ESTIMA
Brazilian Journal of Enterostomal Therapy

REVIEW ARTICLE
https://doi.org/10.30886/estima.v22.1479_IN

Topical agents for the prevention of radiodermatitis in cancer patients: A systematic review

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ABSTRACT

Objective: To analyze the evidence on the effect of topical agents to prevent radiodermatitis in cancer patients. **Methods:** Systematic review of double-blind randomized clinical studies built according to JBI recommendations and search in the databases MEDLINE/PubMed, CINAHL, LILACS, Web of Science, Embase and Scopus, in addition to the Gray Literature. The JBI critical assessment tool for randomized clinical trials was used to assess the possibility of bias, GRADE for the quality of evidence, and Gradepro® to recommend them. **Results:** Thirteen studies were selected that evaluated different topical agents to prevent radiodermatitis, namely: corticosteroids, with antioxidant action and herbal medicines. The methodological quality of each study was appropriate. Still, the quality of evidence generated by pooling them was low, regardless of the type of topical agent employed, suggesting that confidence in its effect is limited and weakening the strength of the recommendation. **Conclusions:** Some topical agents have shown promise for the prevention of radiodermatitis, but the evidence gathered here about their effectiveness does not indicate their use for the prevention of radiodermatitis in cancer patients.

DESCRIPTORS: Radiotherapy. Radiodermatitis. Protective agents. Systematic review. Evidence-based practice. Enterostomal therapy.

Agentes tópicos para prevenção de radiodermatite em pacientes com câncer: revisão sistemática

RESUMO

Objetivo: Analisar as evidências sobre o efeito dos agentes tópicos empregados para a prevenção da radiodermatite em pacientes com câncer. **Método:** Revisão sistemática de estudos clínicos randomizados duplos-cegos construída conforme recomendações do Joanna Briggs Institute e busca nas bases de dados MEDLINE/PubMed, CINAHL, LILACS, Web of Science, Embase, Scopus, além da literatura cinzenta. Utilizaram-se a ferramenta de avaliação crítica do JBI para ensaios clínicos randomizados para avaliar a possibilidade de viés, o Grading of Recommendations, Assessment, Development and Evaluation para a qualidade das evidências e o Gradepro® para recomendá-las. **Resultados:** Selecionaram-se 13 estudos que avaliaram diferentes agentes tópicos para prevenir a radiodermatite, a saber: corticosteroides, de ação antioxidante e fitoterápicos. A qualidade metodológica de cada estudo foi apropriada, mas a qualidade da evidência gerada pela reunião deles foi baixa, independentemente do tipo de agente tópico empregado, sugerindo que a confiança no seu efeito é limitada e tornando a força de recomendação fraca. **Conclusão:** Alguns agentes tópicos mostraram-se

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Section Editor: Manuela de Mendonça F. Coelho
Received: Sep. 08, 2023 | Accepted: Dec. 27, 2023
How to cite: Perse GTG, Jomar RT, Simões FV, Lins SMSB, Oliveira BGRB. Topical agents for the prevention of radiodermatitis in cancer patients: A systematic review. ESTIMA, Braz J Enterostomal Ther. 2024;22:e1479. https://doi.org/10.30886/estima.v22.1479_IN

promissores para a prevenção de radiodermatite, mas as evidências aqui reunidas sobre a eficácia deles não permitem indicar seu uso para a prevenção de radiodermatite em pacientes com câncer.

DESCRITORES: Radioterapia. Radiodermatite. Substâncias protetoras. Revisão sistemática. Prática clínica baseada em evidências. Estomaterapia.

Agentes tópicos para la prevención de radiodermatitis en pacientes con cáncer: una revisión sistemática

RESUMEN

Objetivo: Analizar la evidencia sobre el efecto de los agentes tópicos utilizados para la prevención de la radiodermatitis en pacientes con cáncer. **Método:** Revisión sistemática de estudios clínicos aleatorizados, doble ciego, elaborados según las recomendaciones del JBI y buscados en MEDLINE/PubMed, CINAHL, LILACS, *Web of Science*, Embase y Scopus, además de literatura gris. Se utilizó la herramienta de evaluación crítica JBI para ensayos clínicos aleatorios para evaluar la posibilidad de sesgo, GRADE para la calidad de la evidencia y Gradepro® para recomendarla. **Resultados:** Se seleccionaron trece estudios que evaluaron diferentes agentes tópicos para prevenir la radiodermatitis, a saber: corticosteroides, con acción antioxidante y fitoterapia. La calidad metodológica de cada estudio fue apropiada, pero la calidad de la evidencia generada al combinarlos fue baja, independientemente del tipo de agente tópico empleado, lo que sugiere que la confianza en su efecto es limitada y debilita la fuerza de la recomendación. **Conclusión:** Algunos agentes tópicos se han mostrado prometedores para la prevención de la radiodermatitis, pero la evidencia aquí reunida sobre su eficacia no nos permite indicar su uso para la prevención de la radiodermatitis en pacientes con cáncer.

