		34.02	[27.39; 41.15]	2.8%
Cousins et al. 2005	132 273	- 1998 - 1998	48.35 [4	2.29; 54.45]	2.9%		Random effects model		÷		43.24	[23.99; 62.49]	30.5%
Jessurun et al. 2022	367 614		59.77 [5	5.77; 63.68]	2.9%		Heterogeneity: /~ = 100% [100%, 100%	p = 0					
Lyons et al. 2018	240 2008	1	11.95 [1	0.56; 13.45]	2.9%								
Rodriguez-Gonzalez et al. 2012	479 2314	•	20.70 [1	9.07; 22.41]	2.9%		Administration			_			
Taxis e Barber 2003	212 430		49.30 [4	4.48, 54.13]	2.9%		Berdot et al. 2012	430	1501		28.65	[26.37; 31.01]	2.8%
Wirtz, Taxis e Barber 2003	181 610	100 C	29.67 [2	6.07, 33.47]	2.9%		Blandford et al. 2019	71	3172 •		2.24	[1.75; 2.82]	2.8%
Random effects model		-	35.37 [22	2.52; 48.22]	20.6%		Fekadu et al. 2017	169	366		46.17	[40.98; 51.43]	2.8%
Heterogeneity: /~ = 99% [99%; 99%],	p < 0.01						Felek, Mulatu e Yesmaw 2015	353	360		98.06	[96.03; 99.21]	2.8%
Marchin Reservation							Han, Coombes e Green 2005	126	639	+	19.72	[16.70; 23.02]	2.8%
North America Rightford et al. 2010	71 2172		224 1	175-000	2.00		Helmons et al. 2009	47	374 +		12.57	[9.38; 16.36]	2.8%
Dianarona e Dogram 2016	110 216	100	E0.02 M	1.06: 57.771	3.0%		Hoefel e Lautert 2006	79	99		79.80	[70.54; 87.20]	2.7%
Holmons et al. 2000	47 374 =	4	12.57	4.00, 37.17]	2.9%		Husch et al. 2005	285	426	-	66.90	[62.21:71.36]	2.8%
Hertin et al. 2005	260 329	10 100 100 100 100 100 100 100 100 100	79.03 17	4 22: 83 301	2.9%		I vons et al. 2018	240	2008 +		11.95	[10.56] 13.45]	28%
Husch et al. 2005	285 426		66 90 16	221 71 36]	2.9%		Mendes et al. 2018	54	303 +		17.82	[13 68 22 60]	2.8%
Owens et al. 2020	20 676 +	-	2.96	1.82 4.53	2.9%		Owens et al. 2020	20	676 +		2.96	[182 453]	2.8%
Schnock et al. 2017	699 1164		60.05 f5	7.17: 62.881	2.9%		Rodriguez-Gonzalez et al. 2012	479	2314	+	20.70	[19 07: 22 41]	28%
Skog et al. 2022	144 350	*	41.14 [3	5.94; 46.50]	2.9%		Schnock et al 2017	600	1164		60.05	[57 17:62 88]	2.8%
Wright et al. 2017	22 1530 *		1.44 [0.90; 2.17]	3.0%		Silva a Camarini 2012	355	267		06.73	[01.17, 02.00]	2.010
Random effects model			35.18 [18	5.02; 55.35]	26.5%		Skog et al 2022	144	350	100	A1 1A	[34.00, 30.00] [25.04: 46.50]	2.010
Heterogeneity: 1 ² = 100% [100%; 1009	%], p = 0						Weathreak et al. 2011	400	500	1 1	72.04	[30.94, 40.00]	2.076
							Witz Tavis a Barbar 2002	420	000		24.07	[20.10,77.01]	2.0.10
