PATIENT SAFETY IN THE ADMINISTRATION OF ANTINEOPLASTIC CHEMOTHERAPY AND OF IMMUNOTHERAPICS FOR ONCOLOGICAL TREATMENT: SCOPING REVIEW

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ABSTRACT

Objective: to identify and synthesize the scientific evidence on cancer patient safety in the administration of antineoplastic and immunotherapeutic chemotherapeutic agents.

Method: a scoping review, according to the Joanna Briggs Institute and to the recommendations of the PRISMA-ScR international guide. The research was conducted in five electronic databases, the Cochrane Library and eight catalogs of theses and dissertations. The inclusion criteria were the following: studies related to patient safety in the administration of antineoplastic and immunotherapeutic chemotherapy by nurses in places where cancer care occurs, published entirely in Portuguese, Spanish and/or English, with no time limit. The extracted data were analyzed and synthesized in narrative form.

Results: a total of 14,444 records were retrieved and 47 studies were kept for review. Most publications (44.7%) had a qualitative approach, while 40.4% were quantitative and 14.9%, mixed. When summarizing the findings, the following themes emerged: Safety standards in parenteral administration of antineoplastic chemotherapy; Good practices for patient safety using oral antineoplastic therapy; Administration and safe handling of immunotherapies; Prevention and management of errors related to the administration of antineoplastic and immunotherapeutic chemotherapeutic agents.

Conclusion: patients safety with cancer in the administration of antineoplastic therapy occurs when there is implementation of evidence-based protocols, continuing education of nurses and implementation of safety standards and processes, as a strategy to prevent errors in drug administration.


SEGURANÇA DO PACIENTE NA ADMINISTRAÇÃO DE QUIMIOTERAPIA ANTINEOPLÁSICA E IMUNOTERÁPICOS PARA TRATAMENTO ONCOLÓGICO: SCOPING REVIEW

RESUMO

Objetivo: identificar e sintetizar as evidências científicas sobre segurança do paciente oncológico na administração de quimioterápicos antineoplásicos e imunoterápicos.

Método: scoping review, conforme Joanna Briggs Institute e as recomendações do guia internacional PRISMA-ScR. Realizou-se pesquisa em cinco bases de dados eletrônicos, Biblioteca Cochrane e oito catálogos de teses e dissertações. Os critérios de inclusão foram: estudos relacionados à segurança do paciente na administração de quimioterapia antineoplásica e imunoterápicos, por enfermeiros, em locais onde ocorre o cuidado oncológico, publicados integralmente nas línguas portuguesa, espanhola e/ ou inglesa, sem limite temporal. Os dados extraídos foram analisados e sintetizados na forma narrativa.

Resultados: foram recuperados um total de 14.444 registros e mantidos 47 estudos para a revisão. A maioria das publicações (44,7%) tinha abordagem qualitativa, enquanto 40,4% eram quantitativas e 14,9% mistas. Na sumarização dos achados emergiram as seguintes temáticas: Padrões de segurança na administração de quimioterápicos antineoplásicos via parenteral; Boas práticas para segurança do paciente em uso de terapia antineoplásica oral; Administração e manuseio seguro de imunoterápicos; Prevenção e manejo dos erros relacionados à administração de quimioterápicos antineoplásicos e imunoterápicos.

Conclusão: a segurança do paciente oncológico na administração da terapia antineoplásica ocorre quando há a implementação de protocolos, baseados em evidências, educação permanente dos enfermeiros e efetivação de padrões e processos de segurança, como estratégia para prevenção de erros na administração dos fármacos.


LA SEGURIDAD DEL PACIENTE EN LA ADMINISTRACIÓN DE QUIMIOTERAPIA ANTINEOPLÁSICA E INMUNOTERÁPICOS PARA EL TRATAMIENTO ONCOLÓGICO: SCOPING REVIEW

RESUMEN

Objetivo: identificar y sintetizar las evidencias científicas sobre la seguridad del paciente oncológico en la administración de quimioterápicos antineoplásicos e inmunoterápicos.

Método: scoping review, de acuerdo con el Joanna Briggs Institute y con las recomendaciones de la guía internacional PRISMA-ScR. La investigación se realizó en cinco bases de datos electrónicos, en la Biblioteca Cochrane y en ocho catálogos de tesis y disertaciones. Los criterios de inclusión fueron los siguientes: estudios relacionados con la seguridad del paciente en la administración de quimioterapia antineoplásica e inmunoterápicos a cargo de enfermeros, en los lugares donde se ofrecen cuidados oncológicos, publicados por completo en portugués, español y/o inglés, sin límite de tiempo. Los datos extraídos se analizaron y sintetizaron de forma narrativa.