DESCRIPTORES: Radioterapia. Radiodermatitis. Sustancias protectoras. Revisión sistemática. Práctica clínica basada en la evidencia. Estomaterapia.

INTRODUCTION

One of the main therapeutic methods for cancer treatment indicated for around 50% to 60% of patients is radiotherapy, capable of destroying tumor cells using beams of ionizing radiation leading them to lose their clonogenicity with less damage to surrounding normal cells[1]. Ionizing radiation can destroy basal cells of the epidermis, resulting in radiodermatitis, which is characterized by hypersensitivity, hyperpigmentation, pain, itching, and peeling[2]. Depending on the severity, radiodermatitis can lead to the suspension of radiotherapy, causing delays and compromising therapeutic success[3], in addition to interfering with the patient's quality of life due to the discomfort and pain it generates[4].

Radiodermatitis is associated with intrinsic and extrinsic factors that directly influence its severity, such as age, size of the irradiated area, body mass index, skin color, smoking, nutritional status, pre-existing diseases (such as diabetes *mellitus*), dose, volume and fractionation of radiation and concomitant chemotherapy[5-7]. A high incidence of radiodermatitis has been described in several studies, up to 100% in patients with head and neck cancer, 48% in patients with pelvic cancer, and ranging from 47 to 98% in those with breast cancer[7-9].

To prevent radiodermatitis, there are several topical agents available, although the quality and quantity of studies on their efficacy are insufficient to safely indicate the use of a specific one. Although there is some consensus on the provision of skin care guidelines that patients should follow during radiotherapy treatment (use neutral soap, do not take hot showers, dry the skin with a soft towel, minimize trauma, avoid perfumes, talcs, deodorants, creams and sun exposure)[10-12], the choice of topical agent to prevent radiodermatitis is usually based basically on the experience of professionals working in radiotherapy centers, which makes it difficult to homogenize recommendations for clinical practice worldwide[13].

Since radiodermatitis is a highly relevant multidisciplinary challenge, the Skin Toxicity Group of the Multinational Association of Supportive Care in Cancer, in an attempt to standardize its treatment, published a clinical practice guideline

in 2013[14], which, however, lacked definitive recommendations given the lack of high-quality evidence. A narrative review that compared clinical practice guidelines for radiodermatitis published between 2010 and 2021 by multiple oncology organizations in developed countries revealed significant discrepancies between them, pointing to the need for updated, evidence-based recommendations[13].

In view of this, the Multinational Association of Supportive Care in Cancer conducted a systematic review[15] to summarize the evidence on interventions for the prevention and treatment of radiodermatitis and a Delphi consensus[16] to compile international expert opinions on care for people with radiodermatitis. However, the interventions analyzed could not be recommended due to the limited high-quality evidence and the lack of consensus to support their use, reinforcing the need for more research on the subject.

Conducting a new systematic review with an emphasis on topical agents used to prevent radiodermatitis is therefore relevant and justifiable, since radiodermatitis is a highly frequent adverse reaction among cancer patients, despite technological advances to improve dose homogeneity in the skin and reduce the severity of the reaction, such as intensity-modulated radiotherapy and skin preservation techniques. Therefore, this study aimed to analyze the evidence on the effect of topical agents used to prevent radiodermatitis in cancer patients.

METHOD

This is a systematic review built according to the steps recommended by the Joanna Briggs Institute (JBI): elaboration of the research question, definition of inclusion and exclusion criteria, literature search, selection of studies, risk of bias analysis, data extraction, data analysis and synthesis, presentation and interpretation of results and assessment of the quality of the evidence[17].

The question the systematic review aimed to answer was: "What is the effect of topical agents used to prevent radiodermatitis in cancer patients?". It was built using the anagram PICOS: P – population; I – intervention; C – comparison; O – outcome; and S – study type.