Africa	18643 101211		105712	2010/2010			Winz, Taxis e Daiber 2003	30	213	- 100	0.24	[20.40, 40.02]	2.0.10
Fekadu et al. 2017	169 366	100	46.17 [4	0.98; 51.43]	2.9%		Verseficitiet al. 2010	242	1012	101	9.01	[0.22, 10.43]	2.0.0
Felek, Mulatu e Yesmaw 2015	353 360		98.06 [9	6.03; 99.21]	2.9%		Touser et al. 2022	910	1012	10 A	09.92	[01.90, 91.11]	2.0%
Random effects model	1		12.18 [2]	.33, 100.00]	0.9%		Anseimi, Peduzzi e dos Santos 2007	00	1313 🔳		20.C	[3.90, 0.34]	Z.8%
Heterogeneity: / = 100% (100%, 100%	%], p < 0.01	1					Random effects model		*.:		40.85	[26.30] 55.41]	00.0%
Oceania							Heterogeneity: /~ = 100% [100%; 100%	p = 0					
Han Coombes e Green 2005	126 639	#	19.72 [1	670 23 021	2.9%								
Westbrook et al. 2011	420 568		73.94 [7]	0.13: 77.511	2.9%		Preparation		1211217	1000			
Wiseman et al. 2018	242 2599		931 L	8.22: 10.491	3.0%		Burger e Degnan 2016	110	216		50.93	[44.06; 57.77]	2.8%
Random effects model			34.30 I (0.00: 73.551	8.8%		Jessurun et al. 2022	367	614	_ 1 音	59.77	[55.77; 63.68]	2.8%
Heterogeneity: / ² = 100% [100%; 1009	%], p < 0.01		0.0000				Wirtz, Taxis e Barber 2003	88	337	±	26.11	[21.50; 31.15]	2.8%
							Wright et al. 2017	22	1530 +		1.44	[0.90, 2.17]	2.8%
South America							Anselmi, Peduzzi e dos Santos 2007	118	1391 +		8.48	[7.07; 10.07]	2.8%
Hoefel e Lautert 2006	79 99	-11-	79.80 [7	0.54; 87.20]	2.9%		Random effects model				29.24	[6.80; 51.69]	13.9%
Mendes et al. 2018	54 303	±	17.82 [1	3.68; 22.60]	2.9%		Heterogeneity: /2 = 100% [100%; 100%], p < 0.01					
Silva e Camerini 2012	355 367	_ =	96.73 [9	4.36, 98.30]	2.9%								
Volpe et al. 2014	416 484	10 E	85.95 [8	2.53; 88.92]	2.9%		Random effects model			-	39.97	[29.66; 50.29]	100.0%
Romero et al. 2013	66 194		34.0Z [2	7.39; 41.15]	2.9%		Heterogeneity: /2 = 100% [100%: 100%	0 = 0					
Anselmi, Peduzzi e dos Santos 200	184 2706		6.80 [[5.88; 7.81]	3.0%		Test for subgroup differences: $p = 0.6$	1	2	0 40 60 80			
Random effects model			03.01 [22	2.07; 84.44]	17.0%		1950) S.		1	1999 - 1999 - 1999 - 1999			
meterogeneity: $r = 100 $ m $(100 $ m, $100 $	m], $p = 0$												
Random effects model		-	41.23 130	0 51: 51 961	100.0%								
Heterogeneity: /2 = 100% [100% 100%	%l.p=0	TITI	41.84 [00										
Test for subgroup differences: $\rho = 0.7$	71 0	20 40 60 80 100)										