Resultados: se recuperó un total de 14.444 registros y se mantuvieron 47 estudios para la revisión. La mayoría de las publicaciones (44,7%) tuvo un enfoque cualitativo, mientras que el 40,4% fue cuantitativo y el 14,9% combinado. En el resumen de los hallazgos emergieron las siguientes temáticas: Estándares de seguridad en la administración de medicamentos antineoplásicos para la quimioterapia vía parenteral; Buenas prácticas para la seguridad del paciente en el uso de la terapia antineoplásica oral; Administración y manipulación seguras de los medicamentos inmunoterápicos; Prevención y manejo de los errores relacionados con la administración de quimioterápicos antineoplásicos e inmunoterápicos para la quimioterapia.

Conclusión: la seguridad del paciente oncológico en la administración de la terapia antineoplásica se materializa cuando se implementan protocolos basados en evidencias, educación permanente de los enfermeros y efectivización de estándares y procesos de seguridad, como estrategia para prevenir errores en la administración de los fármacos.

INTRODUCTION

Cases of malignant neoplasms are growing every day in the world. It is estimated that by 2030 the number of people with this disease will be around 21.4 million, and that 13.2 million will die, due to the impact of changes in the sociodemographic and epidemiological patterns of the world population.\(^1\) In Brazil, the estimate for the 2018-2019 biennium was 600,000 new cases of cancer each year.\(^2\)

The treatment of malignant neoplasms is complex, multidisciplinary and essentially depends on their clinical staging, on the pathological characteristics of the tumor and on predictive and prognostic factors.\(^1,3\)

Antineoplastic chemotherapy (CTX) is one of the most preferred modalities for the treatment of malignant neoplasms. According to its purpose, CTX can be classified as adjuvant, following curative surgery; neoadjuvant, indicated for partial tumor reduction; curative, used to achieve complete tumor control; and palliative, which aims to minimize the symptoms arising from tumor proliferation with increased survival.\(^3-5\)

In addition to CTX, surgery, radiotherapy, (teletherapy and brachytherapy), other treatments – such as hormone therapy, immunotherapy, nanotechnology, and gene and molecular therapies – are used to treat some types of tumors. These techniques can be employed alone or in combination to provide better results.\(^3,6\)

Regarding immunotherapy, clinical trials provide information on the efficacy of these agents in different types of malignant neoplasms. Thus, there is a need for protocols and bundles that have guidelines with an emphasis on patient safety in the administration of immunotherapies to enable them to provide safe and evidence-based care.\(^7-8\)

It is noteworthy that immunotherapies differ in their pathophysiology and have high specificity for tumor cells, in addition to limited toxicity to normal cells, unlike conventional cancer therapies.\(^6-7\) Therefore, it is essential to identify the scientific evidence of patient safety in the administration of both chemotherapeutic and immunotherapeutic agents.

In this context, ensuring the safety of patients is challenging, since incidents related to CTX preparation and administration have an incidence of approximately 2% to 5% per year. Thus, implementing actions to improve patient safety and quality in cancer services are based, above all, on the need to implement strategies to prevent adverse events.\(^9\) When considering health care environments for more complex care – such as cancer sectors – the occurrence of undesirable events increases dramatically, since the clinical conditions of the patients and the diversity of treatments require more skill and specific scientific knowledge from the professionals.

Given the above, the relevance of this study is to provide a mapping of the main measures aimed at ensuring the safety of cancer patients during the administration of antineoplastic therapy, as well as providing subsidies for the nursing practice. It is noteworthy that the permanent improvement of the quality of cancer health services needs to be developed, based on solid evidence recognized in the scientific field.

No study was found in the scientific publications that synthesized the evidence available in the literature, in the context of chemotherapeutic and immunotherapeutic administration performed by nurses, to ensure the safety of cancer patients. For this reason, this scoping review was carried out.

