

Safety of cancer patients using morphine: scoping review protocol

Segurança do paciente oncológico em uso de morfina: protocolo de escopo
Seguridad de los pacientes con cáncer que utilizan morfina: protocolo de alcance

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ABSTRACT

Objective: To map the patient safety practices performed in palliative cancer patients using morphine for pain control. **Method:** A scoping review to answer the following question: What is the evidence on the patient safety practices performed in palliative cancer patients using morphine for pain control? The search will be carried out in the MEDLINE, LILACS, Scopus, Embase, Web of Science, Cochrane and CINAHL databases, as well as in the gray literature. After the search, all citations will be grouped in the Rayyan software and the duplicates will be removed. Titles and abstracts will be selected by two independent reviewers. The full text of the selected citations will be evaluated in detail in relation to the inclusion criteria by two independent reviewers. The extracted data will be presented in diagram or table formats so that it aligns with the objective of this scoping review, and a narrative abstract will be provided.

DESCRIPTORS: Research in Nursing Administration; Patient Safety; Pain Management; Morphine; Drug-Related Side Effects and Adverse Reactions.

RESUMO

Objetivo: Mapear as práticas de segurança do paciente realizadas em pacientes oncológicos paliativos em uso de morfina para o controle da dor. **Método:** Revisão de escopo para responder à pergunta: Quais as evidências sobre as práticas de segurança do paciente realizadas em pacientes oncológicos paliativos que fazem uso de morfina para o controle da dor? A busca será realizada nas bases de dados MEDLINE, LILACS, Scopus, Embase, Web of Science, Cochrane e CINAHL e literatura cinzenta. Após a busca, todos as citações serão agrupadas no software Rayyan e as duplicatas removidas. Os títulos e resumos serão selecionados por dois revisores independentes. O texto completo das citações selecionadas será avaliado em detalhes em relação aos critérios de inclusão por dois revisores independentes. Os dados extraídos serão apresentados em um diagrama ou forma tabular de maneira que se alinhe com o objetivo desta revisão de escopo, e um resumo narrativo será fornecido.

DESCRITORES: Pesquisa em Administração de Enfermagem; Segurança do Paciente; Manejo da Dor; Morfina; Efeitos Colaterais e Reações Adversas Relacionados a Medicamentos.

RESUMEN

Objetivo: Mapear las prácticas de seguridad del paciente realizadas en pacientes con cáncer paliativo que utilizan morfina para el control del dolor. **Método:** Revisión de alcance para responder a la pregunta: ¿Cuál es la evidencia sobre las prácticas de seguridad del paciente que se implementan en pacientes con cáncer paliativo que utilizan morfina para el control del dolor? La búsqueda se realizará en las bases de datos MEDLINE, LILACS, Scopus, Embase, Web of Science, Cochrane y CINAHL y literatura gris. Después de la búsqueda, todas las citas se agruparán en el software Rayyan y se eliminarán los duplicados. Los títulos y resúmenes serán seleccionados por dos revisores independientes. El texto completo de las citas seleccionadas será evaluado en detalle según los criterios de inclusión por dos revisores independientes. Los datos extraídos se presentarán en un diagrama o en forma de tabla para que se alineen con el objetivo de esta revisión de alcance, y se proporcionará un resumen narrativo.

DESCRIPTORES: Investigación en Administración de Enfermería; Seguridad del Paciente; Manejo del Dolor; Morfina; Efectos Colaterales y Reacciones Adversas Relacionadas con los Medicamentos.

INTRODUCTION

In 2019, the Institute of Healthcare Improvement published the *Advancing the Safety of Acute Pain Management* guide with recommendations for patient safety, due to its high prevalence in hospitalized patients, which makes them vulnerable to the occurrence of errors and adverse events in health⁽¹⁾. Expressive morbidity, avoidable mortality and additional expenses are evident when health care is unsafe, and they can be avoided⁽²⁾.

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

Pain affects 60% to 80% of the cancer patients, with 25% to 30% already reporting pain at the time of diagnosis, and 70% to 90% of the patients with advanced disease presenting moderate to severe pain⁽¹⁾. There is evidence that the control of the cancer-related symptoms contributes to improved survival, with emphasis on pain control and a direct impact on quality of life^(3,4).

Although analgesic treatment is available for 70% to 90% of the cancer patients, it is inadequate in 40% to 50% of the cases. Pain undertreatment is a reality in several developing countries⁽⁵⁾. 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^(2,6).

