Safety of palliative cancer patients using morphine for pain control: scoping review

Segurança do paciente oncológico paliativo em uso de morfina para o controle da dor: revisão de escopo

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ABSTRACT

BACKGROUND AND OBJECTIVES: The objective of this study was to map the safety practices of morphine use for pain control in palliative cancer patients.
CONTENTS: This is a scoping review that followed the methodology of the Joanna Briggs Institute (JBI) to answer the question: what is the evidence on safety practices for the use of morphine for pain control in palliative cancer patients? The search was carried out in the Medline, LILACS, Scopus, Embase, Web of Science, Cochrane and CINAHL databases, as well as in the gray literature. The titles and abstracts were evaluated by two independent reviewers, and the selected papers were read in full. The data extracted is presented in the form of tables accompanied by a narrative summary. The 21 articles selected identified 14 service management practices in the use of morphine, 24 safety practices related to the prescription of morphine, 15 safety practices related to the preparation and administration of morphine and characterized 16 risks and 8 adverse reactions.
CONCLUSION: Through the identified practices, professionals can plan safe care, managing risks, adverse reactions, and promoting better control of cancer pain.
Keywords: Adverse effects, Drug-related adverse reactions, Morphine, Pain management, Patient safety.

RESUMO

JUSTIFICATIVA E OBJETIVOS: O objetivo deste estudo foi mapear as práticas de segurança do uso de morfina para o controle da dor em pacientes oncológicos paliativos.
CONTEÚDO: Trata-se de uma revisão de escopo que seguiu a metodologia do Instituto Joanna Briggs (JBI) para responder à pergunta: quais as evidências sobre as práticas de segurança do uso de morfina para o controle da dor em pacientes oncológicos paliativos? A busca foi realizada nas bases de dados Medline, LILACS, Scopus, Embase*, Web of Science*, *Cochrane* e CINAHL, bem como na literatura cinzenta. Os títulos e resumos foram avaliados por dois revisores independentes, e os trabalhos selecionados foram lidos na íntegra. Os dados extraídos estão apresentados em forma de tabelas acompanhadas de resumo narrativo. Dos 21 artigos selecionados, foram identificadas 14 práticas de gestão dos serviços no uso da morfina, 24 práticas de segurança relacionadas à prescrição de morfina, 15 práticas de segurança relacionadas ao preparo e administração de morfina, e caracterizados 16 riscos e 8 reações adversas.
CONCLUSÃO: Por meio das práticas identificadas, os profissionais podem planejar um cuidado seguro, gerenciando riscos, reações adversas e promovendo um melhor controle da dor oncológica.
Descritores: Efeitos adversos, Manejo da dor, Morfina, Reações adversas relacionadas a fármacos, Segurança do paciente.

INTRODUCTION

In 2019, the Institute of Healthcare Improvement published the Advancing the Safety of Acute Pain Management guide with recommendations for patient safety in pain management, due to the high prevalence of pain in hospitalized patients, which makes them vulnerable to the occurrence of errors and adverse health events[1]. Unsafe healthcare, which can be avoided, is related to increased morbidity, avoidable mortality and additional costs[2].

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HIGHLIGHTS
- Pain control
- Best practices in morphine use
- Risk and adverse event management

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Pain is a symptom much feared by cancer patients and is associated with great suffering, a worsening of the patient's quality of life (QoL) and feelings related to death. From an oncology perspective, pain transcends the physical aspect, as the spiritual, cultural and social dimensions are also involved. Its relief, in all its dimensions, is the basis of Palliative Care (PC), which permeates the work of all professionals in interdisciplinary care[3].

Pain affects 60% to 80% of cancer patients, with 25% to 30% already reporting pain at the time of diagnosis, and 70% to 90% of patients with advanced disease having moderate to severe pain[1]. There is evidence that controlling cancer-related symptoms contributes to improved survival, especially pain control, which has a direct impact on QoL[3,4].

Although analgesic treatment is available for 70% to 90% of cancer patients, in 40% to 50% of cases it is inadequate. Undertreatment of pain is a reality in several developing countries[5]. Noteworthy is Resolution No. 33 of January 14, 2000, from the Brazilian Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária* - ANVISA), which updates and regulates the list of substances subject to special control, including morphine and its derivatives (salts and isomers) in the list of narcotic substances; It must be prescribed on an A (yellow) prescription form, and can only be sold with a prescription withheld[6], a situation which can make it difficult for the target public who would benefit most from the drug to access it.

There are several reports in the literature about inadequate pain control in cancer patients and the occurrence of adverse events related to the use of morphine[2,7]. Morphine is a strong opioid, chosen when the use of non-steroidal anti-inflammatory drugs and weak opioids are no longer effective for the patient. Morphine does not have a dose ceiling, the dose limit being that which provides pain relief, limited by uncontrollable or intolerable adverse effects[8]. The dose is adjusted to achieve analgesia, without excessive sedation, and is reduced when the pain subsides[9].