Thus, the objective was to identify and synthesize the scientific evidence of cancer patient safety in the administration of antineoplastic and immunotherapeutic chemotherapies.
METHOD

It is a scoping review, research protocol registered in the OpenScience Framework (https://osf.io/c7g94/), developed from the recommendations of the PRISMA-ScR\textsuperscript{10} international guide and from the method proposed by the Joanna Briggs Institute, Reviewers Manual 2017,\textsuperscript{11} which establishes five steps, namely: 1) identification of the research question; 2) identification of relevant studies; 3) study selection; 4) data analysis; and 5) grouping, synthesis and presentation of data.\textsuperscript{11}

This type of review provides a mapping of the main concepts that support a research area, as well as it clarifies the working definitions and/or conceptual boundaries of a topic through available evidence. It is intended to achieve comprehensive results.\textsuperscript{10–11}

The participants, concept and context (PCC) strategy was used,\textsuperscript{1} where P (participants) – cancer patient, C (concept) – patient safety and C (context) – CTX and immunotherapy administration by nurses. The research question established was the following: What scientific evidence in the context of chemotherapy and immunotherapy administration by nurses is available to ensure the safety of cancer patients?

The study population consisted of research studies related to patient safety in the administration of CTX and immunotherapies performed by nurses, in places where cancer care occurs, published entirely in Portuguese, Spanish and/or English, with no time limit. Editorials, reviews, letters, experience reports, theoretical essays, single case studies, narrative and integrative reviews were excluded.

The search was performed in June and July 2018, in the following databases: U.S. National Library of Medicine (PubMed), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, Scopus, Latin American and Caribbean Health Sciences Literature (LILACS); the Cochrane Library, besides searching the CAPES Catalog of Theses and Dissertations; Europe E-Theses Portal (DART); Electronic Theses Online Service (EThOS); Open Access Scientific Repository of Portugal (Repositório Científico de Acesso Aberto de Portugal, RCAAP); National ETD Portal; Theses Canada, Latin American Thesis Portal and WorldCat Dissertations and Theses.

Initially, a search was conducted in the PubMed and CINAHL databases, in order to identify the most frequently used keywords and descriptors in studies that addressed the topic of interest. The publications were then analyzed to identify the keywords for each PCC strategy item.

The general strategy adopted was the search for studies using Boolean operators: (Antineoplastic Agents OR Drug Therapy OR Drug Therapy, Combination OR Chemotherapy, Adjuvant OR Induction Chemotherapy OR Consolidation Chemotherapy OR Immunotherapy OR Maintenance Chemotherapy OR Medication Therapy Management OR Antineoplastic Combined Chemotherapy Protocols) AND (Patient Safety OR Risk Management OR Medication Errors) AND (Nursing OR Oncologic Nursing). The search strategy was adapted to the specificities of each database and the similar combination of descriptors was maintained.

The titles and abstracts of the articles retrieved from the search, when available, were read and analyzed by four reviewers, who worked in pairs, to identify those potentially eligible for the study. In cases of doubt, the articles remained for the next phase, which involved the full reading of each of the articles selected by two independent reviewers, aiming to: a) confirm the pertinence to the review question and, if so, b) extract the data of interest. Inconsistencies or doubts were resolved by consensus among the authors.

For the separation, summarization and reporting of the essential elements found in each study, a structured instrument was used. This instrument allowed for synthesis, interpretation of data and basic numerical analysis of the extent, nature and distribution of the studies incorporated in the review. Items such as type of study (article, dissertation or thesis), year of publication, country of
origin, objectives, method, description of care used to ensure patient safety in the administration of CTX and immunotherapeutic drugs used for oncological treatment, and the conclusions were grouped. Thus, in each publication the main focuses involved in the conjecture of the problem, in the contexts, methods, discussions and conclusions were identified and extracted. The articles, dissertations and thesis found were analyzed, turning to the full texts, whenever necessary. The findings were summarized by thematic approximation and the synthesis of the results was presented in descriptive form, using tables and figures. Descriptive statistics was used for material analysis, using absolute and relative frequency calculations. There was no need for any ethical consideration, since the work was done with public domain data.

The level of evidence and the degree of recommendation of the studies were classified according to the proposal of the Joanna Briggs Institute,12 namely: the levels of evidence are categorized from one to five and the degrees of recommendation in A and B.

Data mapping using a structured instrument proposed by the Joanna Briggs Institute, Reviewers,11 allowed the identification of the essential elements of the studies, which enabled the synthesis and interpretation of the data, and to generate the basic numerical analysis of the extent, nature and distribution of the studies incorporated in the review.

