Topical treatments for the prevention of radiodermatitis in cancer patients: a scoping review protocol[*]

Tratamentos tópicos para prevenção da radiodermatite em pacientes oncológicos: um protocolo de revisão de escopo

Gilma Teresa Guimarães Perse[1]
ORCID: 0000-0002-0311-6362

Beatriz Guitton Renaud Baptista de Oliveira[1]
ORCID: 0000-0001-7494-7457

Sílvia Maria de Sá Basílio Lins[2]
ORCID: 0000-0002-6717-9223

[1]Fluminense Federal University, Niterói, RJ, Brazil
[2]State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil

Editors:
Ana Carla Dantas Cavalcanti
ORCID: 0000-0003-3531-4694

Paula Vanessa Peclat Flores
ORCID: 0000-0002-9726-5229

Corresponding author:
Gilma Teresa Guimarães Perse
E-mail: gtperse@gmail.com

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ABSTRACT

Objective: To map the available evidence on topical treatments used to prevent radiodermatitis in cancer patients. **Method:** Scoping review protocol developed following the Joanna Briggs Institute (JBI) methodology. The search strategy is subdivided into three steps using the MEDLINE, CINAHL, LILACS, Web of Science (WoS), and grey literature databases (theses, dissertations, guidelines, expert opinions, and promotional material from companies that own specific products), with no language or time restriction. Two independent reviewers will select articles, and data extraction will take place through a form built for this purpose. The extracted data will be presented in diagrams or tables, aligned with the objective of this scoping review, closing with a narrative synthesis.
Descriptors: Radiodermatitis; Neoplasms; Disease Prevention.

RESUMO

Objetivo: Mapear as evidências disponíveis sobre os tratamentos tópicos utilizados na prevenção da radiodermatite no paciente oncológico. **Método:** Protocolo de revisão de escopo seguindo a metodologia do Joanna Briggs Institute (JBI). A estratégia de busca subdivide-se em três etapas utilizando os bancos de dados MEDLINE, CINAHL, LILACS, Web of Science (WoS) e literatura cinzenta (teses, dissertações, *guidelines*, opiniões de especialistas e material de divulgação de empresas detentoras de produtos), sem restrição de idioma ou temporal. A seleção dos artigos será realizada por dois revisores independentes e a extração de dados se dará através de um formulário construído para esse propósito. Os dados extraídos serão apresentados em diagramas ou tabelas, alinhados com o objetivo dessa revisão de escopo, concluindo com um resumo narrativo.
Descritores: Radiodermatite; Neoplasias; Prevenção de Doenças.

INTRODUCTION

According to the most recent global estimate for 2020, released by the International Center for Research on Cancer (IARC), cancer continues to progress at an alarming rate worldwide, with 19.3 million new cases and 10.0 million expected deaths. Increased incidence and mortality have been associated with aging, population growth, and changes in the distribution and prevalence of risk factors for cancer, especially when associated with socioeconomic development[1]. In the Brazilian scenario, an estimate was recently released that there will be 625,000 new cancer cases each year in 2020-2022[2]. Worldwide, colorectal cancer has the third highest incidence, affecting 10.0% of patients with cancer and ranking second as a cause of death from cancer[3]. One of the main therapeutic methods for cancer treatment is radiotherapy, which is indicated for 50% of all cancer patients[4]. This treatment method can destroy tumor cells using beams of ionizing radiation sufficient to alter the DNA structure of cancer cells, leading to cell death with the least possible damage to surrounding normal cells[5].

Treatment with radiotherapy can be exclusive or associated with other therapeutic modalities, such as surgery and chemotherapy[2]. This radiation

can result in an adverse skin reaction called radiodermatitis, but also known in hospitals as radiodermatitis, actinic dermatitis, and radioepithelitis. In this protocol, we chose to use the term radiodermatitis, which is standardized in the international literature, and listed in the Medical Subject Headings (MeSH).

Radiodermatitis is defined as a set of skin reactions resulting from the destruction of basal cells due to exposure to ionizing radiation of the epidermis[6]. These lesions are characterized by hypersensitivity, hyperpigmentation, pain, itching, and scaling. The degree of severity of the skin reaction can lead to treatment suspension, causing delays and compromising therapeutic success[7]. In addition, it can directly interfere with the patient's quality of life due to the resulting discomfort, itching, and pain. The occurrence of this event may be related to intrinsic and extrinsic factors directly influencing the severity of radiodermatitis. Among the intrinsic factors are age, size of the irradiated area, body mass index, skin color, smoking, nutritional status, and preexisting disease, such as diabetes mellitus. The extrinsic ones relate to radiotherapy treatment, such as total dose, treatment volume, fractionation, and concomitant chemotherapy[8].