The eligibility criteria determined by the PICOS anagram were respected (P – patients with cancer undergoing exclusive radiotherapy; I – topical agent for the prevention of radiodermatitis; C – other agents or no comparator; O – prevention of radiodermatitis; S – double-blind randomized clinical trial) without establishing a time cut-off or limiting the languages of publication.

The search strategy, conducted in December 2020, was carried out in three stages. The first involved an initial search in the Medlars online (MEDLINE/PubMed) and Web of Science databases, via the *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES) portal, in which an analysis was made of the words contained in the title, abstract and index of the articles retrieved to broaden the terms used in the final search strategy.

The second stage used all the keywords identified in the previous stage to produce a broad mapping that was applied to the MEDLINE/PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), *Literatura Latinoamericana em Ciências da Saúde* (LILACS), Web of Science, Embase and Scopus databases. A search was also made for Gray Literature in thesis and dissertation banks, oncology society websites, product supplier company websites, and free *web* searches.

In the last stage, a manual search was carried out on the reference lists of the selected studies to identify other relevant ones that the electronic search in the databases had not captured.

The entire process of mapping the keywords for the evidence search strategy (https://doi.org/10.1079/searchRxiv.2023.00129) and the search itself was carried out by the main author in partnership with a health sciences librarian.

After searching the databases, all the documents found were uploaded to the EndNote Online® bibliographic reference management software, and duplicates were excluded. The next step was to assess the eligibility of the documents by reading the titles and abstracts of the studies, using the Rayyan QCRI® application, developed by the Qatar Computing Research Institute (QCRI), which enabled the eligibility of the documents to be blinded between the reviewers. The studies were selected by two independent reviewers and, in cases of disagreement, a consensus was reached between them.

The JBI critical appraisal tool for randomized clinical trials (https://jbi.global/critical-appraisal-tools) was used to determine the extent to which studies addressed the possibility of bias in their conception, conduct, and analysis. This tool consists of 13 questions with four answer options (yes, no, unclear, or not applicable) for the following aspects of the study: randomization, allocation, existence of similarity at baseline and treatment between the intervention and control groups, blinding of participant and researcher, measurement of outcomes and results, statistical analysis and appropriate design.

Using an instrument developed by the authors themselves, the following data was extracted from each study: author, year of publication, country of conduct, objectives, type of study, population and sample size, area of body irradiated, topical agent under investigation, mode of application of the topical agent, method of evaluation of radiodermatitis, results and conflicts of interest.

The data extracted from the studies was analyzed, summarized, and presented descriptively.

The information extracted from the studies was categorized, highlighting the description of the type of topical agent used to prevent radiodermatitis and the result achieved.

Concerning evaluating the evidence's quality, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) was used, a grading system that provides clear and concise information on both the evidence's quality and the strength of the recommendation[18]. The Gradepro® Guideline Development Tool GDT software was used to obtain the evidence's grade of recommendation, considering the following points: study limitations (e.g. risk of bias), inconsistency of effect, estimation imprecision, indirect effect, and publication bias[18,19].

GRADE considers four levels of evidence: high evidence (A) is given when it is unlikely that other studies will change the estimated confidence in the effect of the intervention and moderate evidence (B) is given when there is moderate confidence in the estimated effect. When confidence in the effect is limited, a low level is considered (C), and when any estimate of effect is uncertain, a very low level is given (D)[19].

RESULTS

According to Figure 1, 1,671 studies were found in the databases consulted, 875 of which were eligible for reading the title and abstract. A total of 192 were pre-selected for full reading, in compliance with the eligibility criteria. After thorough reading, 13 double-blind randomized clinical trials were selected, which then made up this systematic review.

The main characteristics of the selected studies are presented in charts, according to the mechanisms of action of the different topical agents for preventing radiodermatitis, which were categorized as follows: corticosteroids (Chart 1)[10,20-23], antioxidant agents (Chart 2)[24-28] and herbal medicines (Chart 3)[11,12,29]. The studies were conducted on the North American[10,24,29], Asian[11,25-27], European[12,21-23] and Eurasian[28] continents and published over 40 years, between 1979[21] and 2019[11,26,27]. The sample size varied between 36[22] and 390[12] participants. Concerning the method used to evaluate radiodermatitis, four studies[11,12,23,26] used the Radiation Therapy Oncology Group (RTOG) scale and two[10,24] used the Common Terminology Criteria for Adverse Events (CTCAE) scale alone, while another two[25,27] used both. Regarding the authors' conflicts of interest, only two studies[21,22] made no declaration in this regard.