Finally, the stage of compilation and communication of the results took place, with the intention of presenting the view of all the material, through a thematic construction, organized according to the patientent safety with cancer, in the administration of antineoplastic and immunotherapeutic chemotherapeutic drugs by nurses.

RESULTS

The initial search in the databases generated a total of 14,444 studies for title analysis. In the first screening, after examination of the title and abstract (whenever necessary), 145 papers were selected, 23 duplicate studies were excluded and 74 publications did not answer the research question after the analysis of the abstract. 43 articles, two theses and two dissertations remained, which were included in the main analysis. Thus, the sample of this study consisted of 47 papers.

Figure 1 displays the process of searching, deleting and selecting the studies found. It was used as the basis for the analysis elements related to the nature of the studies, the year and the region/country of the papers, the level of evidence of the articles, the journals responsible for the publication of the articles or the institution where the thesis or dissertation was defended, apart from the themes addressed.

The following are the research variables, which were organized according to the approach of the papers, i.e., 21 (44.7%) were qualitative (Chart 1), 19 (40.4%) quantitative (Chart 2) and seven (14.9%) mixed (Chart 3).
### Chart 1 – Presentation of publications, with a qualitative approach, on cancer patient safety in the administration of antineoplastic and immunotherapeutic agents, according to year of publication, type, level of evidence, journal or place of title and authors. Natal, Brazil, RN, 2018

<table>
<thead>
<tr>
<th>Year</th>
<th>Type</th>
<th>EL*</th>
<th>Journal or Institution</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>Article</td>
<td>4A</td>
<td>Australian J Cancer Nurs</td>
<td>Fyfe K, Nowak AK.¹⁴</td>
</tr>
<tr>
<td>2014</td>
<td>Thesis</td>
<td>-</td>
<td>Universidade Federal de Santa Catarina</td>
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<tr>
<td>2012</td>
<td>Article</td>
<td>4A</td>
<td>Clin J Oncol Nurs Forum</td>
<td>Vioral AN, Kennihan HK.¹⁸</td>
</tr>
<tr>
<td>Year</td>
<td>Type</td>
<td>EL*</td>
<td>Journal or Institution</td>
<td>Author(s)</td>
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<td>--------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
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<td>2010</td>
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<td>5A</td>
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<td>Mellinger E, Skinker G, Sears D, Gardner D, Shultz P.</td>
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<tr>
<td>2010</td>
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<td>4B</td>
<td>Oncol Nurs Forum</td>
<td>Schwappach DL, Hochreutener MA, Wernli M.</td>
</tr>
<tr>
<td>2010</td>
<td>Article</td>
<td>4A</td>
<td>European J Cancer Care</td>
<td>Oakley C, Johnson J, Ream E.</td>
</tr>
<tr>
<td>2006</td>
<td>Article</td>
<td>4A</td>
<td>Qual Saf Health Care</td>
<td>van Tilburg CM, Leistikow IP, Rademaker CM, Bierings MB, van Dijk AT.</td>
</tr>
<tr>
<td>2004</td>
<td>Article</td>
<td>4A</td>
<td>J Pediatr Oncol Nurs</td>
<td>Tracy E, DiTaranto S, Womer RB.</td>
</tr>
</tbody>
</table>

*EL= Evidence Level

**Chart 2** – Presentation of publications with a quantitative approach on patient safety with cancer in the administration of antineoplastic and immunotherapeutic agents, according to year of publication, type, level of evidence, journal or place of title and authors. Natal, RN, Brazil, 2018