Adverse drug events are predictable in patients taking opioids continuously[10], both in chronic pain related to the cancer itself and to anti-tumor treatments, and reactions to the drug can occur, such as progressive cognitive disorders with alterations in memory, attention and learning, impregnations that cause drowsiness and a lowered level of consciousness[11], emetic conditions that are difficult to control and constipation, as well as errors that cause adverse events related to prescription, preparation and administration stages[12,13]. Patient safety practices should be implemented to prevent adverse events, with continuous monitoring of the opioid's therapeutic response by nurses[14,15].

Patients taking highly monitored drugs, such as opioid analgesics, are at increased risk of adverse events, whether they are related to an adverse reaction from the drug itself or an error in its administration[10]. It is known that a large proportion of related adverse events occur due to systematic failures. Therefore, knowing the processes related to their administration can identify causes of failure and propose the implementation of safety barriers to help prevent and reduce injuries to patients[16].

Drug-related adverse events must be reported. This is a participatory management strategy that helps to quantify the errors and failures that occur in care processes. Through it, patient safety indicators are generated and actions are planned to reduce the incidence of events[17].

Despite the relevance of the topic, the discussion on patient safety became more notorious with the report by the American Institute of Medicine named "To err is Human: Building a safer health care system", which brought alarming data on adverse events and related deaths. Drug errors featured prominently in the report, since they caused 7,391 deaths annually among Americans in hospitals and more than 10,000 deaths in outpatient institutions[18].

Today, decades after the publication of the "To Err is Human" report, the challenges of patient safety are many. Since then, there has been a major international mobilization with extensive publication in the World Health Organization (WHO), by the Joint Commission and the Agency for Healthcare Research & Quality (AHRQ)[19]. In addition, the creation of the World Alliance for Patient Safety and, later, the Six International Patient Safety Goals, drew the attention of health managers and professionals to the implementation of patient safety protocols and practices[20].

A few primary studies on safety practices for cancer patients using morphine have been published. A preliminary search on PROSPERO, Medline, Cochrane Database of Systematic Reviews and JBI Evidence Synthesis was conducted and no current or ongoing scoping or systematic reviews on the topic were identified.

Given the relevance of the topic, this scoping review on safety practices in cancer patients using morphine can be used to support actions to prevent the occurrence of adverse events related to this drug, as well as to support research in order to identify gaps on the subject and the possibility of a future systematic review. Therefore, the aim of this review was to map patient safety practices carried out in palliative oncology patients using morphine for pain control.

CONTENTS

This scoping review was conducted following the JBI methodology for scoping reviews[21]. The protocol was registered with the Open Science Framework (OSF) under the link osf.io/k4rgq.

The central question of this research was: what is the evidence on patient safety practices carried out in palliative cancer patients who use morphine for pain control?

The following sub-questions were also developed:

- What patient safety practices are carried out in the stages of prescribing, preparing and administering morphine?
- What patient safety practices involve risk management in the use of morphine?

The participants in this review were oncology patients undergoing PC using morphine for pain control. Studies involving adult patients undergoing PC for any oncological disease were included. Patients had to be using morphine for pain control, regardless of the route used.

Concept
This review included studies on patient safety practices and risk management. These are practices aimed at reducing the risk of unnecessary injury associated with healthcare to an acceptable minimum[10,20]. Studies on patient safety during morphine prescription, dose preparation and administration were included, as well as those on the prevention of adverse events related to this drug, including adverse reactions and administration errors.

Context
For the context, studies with hospitalized or outpatient patients were included.

Types of fonts
This scoping review considered experimental and quasi-experimental study designs, including randomized and non-randomized clinical trials, before-and-after studies and time series. Observational studies, including cohort studies, case-control studies and cross-sectional studies, were also included. This review also considered case series and reports, as well as protocols and clinical practice guidelines. Literature reviews, theses and text and opinion articles were also considered for inclusion.
The databases searched included: Medline (Pubmed), LILACS (Regional Virtual Health Library), Scopus, Embase, Web of Science, Cochrane and CINAHL. The search for grey literature included: websites of pain societies and organizations, the Digital Library of Theses and Dissertations, protocols and clinical guidelines recognized by government bodies and the National Institute for Health Care and Excellence (NICE).

Search strategy
A three-stage search strategy was used for this review. An initial search limited to Medline (Pubmed) and CINAHL was carried out, followed by analysis of the words in the text contained in the title and abstract, and the index terms used to describe the article. tables 1 and 2 present the complete search strategies for Medline via Pubmed and CINAHL that were carried out in 2023, using the "advanced search" feature with the descriptors MeSH (Medical Subject Headings) and the controlled vocabulary developed by the U.S. National Library of Medicine and Boolean operators OR and AND.
A full secondary search was carried out on all the databases included, using the keywords and index terms identified in the initial search. To help identify any additional studies, a tertiary literature search was carried out by examining the reference lists of all literature meeting the inclusion criteria of this review. This review considered studies in any language and with no time frame.