Morphine is a potent first-choice opioid when the use of non-steroidal anti-inflammatory drugs and weak opioids is no longer effective for the patient. It presents no dose limit, considering as dose limit the one providing pain relief, limited by the uncontrollable or intolerable side effects⁽⁷⁾. The dose is adjusted to achieve analgesia, without excessive sedation, and reduced when pain decreases⁽⁸⁾.

Drug-related adverse events are predictable in patients on continuous use of opioids, and reactions to the medication can occur, such as impregnations causing drowsiness and decreased level of consciousness⁽⁹⁾, difficult-to-control emetic conditions, and constipation, in addition to errors related to prescription, stages of preparation and administration of the medication^(10,11). Patient safety practices must be implemented in order to avoid adverse events, with continuous monitoring by the nurse in the opioid therapeutic response^(12,13).

Patients using high surveillance medications, such as opioid analgesics, have an increased risk for the occurrence of adverse events, whether related to an adverse reaction to the medication itself, or to an error in medication administration⁽¹⁴⁾. It is known that most drug-related adverse events occur due to failures at the systemic level. Therefore, knowing the processes related to its administration will assist in identifying causes of failures and in proposing the implementation of safety barriers to contribute to the prevention and reduction of harms to the patients⁽¹⁵⁾.

Drug-related adverse events must be notified. This is a participatory management strategy,

which contributes to quantifying the errors and failures occurred in the care processes. Through it, patient safety indicators are generated, and actions are planned aimed at reducing the incidence of the event⁽¹⁶⁾.

Despite the relevance of the topic, the discussion regarding patient safety took on greater prominence through the report by the American Institute of Medicine entitled *To err is Human: Building a safer health care system*, which brought alarming data on adverse events and related deaths. Medication errors were importantly highlighted in the report, since they caused 7,391 annual deaths of Americans in hospitals and more than 10,000 deaths in outpatient institutions⁽¹⁴⁾.

Currently, 20 years after the publication of the *To Err is Human* report, there are many patient safety challenges. Since then, there has been major international mobilization with wide publication by the World Health Organization (WHO), the Joint Commission and the Agency for Healthcare Research & Quality (AHRQ)⁽¹⁷⁾. At the global level, the creation of the World Alliance for patient safety and, subsequently, of the six international goals for patient safety, drew the attention of health managers and professionals towards the implementation of patient safety protocols and practices⁽¹⁸⁾.

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

Considering the relevance of the topic, a scoping review on safety practices in cancer patients using morphine may be used to support actions to prevent the occurrence of adverse events related to this drug, as well as in research, in order to identify gaps on the topic and the possibility of a future systematic review. Thus, the objective of this review is to map the patient safety practices performed in palliative cancer patients using morphine for pain control.

METHOD

The proposed scoping review will be conducted following the JBI methodology for scoping reviews⁽¹⁹⁾. The protocol was registered in the Open Science Framework (OSF) with the following link: osf.io/k4rgq.

Review question

What is the evidence on the patient safety practices performed in palliative cancer patients using morphine for pain control? And as sub-questions:

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

Inclusion criteria

Participants

The participants of this review will be cancer patients in palliative care using morphine for pain control. Studies involving adult patients in palliative care for any oncological pathologies will be included. The patients must be using

morphine for pain control, regardless of the route.

Concept

This review will include studies that address patient safety and risk management practices. These practices aim at reducing, to an acceptable minimum, the risk of unnecessary harm associated with health care^(1,14). Studies that address patient safety during the prescription of morphine, preparation and administration of doses will be included, as well as the prevention of adverse events related to this medication, including adverse reactions and administration errors.

Context

For the context, studies with patients hospitalized or followed-up on an outpatient basis will be included.

Types of sources

This scoping review will consider 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 will also be included. This review will also consider series and case reports, in addition to clinical practice protocols and guidelines. Literature reviews, theses and text and opinion articles will also be considered for inclusion in this scoping review.

The databases to be searched include: MEDLINE (PubMed), LILACS (BVS Regional), Scopus, Embase, Web of Science, Cochrane and CINAHL. The search for gray literature will

include: websites of pain societies and organizations, Digital Library of Theses and Dissertations, clinical protocols and guidelines recognized by governmental bodies and the National Institute for Health Care and Excellence (NICE).