<table>
<thead>
<tr>
<th>Year</th>
<th>Type</th>
<th>EL*</th>
<th>Journal or Institution</th>
<th>Author(s)</th>
</tr>
</thead>
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<tr>
<td>2016</td>
<td>Article</td>
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<td>Clin J Oncol Nurs</td>
<td>Baldwin A, Rodriguez ES.</td>
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<td>2016</td>
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<td>Clin J Oncol Nurs</td>
<td>LeFebvre KB, Felice TL.</td>
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<td>2016</td>
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<td>4A</td>
<td>BMJ Open</td>
<td>Schwappach DLB, Pfeiffer Y, Taxis K.</td>
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<tr>
<td>2015</td>
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<td>J Oncol Pract</td>
<td>Patil VM, Chakraborty S, Bhattacharjee A, Dessai S.</td>
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<tr>
<td>2015</td>
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<td>-</td>
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<tr>
<td>2014</td>
<td>Article</td>
<td>4A</td>
<td>Can Oncol Nurs J</td>
<td>Campbell C.</td>
</tr>
</tbody>
</table>
The analysis of the papers found revealed that the publication of specific papers on patient safety with cancer in the administration of antineoplastic and immunotherapeutic chemotherapies began in 2004. Although research studies on the topic published in the previous decade were found, they were not available in the Internet and therefore were not included in the review. Since then, the number of publications has not followed a linear pattern over the years (Figure 2). In 2010 and 2012, the area reached the maximum number of papers on the theme published in one year (seven), of which six were articles and one, a doctoral dissertation, in 2010, and six articles and a master dissertation, in 2012. In 2008 there was no publication on the subject of this study. In 2018, one article was retrieved, but this is a provisional number since the search was made midway through the year mentioned.
The country with the greatest number of studies performed was United States of America (USA), with 22 studies (46.7%), followed by the United Kingdom, with six (12.8%), Canada, with five (10.6%), Brazil, with three (6.4%), Australia and Switzerland, with two (4.3%) studies each, and the other countries (China, Spain, Netherlands, India, Italy, Turkey, and Sweden) with one (2.1%) paper.

Regarding the journals, two had published seven (14.9%) articles in the *Clin J Oncol Nurs* 6–7,18,28–35 (impact factor 0.881, Journal Citation Reports 2017-2018), six (12.8%) studies in the *Oncol Nurs Forum* 9,17,20,22,26,52 (impact factor 1.785, Journal Citation Reports 2017-2018), five (10.6%) in the *J Oncol Pract* 4,17,38,40,45 (impact factor 2.509, Journal Citation Reports 2017-2018) and in the *Eur J Oncol Nurs* 23,44,46,48,51 (impact factor 1.812, Journal Citation Reports 2017-2018), three (6.4%) publications in the *J Pediatr Oncol Nurs* 5,30,32 (impact factor 1.294, Journal Citation Reports 2017-2018), two (4.3%) in the *Qual Saf Health Care* 25,29 (according to the latest data, not indexed in the Journal Citation Reports). The other studies were published in different health journals 3,13–16,19,21,24–25,31,33,43,36–37,39,42,47,49–50.


Regarding the theme of the studies, the findings were summarized in the following themes:

Safety standards in the administration of parenteral antineoplastic chemotherapy (recommendations for patient safety in parenteral CTX application);4–5,13,40–42,44,48,50,15–21,24,26,32 Good practices for patient safety on oral antineoplastic therapy (specific guidelines for safe administration of oral antineoplastic agents were grouped);4,9,14,16,23,31,35,38–39,43 Safe administration and handling of immunotherapy (expert consensus and opinion on safe application and safe management of immunotherapy);6–7 Prevention and management of CTX and immunotherapy related errors (coping measures and strategies to reduce errors in the application of antineoplastic therapy).4–7,13,19–20,22,24–25,27–30,33–34,36,42,44,47,49–50–53

Safety standards in parenteral administration of antineoplastic chemotherapy

The measures described to provide patient safety in parenteral CTX administration were the following: medical prescription made by a qualified professional (preferably electronic) with the patient's name and a second identifier; date; chemotherapy regimen; cycle number and day (where applicable); all drugs listed using full generic names; written dose of drug; dose calculation data describing the variables used (weight, height, body surface area); diagnostic test results, laboratory tests and patient’s clinical status; changes in values that require confirmation of dosage; date and route of administration; infusion rate; allergies; appropriate supportive care for the regimen (pre-
medications, hydration, growth factors, and hypersensitivity medications); signature and stamp of the responsible professional; validation of the prescription by qualified and skilled nurses and pharmacists to work in the cancer area (double check with increment of a checklist of the items included in the prescriptions); prescription properly documented in patient’s record (verbal orders are not allowed except to maintain or discontinue drug administration).4–5,15–21,24,26,32,40–42,44,46,48,50,52

Intrathecal CTX prescriptions should be performed separately from drugs to be administered by other routes; labeled with warning labels and dispensed at the exact time of patient administration; followed in respect of institutional policies and standards.