Evidence selection
After the search, all the references identified were grouped and organized in Excel spreadsheets and uploaded to the EndNote reference manager software (Clarivate Analytics, PA, USA), with duplicates removed. Titles and abstracts were screened by two reviewers and then the full text of the selected citations was organized into folders and assessed in detail against the inclusion criteria by two independent reviewers. The reasons for excluding full-text studies that did not meet the inclusion criteria were recorded and reported. Disagreements that arose between the reviewers at each stage of the study selection process were resolved through discussion with a third reviewer.
The results of the selection are presented in the PRISMA - ScR flowchart (Preferred Reporting Items for Systematic Reviews and Meta-analyses - extension for Scoping Review)[22].

Data extraction
Data from the included studies was extracted by two independent reviewers, using a data extraction tool developed by the reviewers (Table 3). The extracted data included specific details about the population, concept, context, study methods and main conclusions relevant to the aim of the review. Any disagreements between the reviewers were resolved through discussion with a third reviewer.

Data analysis and presentation
The data extracted is presented in the form of figures and tables, so that it is in line with the aim of this scoping review. The data provides information on the type of study, practices related to the prescription, preparation and administration of morphine, risk management and adverse events. A descriptive and narrative analysis accompanies the tabulated and mapped results, describing how the results relate to the aim and question of the review.

RESULTS

The search in the Virtual Health Library (VHL), CINAHL, COCHRANE, Embase, Medline , Scopus, Web of Science (WOS)

Table 1. Medline database search strategy via Pubmed. Niterói, Rio de Janeiro, 2024

Consult	Mapping of terms	Retrieved records
#1	("Palliative Care"[mh] OR "Palliative Care"[tiab] OR "Palliative Supportive Care"[tiab] OR "Palliative Surgery"[tiab] OR "Palliative Therapy"[tiab] OR "Palliative Treatment"[tiab] OR "Surgery, Palliative"[tiab] OR "Therapy, Palliative"[tiab]) AND (Onco*[tiab] OR Cancer*[tiab] OR Carcinoma*[tiab] OR Malignant*[tiab] OR Neoplasm*[tiab] OR Tumor*[tiab])	42.713
#2	(Morphine[mh] OR Morphine[tiab] OR "Chloride, Morphine"[tiab] OR Duramorph[tiab] OR "MS Contin"[tiab] OR Morphi*[tiab] OR "Oramorph SR"[tiab] OR "SDZ 202 250"[tiab] OR "SDZ 202-250"[tiab] OR "SDZ202 250"[tiab] OR "SDZ202-250"[tiab] OR "Analgesics, Opioid"[tiab] OR Agonist[tiab] OR Opioid*[tiab])	348.765
#3	("Patient Safety"[mh] OR "Patient Safety"[tiab] OR Patient Safet*[tiab])	58.794
#4	#1 AND #2 AND # 3	11

Table 2. CINAHL database search strategy. Niterói. Rio de Janeiro, 2024

Consult	Mapping of terms	Retrieved records
S1	("Palliative Care" OR "Palliative Supportive Care" OR "Palliative Surgery" OR "Palliative Therapy" OR "Palliative Treatment" OR "Surgery, Palliative" OR "Therapy, Palliative")	46.569
S2	(Morphine OR "Chloride, Morphine" OR Duramorph OR "MS Contin" OR Morphi* OR "Oramorph SR" OR "SDZ 202 250" OR "SDZ 202-250" OR "SDZ202 250" OR "SDZ202-250" OR "Analgesics, Opioid" OR "Agonist OR Opioid*)	47.475
S3	("Patient Safety" OR Patient Safet*)	90.771
S4	S1 AND S2 AND S3	49

Table 3. Scope review data extraction tool. Niterói/RJ, 2024

Study	Article data extraction
Identification (author, country, year)	
Journal	
Title	
Type of study	
Prescription-related safety practices	
Preparation-related safety practices	
Safety practices related to administration and dose management	
Risks and adverse events	

databases totaled 478 references, and 15 references were obtained from additional records identified by other sources. After removing duplicates, 313 references were obtained. After reading the title and abstract, 29 articles were selected for reading in full, and after applying the exclusion criteria, 21 articles were included in this review. The article screening process is summarized in figure 1.

The 21 studies selected for this scoping review are categorized in table 4 and coded numerically, respecting a decreasing time frame, separated by year of publication, authors, and the journal responsible for publication and type of study.