Search strategy

A three-stage search strategy will be used for this review. A limited initial search in MEDLINE (Pubmed) and CINAHL was carried out, followed by the analysis of the words of the text contained in the titles and abstracts, and the index terms used to describe the articles. Charts 1 and 2 present the complete search strategies for MEDLINE via PubMed and CINAHL that were carried out on March 1st, 2021, using the "advanced search" feature with the MeSH (Medical Subject Headings) descriptors and the controlled vocabulary developed by the US National Library of Medicine and *OR* and *AND* Boolean operators.

Chart 1 - Search strategy for the MEDLINE database via PUBMED. Niterói. Rio de Janeiro, 2021.

Query	Mapping of the terms	Records retrieved
#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 Malignant*[tiab] OR Neoplasm*[tiab] OR Tumor*[tiab])	36,436

#2	(<i>Morphine</i> [mh] OR <i>Morphine</i> [tiab] OR " <i>Chloride, Morphine</i> "[tiab] OR <i>Duramorph</i> [tiab] OR " <i>MS Contin</i> "[tiab] OR <i>Morphi*</i> [tiab] OR " <i>Oramorph SR</i> "[tiab] OR "SDZ 202 250"[tiab] OR "SDZ 202-250"[tiab] OR "SDZ202 250"[tiab] OR "SDZ202-250"[tiab] OR " <i>Analgesics, Opioid</i> "[tiab] OR <i>Agonist</i> [tiab] OR <i>Opioid*</i> [tiab])	301,377
#3	("Patient Safety"[mh] OR "Patient Safety"[tiab] OR <i>Patient Safet*</i> [tiab])	47,135
#4	#1 AND #2 AND # 3	10

Source: Elaborated by the authors, 2021.

Chart 2 - Search strategy for the CINAHL database.

Niterói. Rio de Janeiro, 2021.

Query	Mapping of the terms	Records retrieved
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	(<i>Morphine</i> OR " <i>Chloride, Morphine</i> " OR <i>Duramorph</i> OR " <i>MS Contin</i> " OR <i>Morphi*</i> OR " <i>Oramorph SR</i> " OR "SDZ 202 250" OR "SDZ 202-250" OR "SDZ202 250" OR "SDZ202-250" OR " <i>Analgesics, Opioid</i> " OR " <i>Agonist</i> " OR <i>Opioid*</i>)	47,475
S3	("Patient Safety" OR <i>Patient Safet*</i>)	90,771
S4	S1 AND S2 AND S3	49

Source: Elaborated by the authors, 2021.

A complete secondary search will be performed in all databases included, using the keywords and index terms identified in the initial search. In order to help identifying any additional studies, a tertiary literature search will be carried out by examining the reference lists of

all the literature that meets the inclusion criteria for this review. If applicable, the reviewers may contact the authors of the primary studies for more information. This review will consider studies in any language and without time restrictions.

Evidence selection

After the search, all identified citations will be grouped and loaded into the Rayyan software (Qatar Computing Research Institute, Doha, Qatar) and the duplicates will be identified and removed by the software. The titles and abstracts will be selected by two reviewers and then imported into the *EndNote* reference manager (*Clarivate Analytics*, PA, USA). The full text of the selected citations will be organized into folders and evaluated in detail by two independent reviewers in relation to the inclusion criteria. The reasons for excluding full-text studies that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that could arise between the reviewers at each stage of the study selection process will be resolved through discussion or with the participation of a third reviewer.

The selection results will be presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses for Scoping Reviews (PRISMA -ScR) flow chart⁽²⁰⁾.

Data extraction

The data from the studies included in the scoping review will be extracted by two independent reviewers, using a data extraction tool developed by the reviewers (Chart 3). The extracted data will include specific details

about the population, concept, context, study methods and main conclusions relevant to the review objective. Any differences that could arise between the reviewers will be resolved through discussion or with a third reviewer.

morphine, risk management and adverse events. A descriptive and narrative analysis will accompany the tabulated and mapped results, describing how the results relate to the review objective and question.

Chart 3 - Data extraction instrument

Study	Extraction of data from the article
Identification (author, country, year)	
Journal, Impact Factor	
Title	
Type of study	
Type of cancer disease	
Morphine dose in use	
Administration route, use of analgesia pump	
Safety practices related to prescription	
Safety practices related to preparation	
Safety practices related to administration, and dose management	
Safety practices related to risk management and adverse events	

Source: Elaborated by the authors, 2020.