Subgroup analysis by type of error revealed high heterogeneity in all groups, with the highest prevalence of errors among studies that evaluated administration together with preparation (43.24%; 95%CI 23.99-62.49%), followed by administration only (40.85%; 95%CI 26.30-55.41%) and preparation only (29.24%; 95%CI 6.80-51.69%) (Figure 3 - B).

The meta-regression indicated that none of the selected variables contributed as a source of heterogeneity to the analyses (Table 2).

~ -				
Subgroup	Number of studies	Estimated	CI 95%	р
Year				
> 2017	21	0,00	-	-
≥2017	13	-0,19	-0,44 a 0,07	0,1474
ICU				
No	24	0,00	-	-
Yes	10	-0,08	-0,29 a 0,13	0,4527
Doses evaluated				
< 1000	21	-	-	-
≥ 1000	13	-0,12	-0,36 a 0,12	0,3165
Methodological quality				
High	19	0,00	-	-
Moderate	15	-0,23	-0,47 a 0,01	0,0570
Low	0	-	-	-
<u>I</u> ²		99,89%		

 Table 2 - Meta-regression according to selected covariates.

Legend: CI: Confidence interval; p: p-value; Source: Prepared by the authors (2023).

The prevalence of errors in the preparation and administration of medicines reveals significant limitations in the quality of care and reflects the ineffectiveness of the patient safety strategies implemented in the services (Brazil, 2013).

In Brazil, in 2019, 12,181,726 hospitalizations were recorded in the single health system in Brazil (Brazil, 2021). The literature estimates that on average 70% of hospitalized patients (8,527,208) use peripheral intravenous therapy (Zingg, Pittet, 2009). Based on this meta-analysis, the average prevalence of intravenous drug errors in hospitals in South America being 53% and taking the average number of patients using peripheral intravenous therapy as a basis (Zingg, Pittet, 2009), the estimated absolute frequency would be 4,519,420 errors in the preparation or administration of peripheral intravenous drugs in 2019, considering the patient as the unit of analysis for the error.

These data reflect that even with the worldwide commitment to patient safety through the targets set by the World Health Organization (WHO, 2017), reducing errors in the medication process by 50% is a major challenge for health services. Considering the estimated average prevalence of errors in South American hospitals in this study, the appropriate prevalence based on the target set by the WHO would be 26.5% errors.

Mitigating care insecurity in the medication process consists of engaging the strategic dimensions: system/organization/professional/patient (Pena; Melleiro, 2017) in the various health systems. In addition to overcoming the barriers of underreporting, establishing a culture of safety that results in safe systems for health workers and patients.

This study highlighted that in the continents with the highest levels of socio-economic development (Asia (38%), Europe (35%), Oceania (34%) and North America (35%)) there was a low variability in the average prevalence of errors, while the socio-economically underdeveloped continents (Africa (72%) and South America (53%)) showed the highest average prevalence of errors, reflecting the challenges of the different scenarios for implementing safety in the medication process, such as investments in infrastructure, technology and personnel.

On the one hand, health systems in developed countries are emerging with structural investments and the incorporation of modern technologies, which, if properly implemented, can mitigate health problems. On the other hand, health systems in developing countries have shortcomings that are mainly related to structural limitations and the inadequate distribution of resources (Silva da & Elias, 2019; Souza, 2020).

The underfunding of public health services is recognized as the main obstacle to safe care, as it limits managers in implementing a culture of patient safety, including adjustments to the systems, structure, work process and management of health services (Souza, 2020). The literature shows that the cost of errors is still unknown by health institutions, involving increased hospitalization time and use of inputs, compensation, as well as affecting the prestige of the service in the eyes of clients (Couto et al., 2018; Paulino et al., 2021).

However, it is worth highlighting that errors in the preparation and administration of intravenous medications can be prevented in services that focus on implementing a safety culture as clear language (WHO, 2017; Nguyen et al., 2015; Rodriguez-Gonzalez et al., 2012). On the other hand, insecurity in the medication process interferes with the effectiveness of medication therapy (Nguyen et al., 2015; Abbasinazari, 2013), increase hospitalization time and healthcare costs (Paulino et al., 2021; ASHP, 2018), reduce life expectancy, predispose to irreversible injuries (Figueredo et al., 2022; Nguyen et al., 2015), including causing death of the patient (Nguyen et al., 2015).

In this study, the average prevalence of errors in the administration of intravenous medication (41%) was higher than during preparation (29%), in the studies that analyzed these stages separately. The stages of preparation and administration of a dose of intravenous medication involve 20 - 30 actions, and it is important to know the stages and/or actions in which errors are most prevalent in order to implement effective interventions. Studies that consider preparation and administration as a single process may incur in generalizing the results, making the identification of errors inaccurate for establishing strategies.

Preparing the medication is the stage under the responsibility of the nursing team where errors can be prevented from causing harm to the patient, known as "Near Miss" (Reason, 2000). It is also the stage where errors can be omitted or underreported by the team, as they may not be so obvious. However, administration errors involve a series of procedures aimed at reducing risks to patients and become more evident due to the risk of adverse events, requiring compliance with protocols, including incident reporting (Reason, 2000; NCC MERP, 2018).