The majority of the studies found were from the United States of America with 07 studies, followed by Australia with 05 studies, Brazil with 04 studies, England with 02 studies, Canada

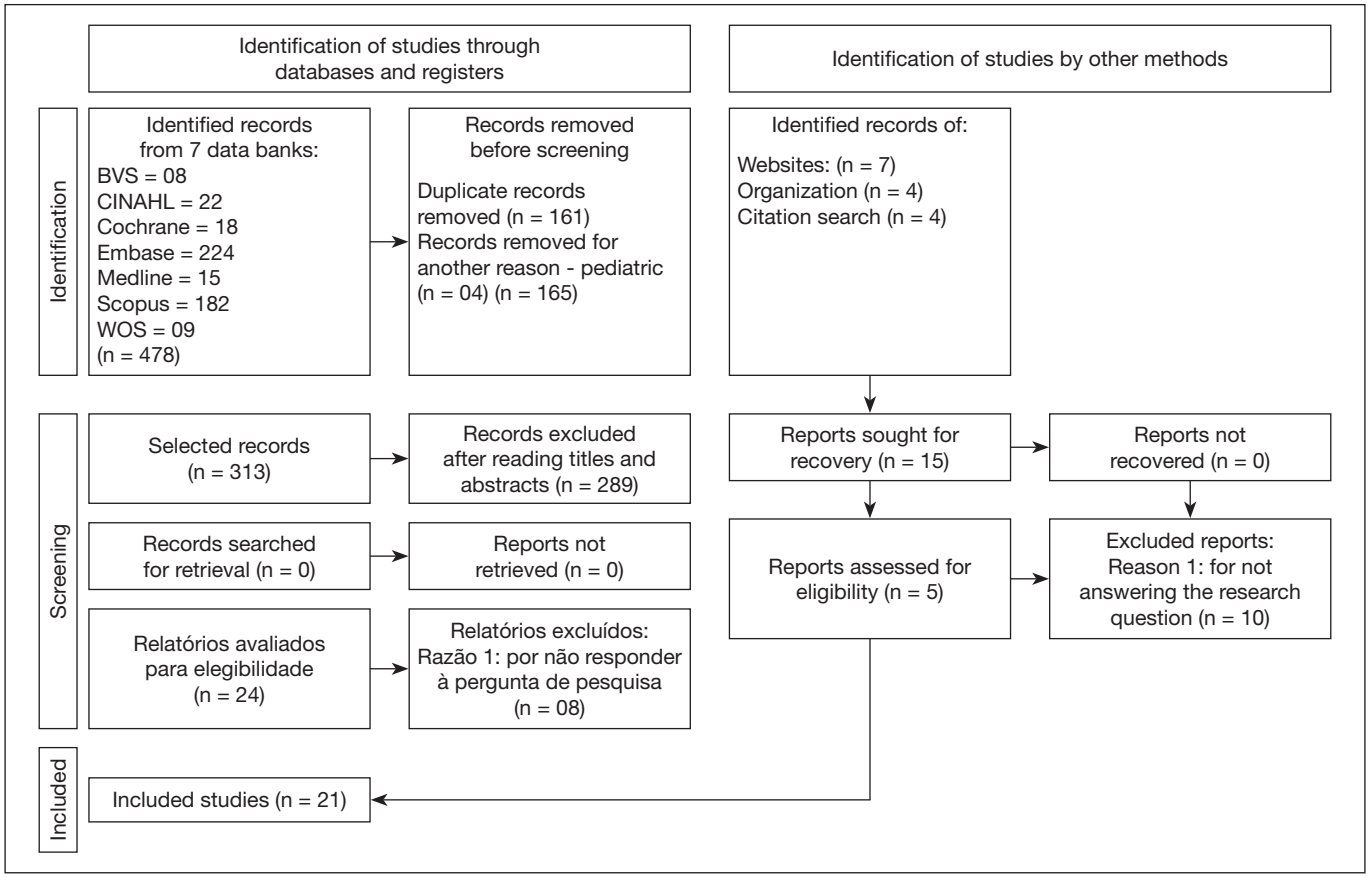

Figure 1. Prisma flowchart. Niterói/RJ, 2024.

From: Page, Matthew J et al. "The PRISMA 2020 statement: an updated guideline for reporting systematic reviews." BMJ (Clinical research ed.) vol. 372 n71. 29 Mar. 2021, doi:10.1136/bmj.n71

with 01 study and the European Union with 02 studies. We identified 04 literature reviews, 02 systematic reviews, 03 retrospective studies, 02 quantitative studies, 02 guidelines, 02 manuals-protocols, 01 qualitative study, 04 expert consensus and 01 cohort study.

Table 4 shows the distribution of the studies (E), identified in descending order by year of publication, with identification of the place of publication, authors responsible for the study, title, journal responsible for publication and type of study.