DATA ANALYSIS AND PRESENTATION

The extracted data will be presented in the form of tables and diagrams, so that they align with the objective of this scoping review. The data shall inform about the type of study, type of cancer disease, morphine dose in use, administration route, practices related to prescription, preparation and administration of

REFERENCES

1. Institute of Healthcare Improvement. Advancing the Safety of Acute Pain Management [internet]. Boston, Massachusetts. 2019 [Cited 2020 jul 30]. Available from: <http://www.ihl.org/resources/Pages/Publications/Advancing-the-Safety-of-Acute-Pain-Management.aspx>.
2. Shafi S, Collinsworth AW, Copeland LA, Collinsworth AW, Ogola GO, Qiu T et al. Association of Opioid-Related Adverse Drug Events With Clinical and Cost Outcomes Among Surgical Patients in a Large Integrated Health Care Delivery System. *JAMA Surg* [internet]. 2018 [Cited 2020 jul 30];153(8):757–763. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6142954/>. doi: <https://doi.org/10.1001/jamasurg.2018.1039>.
3. Knaul FM, Bhadelia A, Rodriguez NM, Arreola-Ornelas H, Zimmermann C. The Lancet Commission on Palliative Care and Pain Relief—findings, recommendations, and future directions. *The Lancet Global Health* [internet]. 2018 [Cited 2020 jul 30];6:S5–6. Available from: [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(18\)30082-2/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30082-2/fulltext). doi: [https://doi.org/10.1016/s2214-109x\(18\)30082-2](https://doi.org/10.1016/s2214-109x(18)30082-2).
4. Henson L A, Maddocks M, Evans C, Davidson M, Hicks S, & Higginson IJ. Palliative Care and the Management of Common Distressing Symptoms in Advanced Cancer: Pain, Breathlessness, Nausea and Vomiting, and Fatigue. *J Clin Oncol* [Internet]. 2020 [Cited 2020 jul 30];38(9):905–14. Available from: <https://pubmed.ncbi.nlm.nih.gov/32023162/>. doi: <https://doi.org/10.1200/JCO.19.00470>.
5. Garcia JBS, Lopez MPG, Barros GAM, Muñiz HGM, Olea MAOA, Bonilla P et al. Latin American Pain Federation position paper on