There are several scales for classifying and evaluating the irradiated skin. The most used worldwide is that of the Radiation Therapy Oncology Group (RTOG), with the following skin toxicity grading criteria: Grade 0: no change from baseline; Grade 1: mild erythema, epilation, dry desquamation and decreased sweating; Grade 2: moderate to bright erythema, patchy moist desquamation, and moderate edema; Grade 3: confluent wet desquamation beyond the skin folds and intense edema; and Grade 4: ulceration, hemorrhage, and necrosis[9].

A recent systematic review analyzed several studies about guidelines for managing radiodermatitis in cancer patients. However, the evidence was insufficient to support or refute any specific product, indicating that there is still no consensus for irradiated skin care[10].

Prevention, in turn, continues to be a highly relevant multidisciplinary challenge; however, currently, there is no consensus among radiotherapy centers in the world regarding the topical treatments used in the prevention of radiodermatitis. Despite years of studies, there is no robust and clear evidence of the superiority of a single topical product in preventing radiodermatitis[11].

The high frequency of this event corroborates the need to deepen knowledge of the proper management of radiodermatitis, as in the study with 117 patients with breast cancer, which showed 81.19% of radiodermatitis[12]. Another study[7] evaluated 112 patients, 31 submitted to irradiation in the head and neck region, 50 in the breast region, and 31 in the pelvic region, showing the involvement of this event in 100% of head and neck, 98% of breast, and 80% of the pelvis cancer patients.

In a preliminary search carried out from June 26 to July 26, 2020, in the databases PROSPERO (International Prospective Register of Systematic Reviews), JBI Evidence Synthesis, and Cochrane Database of Systematic Reviews, no review (published or under development) addressing the list of topical products available to mitigate or prevent radiodermatitis in all irradiated topographies was found. Besides, this preliminary research showed a greater production of studies that evaluated topical products for the prevention and/or treatment of radiodermatitis in patients with cancers that affected the head and neck region and the mammary region, confirming the scarcity of research in other irradiated areas, such as the pelvic region.

Given the reality above, it is necessary to deepen the theme to expand knowledge of the existing arsenal of topical products used to prevent radiodermatitis.

So, to identify the need to develop a future systematic review[13] about the effectiveness of topical agents on the prevention of radiodermatitis, this review aims to map the available evidence on topical treatments used to prevent radiodermatitis in cancer patients.

METHOD

The title of this scoping review is registered in the Open Science Framework (OSF) (https://osf.io/62cq7/). The scoping review will be built according to the Joanna Briggs Institute (JBI) methodology[13], expected to be developed in December 2022. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA –ScR) checklist[14] was used in the reporting of the study.

Research question

What evidence is available on topical treatments to prevent radiodermatitis in non-pediatric cancer patients?

Inclusion criteria

The PCC mnemonic (P - Population, C - Concept, C - Context), recommended by the JBI methodology[13], supported the election of the inclusion criteria for this review protocol, described below.

Population

This review's participants will be studies addressing non-pediatric cancer patients of both sexes undergoing external radiotherapy treatment.

Concept

This review will consider studies that include topical products (gel, ointment, lotion, etc.) used to prevent radiodermatitis. Studies that address oral or intravenous products will not be included.

Context

The context of this scoping review will consist of studies carried out with patients undergoing radiotherapy treatment instituted on an outpatient and/or hospital basis.

Types of fonts

This review will consider studies with quantitative and qualitative research designs. Experimental studies such as randomized clinical trials (RCTs), quasi-experimental, observational, cross-sectional, longitudinal, prospective, retrospective, and descriptive studies will be included. Theses, dissertations, guidelines, expert opinions, and promotional materials from companies that own products will also be considered. There will be no time or language restriction.

Search strategy

The search strategy will follow the JBI recommendation, which advocates carrying out three steps:
First Step: An initial search limited to two online databases relevant to the topic will be carried out. MEDLINE (PubMed) and Web of Science (WOS, Clarivate Analytics) will be searched via the CAPES portal. This preliminary step seeks to analyze the words contained in the titles, abstracts, and indexes of retrieved articles to expand the terms used in the final search strategy.
Second Step: Another search will be carried out using all the keywords identified in the previous step, aiming at the production of a comprehensive mapping that will be applied in the following databases: MEDLINE (PubMed), CINAHL, LILACS, WOS, Embase (Elsevier Medical Database) and Scopus. There will also be a grey literature search in databases of theses and dissertations, onco-logy societies' websites, companies that supply products, and free websites on the web.
Third Step: A manual search will be carried out in the reference lists of the articles retrieved in the databases mentioned in step 2, aiming to identify relevant articles for the review that the electronic search did not capture.