In this study, heterogeneity was present and the meta-regression analysis indicated that none of the selected variables (year of study, hospitalization sector, sample size and methodological quality) contributed as a source of heterogeneity to the analyses. However, it may be associated with differences between the studies, such as the health systems and institutions of the countries, given the peculiarities of health systems around the world, the characteristics of the institutions, the level of technology (Silva da & Elias, 2019; Souza, 2020) the establishment of clinical protocols for the preparation and administration of medicines, the sizing of nursing staff, working conditions, the dynamics of the services, among others (ASHP, 2018; WHO, 2017).

In the studies selected, the definition of error was commonly related to the preparation and administration of medication in disagreement with the prescription, error was also related to any avoidable event that causes the inappropriate use of medication (Nguyen et al., 2015; Abbasinazari, 2013; Ding et al., 2015; Fekadu et al., 2017; Herting et al., 2018; Rodriguez-Gonzalez et al., 2012; Schnock et al., 2017; Silva & Camerini, 2012) and related to the hospital's policies and procedures (Nguyen et al., 2015; Wirtz et al., 2003; Taxis & Barber, 2003). Error in the preparation and administration of medicines has also been defined as an omission in the medication process, with the potential to cause harm to the patient (Fekadu et al., 2017).

The adoption of different definitions of errors in different studies can lead to the search for data representing variability in the measurement of errors, and may represent methodological causes of heterogeneity.

Due to the absence of another meta-analysis on the prevalence of errors in the preparation and administration of medication with peripheral devices, it was not possible to compare with other results.

Improving the safety culture is the basis for effective harm prevention in health services (Figueredo et al., 2022; Rodriguez-Gonzalez et al., 2012). The implementation of a learning culture, with the reinforcement of the role of institutional managers in preventing errors in the medication process, should implement effective strategies to reduce the risk of their occurrence (Romero et al., 2013; Reason, 2000), through changes in systems and clinical practice (Schnock et al., 2017).

Furthermore, the importance of conducting new studies that analyze the safety of the medication process in health institutions around the world is emphasized, in order to broaden the understanding of health systems and work processes that predispose to errors and thus establish strategies to mitigate them.

Among the probable limitations was the collection of data through observation, albeit indirect, of the practice of preparing and administering intravenous drugs, which may have led to changes in performance, hiding some information that portrays reality, interfering with the results of the studies.

The use of different data collection instruments between the studies, with their references, adaptations and stages used and the differences in the scenarios of each study, the period allocated for carrying out each study.

There was also a lack of standardization of the data collection instruments. Some instruments were based on studies previously published in the scientific literature (Ong & Subasyini, 2013; Han et al., 2005; Schnock et al., 2017) and others were developed by the authors based on the stages of the medication process, with one study recommending a pilot test to adapt the instrument for data collection (Volpe et al., 2014). There were differences in the shifts in which the studies were carried out, a fact that directly influences the dynamics of the institutions, the nursing routine and the frequency with which these errors can occur.

Contributions to the areas of nursing and health

Given the evidence demonstrated, mitigating medication errors consists of proving effective health care, reducing incidents and the possibility of causing harm and adverse events to patients, as well as providing the nursing team with the working conditions permitted for the development of care with safety.

4. Conclusion

The prevalence of errors in the preparation and administration of intravenous medicines in developed countries differs from the prevalence in developing countries, highlighting the need for public policies aimed at safety of care with medicines in health institutions.

Preventing medication errors involves investments in technologies, infrastructure and process and personnel management, linked to the Safety Culture of each service, making it necessary to adapt the public health budget with financial transfers allocated to Patient Safety in the hospital environment.

It is important that patient safety is prioritized in the strategic planning of health institutions, with operational objectives, such as the analysis and adaptation of the environment for preparing and administering medicines; aligned with tactical and strategic objectives, such as adequate staffing and the establishment of mental health programs for health professionals, which will allow the Patient Safety Culture to become a predominant language in the management of health services, reflecting positively on quality of care indicators.

The results of this study point to the need for health institutions to know internal drug safety indicators in order to implement effective strategies, such as error reports in clinical practice, emphasizing communication between members of the interprofessional team.

Furthermore, the lack of official data from health systems on the reporting of errors in institutions and omission makes the prevalence of errors underestimated. It is important to carry out new studies, in order to survey prevalence and causes, which are the basis for the effective strategies that ensure for patient safety in the process of preparing and administering intravenous drugs.

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