With the studies selected, the data was extracted and it was possible to categorize: 14 service management practices in the use of morphine, 04 of which related to patient management and 10 related to service organization; 24 safety practices related to the prescription of morphine; 15 safety practices related to the preparation and administration of morphine; and 16 risks and 08 adverse reactions related to the use of morphine were characterized.

The process of managing patient care and follow-up is necessary, as well as setting treatment targets, monitoring abuse and tolerance indicators, and managing possible adverse events. Services should establish clear policies on the treatment of pain and the use of morphine, and establish leadership strategies and staff training, with a view to strengthening the institutional safety culture (Table 5).

Table 4. Characterization of the selected studies, indicating the year of publication, location, author(s), title, journal and type of study. Niterói/RJ, 2024

E1[23]	2024	USA	Kollas, Ruiz and Laughlin	Cohort study
E2[24]	2023	UK	Ismail-Callaghan et al.	Retrospective and Prospective
E3[25]	2023	USA	Paice et al.	Experts' consensus
E4[26]	2022	USA	Yeh et al.	Retrospective and observational
E5[27]	2022	CAN	Lau et al.	Experts' consensus
E6[28]	2020	USA	Curseen, Taj and Grant	Literature Review
E7[29]	2020	BRA	Maiello et al.	Handbook - Protocol
E8[30]	2019	BRA	Abreu	Handbook - Protocol
E9[31]	2019	AUS	Heneka et al.	Qualitative study
E10[32]	2018	AUS	Heneka et al.	Quantitative study
E11[33]	2018	AUS	Heneka et al.	Quantitative study
E12[34]	2018	BRA	Ercolani, Hopf and Schwan	Literature review
E13[35]	2018	AUS	Heneka et al.	Retrospective study
E14[36]	2017	USA	Copenhaver et al.	Literature review
E15[37]	2016	UK	England. National Institute for Health and Care	Guideline
E16[38]	2016	AUS	Heneka et al.	Systematic review
E17[39]	2016	USA	Wiffen, Wee and Moore	Literature review
E18[40]	2014	BRA	Wiermann et al.	Experts' consensus
E19[41]	2012	UK	National Collaborating Centre For, C. National Institute for Health and Clinical Excellence: Guidance.	Guideline
E20[42]	2012	USA	Gudin	Literature review
E21[43]	2010	UK	Raphael et al.	Experts' consensus

Table 5. Service Management Practices in the use of morphine. Niterói/RJ, 2024

1. Management of patient care[33,39-42]	• Setting goals and treatment plans. • Monitoring abuse indicators. • Monitoring tolerance, changes in symptoms and whether discontinuation is possible. • Managing and relieving adverse events.
2. Service Organization[39,40]	• Availability and operation of equipment and supplies. • Existence of clear lines of responsibility, clarifying the responsibility of team members and outlining the work role.
2.1 Staff management and staff levels	• Proper management and allocation of staff to ensure the right mix of skills and personnel for the workload. • Have direct supervision and leadership available at the workplace.
2.2 Policies and procedures	• Existence of formal, written guidance for the proper conduct of work tasks and processes. This can also include situations where procedures are available but contradictory, incomprehensible or of poor quality.

Continue...

Table 5. Service Management Practices in the use of morphine. Niterói/RJ, 2024 – continued

2.3 Hospitalization scheduling and management	• Proper scheduling to manage patient processing, minimizing delays and excessive workload.
2.4 Central support	• Availability of centers to support the operation of the wards / units. This can include information technology support, human resources, concierge services or clinically related services such as radiology and pharmacy.
2.5 Continuous training and education of staff	• Access to correct, timely and appropriate training, both specific, related to the task, and general, related to the organization.
2.6 Communication systems	• Effectiveness of communication processes and systems for exchanging and sharing information between staff, patients, groups, departments and services, including written (documentation), verbal (transfers) and digital (institutional programs) communication systems.
2.7 Safety culture	• Organizational values, beliefs and practices around safety management and learning from mistakes.

The main safety practices related to the prescription of morphine, which should guide the best conduct of the nursing team in order to avoid errors and adverse events for patients on continuous opioid use, are shown in table 6.

Effective communication with the patient is essential. When offering pain treatment with strong opioids to a patient with progressive disease, questions should be asked about: addiction, tolerance, adverse effects and fears about treatment in the final stages of life. Provide verbal and written information about treatment with strong opioids to patients and caregivers, including the following: when and why strong opioids are used to treat pain; how effective they can be; how long pain relief should last; adverse effects and signs of toxicity; follow-up and additional prescribing (rescues); information about who to contact out of hours, especially during the start of treatment (table 7).