In order to avoid permanent sequelae and unnecessary tragic deaths as a result of intrathecal administration of vinca alkaloids, several procedures are recommended in institutions where intrathecal medications are administered: handling vincristine in an infusion bag (minibags), eliminating the risk of exchange with intrathecal syringes; labeling the infusion bags with vincristine preparations with an alert (for intrathecal use only); establishing a differentiated procedure for intrathecal drug administration, in another location and/or at times or days different from the intravenous medications (if this procedure is not possible, as for people receiving medication via both routes, a procedure must be performed so that intravenous vincristine is not dispensed until the confirmation of the end of intrathecal administration or vice versa); not using an infusion pump to infuse intrathecal vincristine (higher likelihood of leakage).4,13

In the CTX administration phase, the following is recommended double-check by nurses for patient identification; check if the patient is wearing the identification bracelet with at least two identifiers; check for allergies to the drugs to be administered; identify drug name, dose, volume, route of administration, start and end date; check the appearance of the drug; put the signature and stamp on the prescription of all professionals (doctor, nurse and pharmacist); analyze if the CTX scheme was observed (adequate time since last cycle); identify treatment-related toxicity (if applicable); confirm if there are supportive medications; recalculate CTX doses; compare diluted drug labels with prescription and antineoplastic regimen; check for specific prescribed sequence; guide the patient verbally and deliver in writing (manual, folder); monitor the patient before, during and after drug administration; perform monitoring after CTX administration, including adherence, toxicity and complications.4–5,15–21,24,26,32,40–42,44,46,48,50

Studies have shown that the implementation of evidence-based care protocols improves care, organizes health services with the establishment of flows, and that they are imperative to improve the quality of care and patient safety.26,32,50

Good practices for patient safety using oral antineoplastic therapy

Due to the increasing use of oral antineoplastic chemotherapy, challenges have increased, especially regarding prescription, dispensation, reimbursement, adherence, and patient and family education. In the standards and specific recommendations for the safe administration of oral anticancer drugs, the following were highlighted: prescriptions for oral chemotherapy (health sectors or other institution as residence) should include the patient’s name, have a second individual identifier; full generic name of the drug; date of request, dose of drug with calculation methodology; administration schedule, administration mode, special instructions (if applicable); amount of drug to be dispensed and duration of therapy (number of cycles); monitoring of oral CTXs with periodic home visits; creation and implementation of institutional protocols (evidence-based care); advise on proper disposal if necessary.4,9,14,16,23,31,35,38–39,43

It is noteworthy that labels for medications dispensed from the health care environment to be taken at home include the following: patient’s name; patient’s second identifier; date of preparation and due date; full generic drug name, dose and dosage; amount dispensed into each vial; administration
schedule; administration instructions related to the ingestion of food and/or other medicines; warning or precautionary statement for storage and handling; warning label attached to the product (hazardous drug); storage conditions; name and number of the class council of the prescribing and responsible pharmacist.4,16,38

Safe administration and handling of immunotherapy

Only two studies6–7 were found on evidence-based administration and safe handling procedures specific for immunotherapies (4.3%), and both with a 5A evidence level,6–7 from consensus and expert opinion, but with a strong recommendation: nurses must have knowledge about the protocols and immunotherapy to be administered; dose reductions are often not an option in immunotherapy treatment plans; immunotherapy doses are administered completely; greater attention to multiple treatment plans (immunotherapy, CTX, teletherapy and/or other antineoplastic agents); the medical history made by nurses needs to include psychiatric assessments with questions about mood and sleep pattern changes secondary to immunotherapeutic drug-induced hypothyroidism or hyperthyroidism and, in physical assessments, include mainly weight, fatigue, and pain monitoring; perform post-administration monitoring including adherence, toxicity and complications.6–7

Prevention and management of errors related to the administration of antineoplastic and immunotherapeutic chemotropics

Errors regarding the administration of antineoplastic drugs pose a serious threat to people with malignant neoplasia. The recommendations found in the studies to avoid them were the following: implement processes to verify CTX regimen prescriptions prior to administration; implement the double-check process, careful and standardized; promote training and continuing education of nurses working in oncology; provide guidelines for patients and families (educational materials appropriate to their level of literacy and understanding, validated by health professionals and target audience); encourage patients to question their treatment and empower them to be able to actively participate in their own care; standardize CTX and immunotherapy administration procedures; perform computerized prescription.4–7,13,19–20,22,24–25,27–30,33–34,36,44,47,49–50,51–53

Diverse studies stood out that signaled as essential the use of tools for managing risks related to drugs, such as the HFMEA (Healthcare Failure Mode and Effect Analysis) and Lean Sigma, methodologies used to map, evaluate and propose the control of incidents before they occur and to detect hidden incidents in the system, error reporting and surveillance systems; a checklist of items for safe administration of antineoplastic drugs.22,25,28,30,37,42,44