The search strategy using descriptors, keywords, and Boolean operators, as described in Figure 1, but improvements will be made after the execution of the first step of the search. The entire process of mapping keywords to the evidence search strategy, as well as the search itself, will be carried out in partnership with a librarian with experience in health sciences.

Selection of studies

After searching the databases, all documents retrieved will be gathered and sent to a bibliographic reference management software, EndNote Online (Clarivate Analytics, PA, USA), for the removal of duplicates.

The next step will be the assessment of the eligible documents. The titles and abstracts of the articles will be screened. The Rayyan QCRI application developed by the Qatar Computing Research Institute, will be used for this step[15]. This tool makes it possible to analyze the eligibility of documents in a blinded way among reviewers. A spreadsheet will be created in Microsoft Excel to organize the articles selected for full-text screening.

Two independent reviewers will conduct the entire study selection process, and, in case of disagreements, a third reviewer will be consulted. An appendix will be created detailing the included and excluded sources, stating the reasons for the exclusions. This step will be detailed using a PRISMA flowchart.

Data extraction

Data will be extracted using an instrument developed by the researchers (Figure 2). Its construction was aligned with the objective of the study. The data to be extracted are 1. Author, 2. Year of publication, 3. Country of origin, 4. Objectives/Purpose, 5. Population and sample size, 6. Type of topical intervention used, 7. Body region irradiated, 8. Results, and 9. Conflicts of interest/Purpose.

During this data extraction process, the instrument may undergo adaptations according to the emerging needs identified by the researchers.

Search	Query	Results
#6	Search: #4 AND #3 AND #2 AND #1 Sort by: Most Recent	2
#5	Search: #4 AND #3 AND #2 Sort by: Most Recent	232
#4	Search: Radiodermatitis OR Radiodermatitides OR (Radiation-Induced Dermatitis) OR (Radiation Induced Dermatitis) OR (Dermatitis, Radiation-Induced) OR (Dermatitides, Radiation-Induced) OR (Dermatitis, Radiation Induced) OR (Radiation-Induced Dermatitides) OR (Radiation Recall Dermatitis) OR(Dermatitides, Radiation Recall) OR (Dermatitis, Radiation Recall) OR (Radiation Recall Dermatitides) OR (Radiation Recall Reaction) OR (Radiation Recall Reactions) OR (Reaction, Radiation Recall) OR (Reactions, Radiation Recall) OR (Recall Reaction, Radiation) OR (Recall Reactions, Radiation) Sort by: Most Recent	3,621
#3	Search: (prevention control) OR (prophylaxis) OR (preventive therapy) OR (preventive measures) OR (prevention) OR (control) Sort by: Most Recent	5,678,153
#2	Search: (Administration, Topical) OR (Drug Administration, Topical) OR (Topical Drug Administration) OR (Topical Administration) OR (Administrations, Topical) OR (Topical Administrations) OR (Administration, Topical Drug) OR (Administrations, Topical Drug) OR (Drug Administrations, Topical) OR (Topical Drug Administrations) OR (Topical therapy) OR (Topical therapeutics) OR (topical therapies) OR (topical administration) OR (Topical Administrations) Sort by: Most Recent	142.072
#1	Search: (Outpatient Clinics, Hospital) OR (Ambulatory Care Facilities, Hospital) OR (Hospital Outpatient Clinic*) OR (Outpatient Clinic, Hospital) OR (Ambulatory Care) OR (Outpatient Care) (Health Services, Outpatient) OR (Outpatient Services) OR (Outpatient Service) OR (Urgent Care) OR (Clinic Visit*) Sort by: Most Recent	247,964

Source: Prepared by the authors, 2020.

Figure 1- MEDLINE search strategy (PubMed). Niterói, RJ, Brazil, 2020

Detailed characteristics of the studies	
Author(s)	
Year of publication	
Country of origin	
Objectives/Purpose	
Population and sample size	
Type of topical intervention used	
Body region irradiated	
Results	
Conflicts of interest/Purpose	

Source: Prepared by the authors, 2020.

Figure 2 – Data extraction tool. Niterói, RJ, Brazil, 2020

Data presentation

The categorization of information from the extracted data will be represented graphically through diagrams, charts, or tables, according with the objective proposed in this scoping review. Emphasis will be given to describing the type of topical treatments used to prevent radiodermatitis and their results. Quantitative variables will be analyzed using simple statistics with relative and absolute frequencies. A narrative summary will accompany the tabulated data.

*Paper extracted from the master's dissertation "Nursing intervention for the preventive manage-

ment of radiodermatitis in cancer patients: a methodological study", presented to the Fluminense Federal University, Rio de Janeiro, RJ, Brazil.

CONFLICT OF INTERESTS
The authors have declared that there is no conflict of interests.

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AUTHORSHIP CONTRIBUTIONS
Project design: Perse GTG
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