When it came to evaluating the possibility of bias in the conception, conduct and analysis of the studies, all of them had at least nine "yes" answers out of a total of 13 and were therefore considered to be of appropriate methodological quality. Four studies[21,23,25,29] did not clarify the true randomization for assigning participants to treatment groups, highlighting that the occultation of the allocation of these groups was carried out in all of them. In none of the studies there was any difference in the baseline characteristics of the treatment groups. About blinding to treatment assignment, in all the studies the participants and those who delivered the treatment were blinded, but one of them[12] was judged to be unclear due to the limited reporting of treatment assignment information. In all the studies, the treatment groups were treated identically in the intervention of interest, the monitoring was complete, and the follow-up was adequately described and analyzed. The participants were analyzed in the groups to which they were randomized, and the outcomes were measured in the same way for the treatment groups, although one study[21] did not measure them reliably or carry out an appropriate statistical analysis with adequate study design and description of the conduct and analysis.

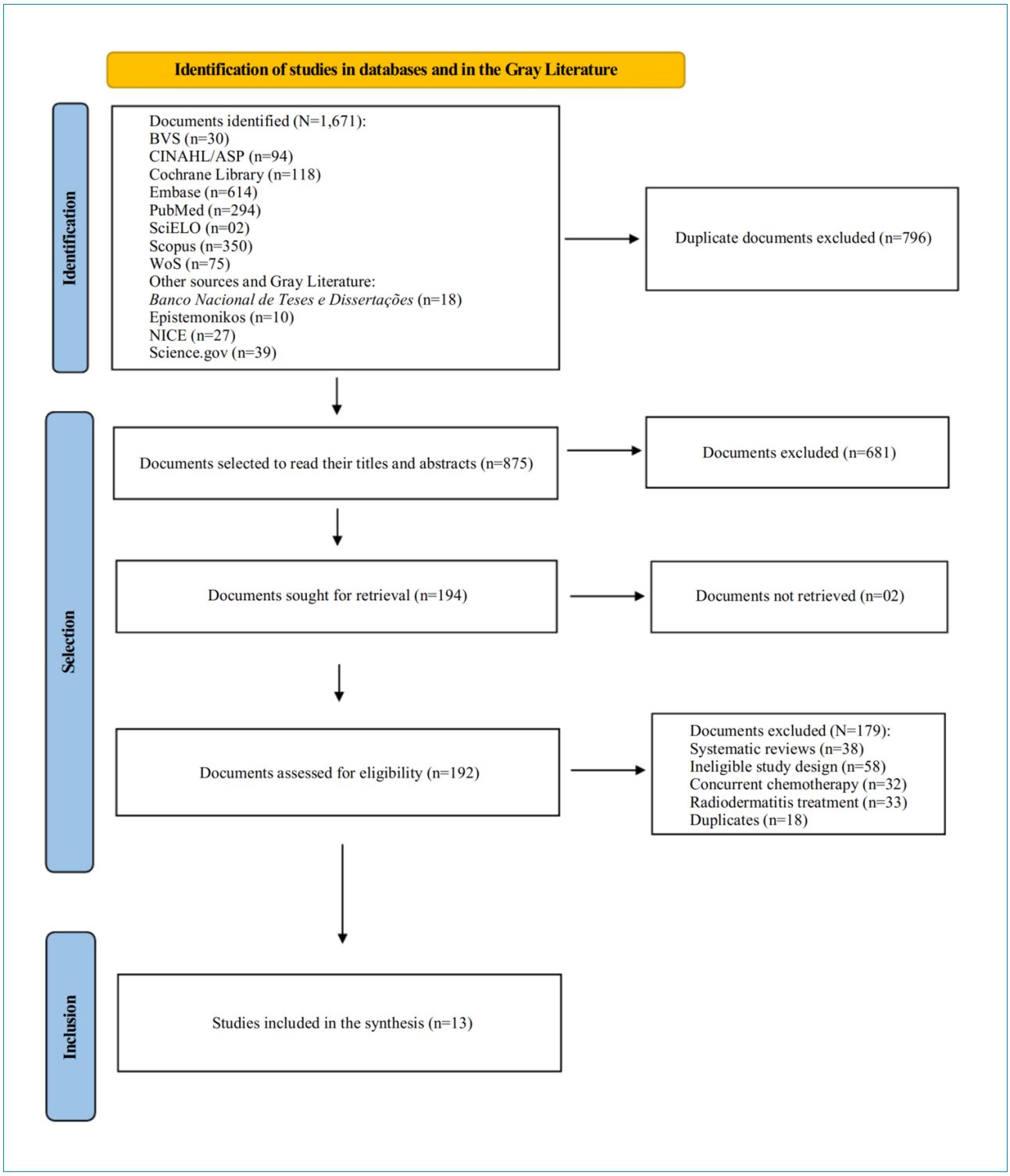

Figure 1. Study selection flowchart. Niterói (RJ), Brazil, 2020.

As shown in Chart 4, the quality of evidence evaluated by GRADE[18,19] was classified as low (C) for the prevention of radiodermatitis, regardless of the type of topical agent used, which suggests that confidence in its effect is limited and weakens the strength of the recommendation. Inconsistency and imprecision were the main factors determining the low quality of the evidence from the studies evaluated.

Chart 1. Characteristics of the studies evaluating topical corticosteroid agents. Niterói (RJ), Brazil, 2020.

Author, country, year	Sample	Radiodermatitis evaluation	Results
Boström et al.[20], Sweden, 2001	N=49 breast cancer patients IG (n=24): mometasone furoate 1% cream CG (n=25): emollient cream (Diprobase)	Evaluation of erythema and pigmentation using spectrophotometry	Mometasone furoate 1% cream combined with emollient cream significantly reduced radiodermatitis (p=0.0033) compared to emollient cream alone
Glees et al.[21], United Kingdom, 1979	N=54 breast cancer patients IG (n=28): hydrocortisone 1% cream CG (n=26): clobetasone butyrate cream 0.05%	Subjective evaluation by physician and patient	No topical agent has been shown to be suitable for the prevention of radiodermatitis