DISCUSSION

This scoping review presented a consistent sample of studies in the area of cancer patient safety in the administration of antineoplastic and immunotherapeutic chemotherapies, more than half (51.0%) published in journals with a high impact factor (stratum A1 according to the Qualis Periodicals of Nursing, 2013-2016 quadrennium) (Brazil). The research proved to be comprehensive as it covered studies from the last 14 years. It is noteworthy that only three studies in Portuguese were found – two dissertations and one thesis –, which demonstrated the lack of research studies on this topic in Brazil. In the last five years, studies on patient safety in the administration of antineoplastic drugs have decreased compared to 2010 and 2012 at the international level.

The country with the highest number of publications was United States of America (46.7%), which is not surprising as it is the source of most guidelines, and therefore with the highest scientific production. Regarding higher education institutions, eight of the top ten universities in the world are in
the USA, which remains the world leader in science and innovation; therefore, they are the promoters of the greatest scientific production in the context of this study.

Regarding safety standards in the administration of parenteral antineoplastic chemotherapy, studies have shown that care protocols are indispensable in all health institutions, and are increasingly complex in order to avoid errors and to favor the maintenance of patient safety. Increased risk awareness in CTX administration processes, coupled with the transition from care to outpatient settings, has accelerated the need to explore ways to reduce risk and increase the safety of chemotherapy prescribing, dispensing and administration.

There are recommendations to minimize the likelihood of an incident occurring and to increase patient safety, such as the use of standardized, preferably electronic, forms prior to each parenteral CTX administration.

The literature supported the use of independent double checking as a means of improving safety. The standards emphasized the importance of conducting a comprehensive review of the medication request, instead of simply comparing the product to the prescription; this has been determined as a valuable method for detecting prescription errors.

It was emphasized that nurses should be qualified and skilled to work in the oncology area, with training and permanent education on drug pharmacokinetics and therapeutic protocols. In addition, they need to record any complications identified or reported by the patient, implement a nursing checklist for the administration of antineoplastic therapy, and guide patients before and after chemotherapy, since their involvement in all stages of treatment enables the detection of failures, making them co-responsible for their safety.

A publication, conducted at an oncology and outpatient unit of a hospital in Switzerland, found that nurses who received additional antineoplastic care education scored higher on a patient and professional safety awareness exam, and were more likely to report risks.

Other articles have pointed out that many organizations do not guarantee that only trained personnel administer cytotoxic agents, mainly due to staff shortages and to a large number of patients to be treated.

As for intrathecal CTX, from 2013 there were no reports of deaths from inadvertent intrathecal injection of vinca alkaloid, as the drug was prepared in a minibag. Specific suggestions have been mentioned for vincristine dilution – such as the need for a cautionary phrase about its exclusive use intravenously – since its incorrect administration may lead to permanent sequelae or death. It is also recommended to dispense vincristine in an infusion bag (minibag) and not in a syringe; administering intrathecal vinca alkaloid, at a different location and/or at times or days disposing of the intravenous medicinal products (if this procedure is not possible, intravenous vincristine should not be dispensed until the confirmation of the end of intrathecal administration or vice versa).

The published literature suggests that extravasation rates are not higher with the administration of a minibag than with syringes. Thus, the professional should be aware during its administration, as it is a vesicant drug with high potential for patient harm.

In relation to oral chemotherapy, until recently it constituted a relatively small proportion of drugs administered to treat malignant neoplasms. However, over the past 15 years, the number of oral antineoplastic drugs and their use has increased significantly and is expected to continue. Due to the increasing use of oral chemotherapy, unique challenges associated with its use have emerged, especially regarding the prescription, dispensation, reimbursement, adherence, and education of the patient and family, with clear guidance on what is considered safe delivery of CTX.