Table 8 shows the risks for the occurrence of adverse events related to morphine, as well as drug errors and adverse reactions. The strategies proposed to reduce error involve raising awareness among all those involved, applying local policies at institutional level on psychoactive drugs and regular training in the preparation process and its administration.

Table 6. Patient safety practices - morphine prescription. Niterói/RJ, 2024

Safety Practices related to the prescription of Morphine
Proposed strategies to reduce error[31,36,37,40]
• Use standardized tools to calculate/convert opioids.
• Awareness and application of the conversion policy. Training.
• Be confident/comfortable when checking calculations and conversions. Do the routine check for each dose.
• Identify wrong conversions and take action.
• Access to the pharmaceutical service for questions.
• Effective communication with the whole team.
• Adjust the dose until there is a good balance between acceptable pain control and adverse effects. If this balance is not achieved after a few dose adjustments, re-evaluate the route and dose.
• Robust assessment of patient history and pain.
• Eliminate underlying physiological conditions.
• Recognize previous opioid use.
• Pharmacological conciliation is indicated in cases of pain that is difficult to control.
• Under-prescribing is just as harmful to the patient as over-prescribing.
• Follow dose titration protocols.
• Avoid concomitant use of two opioids, except in SOS rescue situations.
• Preventive measures for nausea, vomiting and constipation should be started alongside the opioid of choice. These are predictable and avoidable adverse risks.
• Always observe the prescription of laxatives associated with dietary changes to avoid constipation.
• Pay attention to analgesic equipoise: intravenous morphine is three times more potent than oral morphine.
• Attention to the principles of analgesia in patients at risk of opioid abuse.
• Have access to specific information such as: active ingredient and specific characteristics, appropriate dose, instructions for use and pharmacological interactions.
• Prevent withdrawal symptoms and complications - assess opioid load; withdrawal symptoms can be avoided with low doses of opioids.
• Prioritize long-acting opioids to minimize analgesia for the interval. Set a limit and review it frequently.
• Talk to the patient before starting therapy, explaining the limitations and establishing a clear definition - upper limit of opioids before the next review.
• Write instructions clearly for the whole team.
• Use drugs in case of detox and withdrawal: naltrexone (opioid antagonist) is used in detox and in programs to help maintain abstinence. It is long-acting (>48 hours). Buprenorphine (partial agonist) is also used to prevent withdrawal symptoms in opioid-dependent patients. Its action on the receptors reduces the effects of any additional opioids. Average maintenance doses range between 12 and 24 mg per day.

Table 7. Patient safety practices - preparation and administration of morphine. Niterói/RJ, 2024

Safety Practices related to the prescription of Morphine Proposed strategies to reduce error[27,32,38-42]
• Know the type of cancer. • Pain assessments with analgesic scales - VAS and pain faces scale. • Knowing the quality of pain - total pain. • Categorize pain. • Know the factors that relieve and exacerbate pain. • Frequent reassessment. • Reassess pain every 30 minutes after administering SOS rescues. • Reassess the patient with each dose administered. • The tablet should not be crushed and consequently should not be administered by nasoenteral or gastronomic tube due to the risk of excessive rapid release of the drug. • Awareness and application of local drug policies, checking for administration errors. • Keep the team trained. • Recognize the signs and symptoms of opioid toxicity. • Effective communication telling patients that nausea may occur when starting treatment with strong opioids or when increasing the dose, but it is likely to be temporary. • Advise on the risk of drowsiness and falls. • Informing patients that treatment for constipation takes longer to work and compliance is important.

Table 8. Risks and adverse events related to the use of morphine. Niterói/RJ, 2024

Risks related to the use of morphine[32,38,44]	• Absence of drug and conversion tables. • Illegible request in the prescription. • Order delayed for forwarding to the responsible unit and dispensing. • Difficulty with calculations, e.g. volume, mg, decimal points. • Unclear policy around checking calculations. • Risk of error in poly drug compounds. • Punitive culture. • Lack of protocols.
Adverse events (drug errors and pharmacological adverse reactions)	
Drug errors	• Opioid conversion error. • Wrong dose given. • Wrong drug given. • Prescription for the wrong patient. • Incorrect title. • Incorrect dose conversion errors for the new route. • Incorrect calculation of opioid dose and rotation. • Human error due to interruptions in preparation.
Adverse reactions	
1. Constipation	• For an indefinite period. • Start with laxatives, stimulants and osmotics. Control constipation in cases of sedation (2-3 days). • Inform the patient that constipation affects almost everyone who receives treatment with strong opioids.
2. Nausea/ vomiting	• Concomitant use of antiemetics. • Evaluate the reduction and/or rotation of opioids.
3. Central nervous system depression	• Consider psychostimulants (naloxone) if symptoms persist. • Watch for excessive drowsiness or signs of intoxication. • Respiratory depression may be associated. • Oxygen supplementation with a nasal catheter can be considered while waiting for the condition to reverse, as well as intravenous hydration. • Avoid combining opioid therapy with another central nervous system depressant.
4. Delirum	• It has been reported to occur with the use of all opioids. • It can be associated with myoclonus, hyperalgesia and cognitive dysfunction (attention, memory and learning deficits, among others). • It is prevalent in patients with high doses, prolonged treatment, use of concomitant psychoactive agents and reduced renal function.
5. Pruritus	• Assess the need for opioid rotation. • Administration of antihistamines. • In severe cases administer naloxone (opioid antagonist).
6. Endocrinopathy	• Be aware that opioids disrupt the hypothalamic-pituitary-gonadal axis system. • Infertility, fatigue, depression, decreased bone density and increased risk of fractures should be considered.
7. Urinary retention	• More common at the start of treatment. • It can be acute or chronic. • Higher prevalence in the elderly (due to benign prostatic hyperplasia or polypharmacy).
8. Addiction/ dependence	• It is recommended to assess the risk of potential opioid abuse using opioid risk assessment tools before starting pain management therapy. • SOS administration, major rescues. • Reports of pharmacological failure to control pain should be evaluated.