Meghrajani et al.[10], United States, 2016	N=48 breast cancer patients IG (n=21): hydrocortisone 1% cream CG (n=27): placebo cream	CTCAE	The mean radiodermatitis scores were lower in the hydrocortisone 1% group (p=0.024)
Schmuth et al.[22], Austria, 2002	N=36 breast cancer patients IG 1 (n=10): topical methylprednisolone 0.1% IG 2 (n=11): dexpanthenol 0.5% CG (n=15): none	Evaluation of transepidermal water loss levels using an evaporimeter	None of the topical agents reduced the incidence of radiodermatitis
Ulff et al.[23], Sweden, 2013	N=102 breast cancer patients IG 1 (n=53): betamethasone17-valerate cream + Essex® (paraffin-based moisturizer) IG 2 (n=24): Essex® IG 3 (n=25): Canoderm® (urea cream)	RTOG	There was a statistically significant difference (p=0.01) in the incidence of radiodermatitis in favor of the group that used betamethasone17-valerate cream + Essex®

IG: Intervention Group; CG: Control Group; CTCAE: Common Terminology Criteria for Adverse Events; RTOG: Radiation Therapy Oncology Group.

Chart 2. Characteristics of studies evaluating topical antioxidant agents. Niterói (RJ), Brazil, 2020.

Author, country, year	Sample	Radiodermatitis evaluation	Results
Ben-David et al.[25], Israel, 2016	N=47 breast cancer patients IG (n=26): Melatonin cream emulsion CG (n=21): Placebo (cream emulsion without melatonin)	RTOG and CTCAE	The occurrence of acute radiation dermatitis was significantly lower (59 vs. 90%; p=0.038) in the IG
Ghasemi et al.[26], Iran, 2019	N=70 breast cancer patients IG (n=34): atorvastatin 1% gel CG (n=36): placebo gel	RTOG	A 27 percent reduction in hyperemia on irradiated skin in the IG at the 6th week of treatment, without statistical significance (p=0.09)
Karbasforoshan et al.[27], Iran, 2019	N=40 breast cancer patients IG (n=20): silymarin 1% gel CG (n=20): placebo gel	CTCAE and RTOG	Despite the progressive trend of radiodermatitis in both groups, silymarin caused a delay in the incidence and progression of radiodermatitis, especially after three weeks of application
Rollmann et al.[24], United States, 2015	N=42 breast and thoracic cancer patients IG (n=28): Ultra Emu oil CG (n=14): placebo (cottonseed oil)	CTCAE	The average time for hyperemia and peeling was six to seven weeks, suggesting a tendency for Ultra Emu oil to reduce skin toxicity.
Aysan et al.[28], Turkey, 2017	N= 47 breast cancer patients IG (n=23): boron-based gel (sodium pentaborate pentahydrate) CG (n=24): Vaseline gel	RTOG and FPHS	Application of the boron-based gel reduced radiation-induced skin reactions, as the RTOG score was significantly lower in the IG than in the CG (p=0.024) and the FPHS score was higher in the CG than in the IG, without statistical significance (p=0.079)