- appropriate opioid use in pain management. *Pain Rep* [Internet]. 2019 [Cited 2020 jul 30];4(3):e730. Available from: <https://europepmc.org/article/med/31583347>. doi: <https://doi.org/10.1097/PR9.0000000000000730>.
6. Network NCC. NCCN Clinical Practice Guidelines in Oncology [Internet]. Pennsylvania. 2020 [Cited 2020 jul 30]. Available from: https://www.nccn.org/professionals/physician_gls/default.aspx.
 7. Sampiao SG dos SM, Motta LB da, Caldas CP. Medicamentos e Controle de dor: Experiência de um Centro de Referência em Cuidados Paliativos no Brasil. *Rev Bras Cancerol* [Internet]. 2019 out 24 [Cited 2020 jul 30];65(2):e-13365. Available from: <https://rbc.inca.gov.br/revista/index.php/revista/article/view/365>.
 8. doi: <https://doi.org/10.32635/2176-9745.RBC.2019v65n2.365>.
 9. Georgiou E, Paikousis L, Lambrinou E, Merkouris A, Papathanassoglou EDE. The effectiveness of systematic pain assessment on critically ill patient outcomes: A randomised controlled trial. *Aust Crit Care* [Internet]. 2020 [Cited 2021 mar 11];33(5):412-419. Available from: <https://pubmed.ncbi.nlm.nih.gov/31818632/>. doi: <https://doi.org/10.1016/j.aucc.2019.09.004>.
 10. Winn AN, Check DK, Farkas A, Fergestrom NM, Neuner JM, Roberts AW. Association of Current Opioid Use With Serious Adverse Events Among Older Adult Survivors of Breast Cancer. *JAMA Netw Open* [Internet]. 2020 [Cited 2020 ago 3];3(9):e2016858. Available from: <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770642>. doi: <https://doi.org/10.1001/jamanetworkopen.2020.16858>.
 11. Corli O, Roberto A, Bennett MI, Galli F, Corsi N, Rulli E et al. Nonresponsiveness and Susceptibility of Opioid Side Effects Related to Cancer Patients' Clinical Characteristics: A Post-Hoc Analysis. *Pain Pract* [Internet]. 2018 [Cited 2020 ago 3];18:748-757. Available from: <https://pubmed.ncbi.nlm.nih.gov/29220110/>. Doi: <https://doi.org/10.1111/papr.12669>
 12. Els C, Jackson TD, Kunyk D, Lappi VG, Sonnenberg B, Hagtvedt R et al. Adverse events associated with medium- and long-term use of opioids for chronic non-cancer pain: an overview of Cochrane Reviews. *Cochrane Database of Syst Rev* [Internet]. 2017 [Cited 2020 dez 11]; (Issue 10). Art. No.: CD012509. Available from: <https://pubmed.ncbi.nlm.nih.gov/29084357/>. Doi: <https://doi.org/10.1002/14651858.CD012509.pub2>.
 13. Prado BL, Gomes DBD, Usón Júnior PLS, Taranto P, França MS, Eiger D et al. Continuous palliative sedation for patients with advanced cancer at a tertiary care cancer center. *BMC Palliat Care* [Internet]. 2018 [Cited 2021 mar 11];17(1):13. Available from: <https://pubmed.ncbi.nlm.nih.gov/29301574/>. doi: <https://doi.org/10.1186/s12904-017-0264-2>.
 14. Compton P, Blacher S. Nursing Education in the Midst of the Opioid Crisis. *Pain Man Nurs* [Internet]. 2020 [Cited 2020 ago 3];21(1):35-42. Available from: <http://lianxidoors.com/journal/pain-management-nursing/vol/21/issue/1>. doi: <https://doi.org/10.1016/j.pmn.2019.06.006>.
 15. Dzau VJ, Shine KI. Two Decades Since To Err Is Human: Progress, but Still a "Chasm". *JAMA* [Internet]. 2020 [Cited 2021 mar 12];324(24):2489-2490. Available from: <https://pubmed.ncbi.nlm.nih.gov/33351025/>. doi: <https://doi.org/10.1001/jama.2020.23151>. PMID: 33351025.
 16. Idris MK, Al-Talib TA. Assessment of Outpatients' medical Prescriptions' Legibility, completeness, and rational use of medicines: Sudan study. *World Journ of Pharm Res* [Internet]. 2017 [Cited 2021 mar 12];6(3):1-42. Available from: <https://www.semanticscholar.org/paper/ASSESSMENT-OF-OUTPATIENTS%27-MEDICAL-PRESCRIPTIONS%27-Idris-Al-Talib/b4e06c58d78acf1f819b202a38aafb4484ff8921>.
 17. Alves BMCS, Andrade TNG, Santos SC, Goes AS, Santos AS, Lyra Junior DP et al. Harm Prevalence Due to Medication Errors Involving High-Alert Medications: A Systematic Review. *J Patient Saf* [Internet]. 2021 [Cited 2021 mar 12];17(1):e1-9.

- Available from:
<https://pubmed.ncbi.nlm.nih.gov/32217932/>. doi:
<https://doi.org/10.1097/PTS.0000000000000649>.
19. Al-Jumaili AA, Doucette WR. Comprehensive Literature Review of Factors Influencing Medication Safety in Nursing Homes: Using a Systems Model. *J Am Med Dir Assoc* [Internet]. 2017 [Cited 2021 mar 11];18(6):470-488. Available from: <https://pubmed.ncbi.nlm.nih.gov/28242191/>. doi: <https://doi.org/10.1016/j.jamda.2016.12.069>.
20. Santos PRA, Rocha FLR, Sampaio CSJC. Actions for safety in the prescription, use and administration of medications in emergency care units. *Rev Gaúcha Enferm* [Internet]. 2019 [cited 2021 mar 12];40(spe):e20180347. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1983-14472019000200423&lng=en. doi: <https://doi.org/10.1590/1983-1447.2019.20180347>.
21. The Joanna Briggs Institute. JBI Manual for Evidence Synthesis [Internet]. Adelaide: JBI. 2020 [Cited 2021 mar 12]. Available from: <https://wiki.jbi.global/display/MANUAL>.
22. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac, D et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* [Internet]. 2018 [Cited 2020 ago 3];169(7):467-473. Available from: <http://www.prisma-statement.org/Extensions/ScopingReviews>. doi:10.7326/M18-0850.