DISCUSSION

The main reason why pain control is a priority in cancer treatment is the positive impact it offers to cancer patients in terms of survival and QoL. However, opioids, especially morphine, are highly monitored drugs, related to risks and the occurrence of adverse events in these patients.

Thus, it is necessary for services to establish management and safety practices in the use of these drugs1. Opioids have been the mainstay of cancer pain treatment, but there are challenges to their use; experts report a lack of research to guide clinical practice in the population that uses any opioid for pain control[27].

The evidence from this study showed that services need to have policies and protocols in place on the safe use of morphine. In addition, other factors are relevant, such as: supervision and leadership, establishment of lines of responsibility, effective communication between team members and the institution's safety culture, among others.

Patients in PC with cancer pain are eligible for morphine in cases of moderate to severe pain[21,44]. In a study carried out in 2019 at a Federal Hospital in the city of Rio de Janeiro specializing in PC for adult cancer patients, of the 461 episodes of hospitalization over two months, 429 patients (95%) had pain symptoms, and in 35% of cases the pain was not controlled. In these patients, the Visual Numeric Scale (VNS) was quantified as zero after an average of two days in hospital and, according to the WHO analgesic ladder, 82% of these patients used the 3rd rung of the analgesic ladder, with morphine being the most commonly used drug[45].

It is important to highlight the context of potentially dangerous drugs, i.e. those of high alert (HAMs), including morphine, which presents a high risk of causing significant injuries when there is a failure in the medication process. Weakness in the control and correct use of drugs becomes a problem for public health and can generate costs for the health system, therapeutic unfeasibility and even failure, increasing the number of avoidable adverse events, with injuries ranging from mild to catastrophic[45].

A study reinforced the importance of safety in the stages involving the preparation of HAMs, as the research found an occurrence of errors involving opioid medications such as fentanyl, tramadol and morphine[46]. In turn, a retrospective observational study with palliative medicine in a hospital setting evaluated the effectiveness of long-term opioid therapy in patients at the end of life. The research describes continuous opioid infusion can improve patient comfort with persistent or progressive symptoms, but requires clinical experience and attention to pharmacokinetics. The same study found that opioid infusions by active PC teams were potentially inappropriate in the hospital and academic medical center under study, and that this was associated with increased suffering of patients and work teams[28].

The evidence observed in this study showed that hospital management must guarantee a safe environment, mainly by establishing training programs aimed at pain control and the administration of opioid drugs, including morphine, as a practice to reduce adverse events. Board members of the

Canadian Society of Palliative Care Physicians have developed recommendations to promote opioid safety in adult palliative care patients. The recommendations were divided into 6 major domains; domain 2, considered a high priority, concentrates measures that reinforce the need for mandatory training for the healthcare team[46]. The Brazilian National Academy of Palliative Care (*Academia Nacional de Cuidados Paliativos* - ANCP) reiterates this need, stating that institutional protocols and routines must be made available and easily accessible for professionals to consult.

In a hospital environment, errors related to the use of pharmaceuticals are an important concern, and can be favored by factors such as lack of effective communication, as well as lack of access to documentation or distorted information from work teams. A survey with a retrospective analysis[24] of case notes and a prospective study analyzing the improvement of the quality of intervention in an inpatient unit, evaluated how communication was with patients in PC about the appropriate direction of opioid use and applied an improvement report. Three cycles of meetings were held to plan, do, study, act and document. In the retrospective analysis, it was found that communication regarding how to manage the patient in PC was inefficient and after documenting the discussions with everyone involved in this management, the scores improved to an adequate level.