IG: Intervention Group; CG: Control Group; RTOG: Radiation Therapy Oncology Group; CTCAE: Common Terminology Criteria for Adverse Events; FPHS: Five-Point Horizontal Scale.

Chart 3. Characteristics of studies evaluating herbal medicines topical agents. Niterói (RJ), Brazil, 2020.

Author, country, year	Sample	Radiodermatitis evaluation	Results
Rafati et al.[11], Iran, 2019	N=62 breast cancer patients IG (n=31): Nigella sativa gel 5% (black cumin seed) CG (n=31): placebo gel	RTOG	Patients who used Nigella sativa gel developed acute radiation dermatitis less frequently compared to those who used the placebo (p<0.05) in all weeks except week 2 (p=0.36)
Williams et al.[29], United States, 1996	N=195 breast cancer patients IG (n=97): Aloe Vera gel CG (n=98): placebo gel	Own scale: (1) Mild erythema (2) Moderate erythema with or without dry peeling (3) Moist peeling and/or ulceration	Skin dermatitis scores were virtually identical in both groups (p=0.36)
Sharp et al.[12], Sweden, 2013	N=390 breast cancer patients IG 1 (n=194): Calendula officinalis cream (Weleda®) IG 2 (n=196): Aqueous cream (Essex®)	RTOG	No difference was observed in severe acute radiation skin reactions between the groups at any point in the evaluation (p=0.39)

IG: Intervention Group; CG: Control Group; RTOG: Radiation Therapy Oncology Group.

Chart 4. Quality of the evidence corresponding to the results of studies evaluated by the GRADE system. Niterói (RJ), Brazil, 2020.

Topical corticosteroid agents								
Quantity	**Design**	**Risk of bias**	**Inconsistency**	**Indirect evidence**	**Inaccuracy**	**Publication bias**	**Quality**	**Importance**
5	Randomized clinical trial	Not severe	Severe*	Not severe	Severe†	No	Low (C)	Important
Topical anti-oxidant agents								
Quantity	Design	Risk of bias	Inconsistency	Indirect evidence	Inaccuracy	Publication bias	Quality	Importance
5	Randomized clinical trial	Not severe	Severe*	Not severe	Severe†	No	Low (C)	Important
Topical herbal medicine agents								
Quantity	Design	Risk of bias	Inconsistency	Indirect evidence	Inaccuracy	Publication bias	Quality	Importance
3	Randomized clinical trial	Not severe	Severe*	Not severe	Severe†	No	Low (C)	Important

*Divergent results on the efficacy of the topical agents used; †No confidence interval for the estimates.

DISCUSSION

This systematic review included 13 double-blind randomized clinical trials that evaluated different topical agents to prevent radiodermatitis: corticosteroids[10,20-23], antioxidant agents[24-27,29] and herbal medicines[11,12,29]. Even though some of these agents have shown promise, the evidence gathered here does not allow their use to be indicated for the prevention of radiodermatitis in cancer patients.

Several topical corticosteroid agents have shown promising results, most notably hydrocortisone 1%[10], mometasone furoate[20] and betamethasone valerate 0.1%[23]. It is worth mentioning that hydrocortisone 1% showed conflicting results for the prevention of radiodermatitis in two studies: in one it had no beneficial effect at all[21], while it proved effective in another[10].

This difference is probably due to two reasons:

1. The way radiodermatitis was evaluated, since the first study[21] evaluated it subjectively based on the observation of the physician and the patient, and the second[10], using the RTOG scale, the use of which is widely recognized for its clinical usefulness[30]; and

2. The quantity of the agent applied since only one of them presented the application protocol[10].

Regarding topical antioxidant agents, two studies have not proven their benefit in preventing radiodermatitis[26,27]. On the other hand, three others[24,25,28] have shown beneficial effects, with Emu oil standing out since a time to hyperemia and peeling was reported between the sixth and seventh week of radiotherapy, confirming the safety of this agent. Emu oil is derived from adipose tissue collected from certain subspecies of the Emu, an indigenous Australian bird[24].