In response to this need, CTX administration safety standards since 2016 have included specific oral CTX standards as well as the addition of specific oral cancer agent issues such as the need to monitor adherence.
It was observed that the safe administration and handling of immunotherapies is still poorly studied, as only two publications were found and both came from expert opinions and consensus. There are numerous approved and available immunotherapeutic drugs in the Brazilian health system, mostly private, and nurses need to be aware of these drugs before administering them, in addition to having a thorough physical examination and interview, post-administration monitoring, including early detection and continuous screening for adverse events and continuing education of patients and families, with encouragement of early reporting of side effects.\textsuperscript{6–7}

Regarding the prevention and management of errors related to the administration of CTX and immunotherapy, the publications analyzed indicated the need to create strategies to minimize or prevent failures in the administration of antineoplastic therapies – based on institutional protocols for standardization of conduct – and the creation of a multidisciplinary incident prevention and assessment team, in addition to monitoring adverse drug reactions and response to treatment.\textsuperscript{4,17,24,27,53} Stress, lack of staff, lack of experience and unclear orders were cited as factors that may contribute to the occurrence of errors.\textsuperscript{22,34,37}

According to the findings, the workflow implementation as an additional security standard demonstrated its contribution to improving the delivery and secure administration of CTX schemes.\textsuperscript{22,25,28,30,37,42,44}

It is noteworthy that the publications pointed to the need for more research on the possibilities of implementing nursing checklists in the oncology area, as they are useful tools and, when they are of a good quality, aim to guarantee satisfactory results and patient safety.\textsuperscript{13,44}

The studies included in this review concluded that the use of chemotherapeutic and immunotherapeutic risk management tools can prevent adverse events.\textsuperscript{44}

One of the strengths of this review was the variety of countries, adult and pediatric patients, as well as the inclusion of qualitative, quantitative and mixed approaches.

However, some limitations are recognized in this process, as there are studies published in other languages that were not included, as well as a diversity of studies that probably exist in other indexing bases, and the exclusive inclusion of the descriptor immunotherapy was not considered to search the theme of the related research.

**CONCLUSION**

In the studies analyzed in this scoping review, safety of cancer patients in the administration of antineoplastic and immunotherapeutic drugs was found to occur when evidence-based protocols were implemented. In this sense, the continuing education of nurses and the implementation of safety standards and processes help to prevent antineoplastic administration errors.

Recommendations to improve safety included the establishment of standardized processes, adherence to policies and procedures, and the routine conduct of interdisciplinary error reviews to identify areas for improvement, as well as patient and family education.
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NOTES

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There is no conflict of interest.

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ERRATUM:
PATIENT SAFETY IN THE ADMINISTRATION OF ANTINEOPLASTIC CHEMOTHERAPY AND OF IMMUNOTHERAPICS FOR ONCOLOGICAL TREATMENT: SCOPING REVIEW


On page 10, second paragraph, where was written: “In order to avoid permanent sequelae and unnecessary tragic deaths as a result of intrathecal administration of vinca alkaloids, several procedures are recommended in institutions where intrathecal medications are administered: handling vincristine in an infusion bag (minibags), eliminating the risk of exchange with intrathecal syringes; labeling the infusion bags with vincristine preparations with an alert (where it for intrathecal use only); establishing a differentiated procedure for intrathecal drug administration, in another location and/or at times or days different from the intravenous medications (if this procedure is not possible, as for people receiving medication via both routes, a procedure must be performed so that intravenous vincristine is not dispensed until the confirmation of the end of intrathecal administration or vice versa); not using an infusion pump to infuse intrathecal vincristine (higher likelihood of leakage).”

Now read: In order to avoid permanent sequelae and unnecessary tragic deaths as a result of intrathecal administration of vinca alkaloids, several procedures are recommended in institutions where intrathecal medications are administered: handling vincristine in an infusion bag (minibags), eliminating the risk of exchange with intrathecal syringes; labeling the infusion bags with vincristine preparations with an alert (where it for intravenous use only); establishing a differentiated procedure for intrathecal drug administration, in another location and/or at times or days different from the intravenous medications (if this procedure is not possible, as for people receiving medication via both routes, a procedure must be performed so that intravenous vincristine is not dispensed until the confirmation of the end of intrathecal administration or vice versa); not using an infusion pump to infuse intrathecal vincristine (higher likelihood of leakage).
On page 12, seventh paragraph, where was written: “...vincristine in an infusion bag (minibag) and not in a syringe; administering intrathecal vinca alkaloid, at a different location and/or at times or days disposing of the intravenous medicinal products (if this procedure is not possible, intravenous vincristine should not be dispensed until the confirmation of the end of intrathecal administration or vice versa).”

Now read: ...vincristine in an infusion bag (minibag) and not in a syringe; administering intravenous vinca alkaloid, at a different location and/or at times or days disposing of the intrathecal medicinal products (if this procedure is not possible, intravenous vincristine should not be dispensed until the confirmation of the end of intrathecal administration or vice versa).