In this context, it is worth highlighting the Safety Protocol in the Prescription, Use and Administration of Drugs established by Ordinance No. 2095 (2013) of the Brazilian Ministry of Health, with the purpose of promoting safe practices to the use of drugs in healthcare establishments[47].

Among the different types of errors related to morphine, prescription errors are the most common and occur at the beginning of the process of activities that bring the drug to the patient, according to a study[12] carried out in 2018. The most frequent errors involving prescription include drug, route or dose, or the frequency wrong. These errors are responsible for almost 50% of medication errors, and are most often identified by pharmacists and nurses before dispensing and administration occur.

Prompt assessment of pain helps with the analgesia process. In a systematic review that aimed to investigate the use and performance of the EVN pain scale, pain faces scale and Visual Analogue Scale (VAS), it was identified that EVN had better compliance in use in 15 of the 19 studies that addressed the case and was the most recommended tool in 11 studies, with higher compliance rates, better responsiveness, ease of use and good applicability in relation to pain faces scale and EAV. Overall, the studies analyzed agreed that the applicability scores of EVN and EAV are systematically higher[32,37-41,48-50].

According to the Brazilian Consensus on Cancer-Related Pain Control, patients with severe pain should be treated with oral or intravenous opioids when clinically justifiable. The need to continually reevaluate the patient with each new dose is an inherent action in pain treatment[40]. The review of this study also highlights the need for attention to analgesic equipotency. Intravenous morphine is three times more potent than oral morphine, and should not be macerated and administered gastrically due to the risk of impregnation[28,38-40,48]. Patient satisfaction with the relief obtained and the occurrence of adverse events must be systematically reevaluated.

According to the WHO[49], errors arising from pharmacological therapy are the result of faulty processes and procedures during care. Errors are susceptible at any stage of the medication system: prescription, dispensing, preparation, administration and monitoring; being the responsibility of all professionals involved in care. Experts who approved a consensus of guidelines for pain patients using opioids described that these drugs have been the basis of cancer pain treatment, but there are serious challenges to their use, including an impressive lack of research to guide clinical practice[25].

Adverse Drug Reactions (ADRs) are characterized by the hypothesis of a causal relationship between the drug and the harmful or undesirable response that may occur, and are predictable in patients using opioids. In a study carried out in a health network in the state of Minas Gerais[50] from April 2019 to March 2020, 93 ADR notifications were analyzed. Among the main therapeutic classes involved, opioids were detected 6 times, and among opioids, morphine stood out as the most reported drug, 4 times. A recent article, published in 2022, identified body itching in 33.3% of reported occurrences, including: hiccups (8.3%), drowsiness (8.3%), sweating (8.3%), dizziness (8.3%) and vomiting (8.3%)[51].

More up-to-date studies have included the occurrence of endocrinopathies as adverse reactions in the use of opioids, citing erectile dysfunction, reduced libido, infertility and decreased bone density, which may favor the occurrence of fractures[27]. *Delirium* is likely to occur in patients on continuous use of opioids, common in patients with high doses, in prolonged treatment, in use of concomitant psychoactive agents and in cases of reduced renal function. Urinary retention has been mentioned in more up-to-date clinical guidelines[25]. According to these studies, it is common at the beginning of opioid treatment and is more prevalent in the elderly due to benign prostatic hyperplasia or polypharmacy. Therefore, nursing teams need to be aware of these possible adverse reactions.

For best practices in administration, double checking of the prescription between the nurse and the nursing technician stands out, which guarantee the safety of morphine administration[46] and the execution of the "nine rights" of drug administration, which are: patient verification right, right drug, right route, right time, right dose, right record, right action, right form and right response. This verification does not guarantee that administration errors will not occur, but following it can prevent a significant portion of these events, improving the safety and quality of care provided to the patient during the drug administration process[51].

The strength of this production is in presenting the best evidence to support safety practices in palliative cancer patients using morphine. This is a relevant topic for global public health, given the potential for errors with high-alert drugs, especially morphine, and their adverse events.

It is necessary to expand research in this area, with each psychotropic drug being able to be specified in the context of hospital complexity or specifically for patients who use it in home care. Patient safety and especially the correct use of drugs must be reflected from professional training to continuing education for professionals providing care, ensuring safe healthcare practices.

CONCLUSION

This scoping review identified safety practices related to the use of morphine in palliative cancer patients from its prescription, preparation and administration, and addressed risk management and adverse events related to this opioid. Through this study, professionals can plan safe care, promoting better control of cancer pain. This study also contributes to the use of morphine as a treatment proposal, especially for cancer patients undergoing PC who live with intense pain and who benefit greatly from its use, bringing a positive impact on the survival and QoL of these patients.

AUTHORS' CONTRIBUTIONS

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Data Collection, Conceptualization, Project Management, Research, Methodology, Writing - Preparation of the Original, Writing - Review and Editing, Supervision

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