Only one study showed some benefit from a topical herbal medicine, *Nigella sativa* (black cumin seed) compared to placebo gel[11], while two other studies evaluating *Calendula officinalis* cream[12] and Aloe vera gel[29] did not show favorable results for the prevention of radiodermatitis.

It is worth noting that the possibility of selective outcome reporting bias cannot be ignored in some studies included in this review, because when the benefit of the topical agent investigated could not be proven to prevent radiodermatitis, many secondary outcomes were conveniently emphasized and discussed.

Most of the studies evaluated radiodermatitis using scales, which are valuable tools for checking its development and progression. Evaluating radiodermatitis using scales favors and optimizes its documentation, makes it possible to evaluate interventions and consequent results, as well as allows comparisons between studies[30].

The amount of agent used in each application was well described by some studies, which used the expression "apply a thin layer"[11,22,28]. However, another provided confusing guidance to the patient, such as applying a "fingertip" measure[10]. This subjectivity in the guidance on how to apply the agent may have influenced the results in preventing radiodermatitis.

General skincare was used in some studies as additional guidelines to be combined with topical agents[10-12,29]. These guidelines were based on hygienic skin care, such as washing the irradiated area with neutral soap, not taking hot baths, drying the skin with a soft towel with light taps, minimizing trauma (friction, itching, scratches and rubbing of the irradiated area) and, for men, shaving with an electric razor, not exposing the irradiated area to the sun or wind, not using adhesive tape, perfumes, talcs, deodorants and creams on the irradiated area.

The quality of the evidence generated by the studies was classified as low for the prevention of radiodermatitis for all types of topical agents used. This is due to inconsistency, which indicated divergent results in different studies, and imprecision, since no study presented estimates derived from robust statistical analyses, such as the confidence interval. Therefore, these two GRADE items[18,19], inconsistency and imprecision, were responsible for reducing the quality of evidence generated by this systematic review. It should be emphasized that the divergent results between the studies are partly due to the evaluation of the efficacy of different topical agents, even though their mechanisms of action are similar.

The main limitations that can be pointed out in this review are the different sample sizes of the studies (generally very small) and the multiple topical agents investigated with different mechanisms of action. However, one of the aims of this review was to present an overview of the topical agents used in the prevention of radiodermatitis, which, in view of its results, can support future studies, review or research, on the efficacy of one of these agents specifically. Another limitation is the heterogeneity of the studies, which evaluated different topical agents, so it was not possible to carry out a meta-analysis.

The review's strengths include minimizing the risk of publication and language bias since the grey literature was researched and no limits were placed on the language in which the studies were published. In addition, the decision to include only double-blind randomized clinical trials favored its internal validity, since the results of all the primary studies included in it were protected from biased evaluation of the effect of topical agents in preventing radiodermatitis because of the blinding of participants and researchers.

Given that all the studies evaluated here were conducted with participants undergoing radiotherapy treatment for breast cancer, new randomized clinical studies should be conducted with participants with different irradiated anatomical regions and larger sample sizes, which in turn will enable more robust analyses, greater statistical power, and more accurate effect estimates, such as measures of association and confidence intervals.

CONCLUSION

This systematic review shows that some topical corticosteroid (betamethasone valerate, mometasone furoate 1% and hydrocortisone 1%), antioxidant (boron, melatonin and Emu oil) and herbal medicines (*Nigella sativa*) agents are promising for the prevention of radiodermatitis, although the evidence gathered here on their efficacy does not indicate their use for the prevention of radiodermatitis in cancer patients and therefore needs to be investigated further in future randomized clinical trials.

Conflict of interest: None.
Funding: Not applicable.
Authors' contribution: GTGP: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, supervision, validation, visualization, writing – original draft, writing – review & editing. RTJ: conceptualization, formal analysis, investigation, methodology, validation, visualization, writing – original draft, writing – review & editing. FVS: formal analysis, investigation, visualization, writing – review & editing. SMSBL: conceptualization, supervision, visualization, writing – review & editing. BGRBO: conceptualization, supervision,- visualization, writing – review & editing.
Data availability statement: All data were generated or analyzed in the present study.
Acknowledgements: Not applicable.

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