Use of Chamomile and Calendula Creams to Prevent acute Radiodermatitis in Patients with Head and Neck Cancer: a Randomized Double Blind Clinical Trial

doi: https://doi.org/10.32635/2176-9745.RBC.2022v68n2.1963

Uso de Cremes de Camomila e Calêndula na Prevenção de Radiodermatites Agudas em Pacientes com Câncer de Cabeça e Pescoço: Ensaio Clínico Randomizado Duplo-Cego

Uso de Cremas de Manzanilla y Caléndula para Prevenir Radiodermatitis Aguda en Pacientes con Cáncer de Cabeza y Cuello: Ensayo Clínico Aleatorizado Doble Ciego

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ABSTRACT

Introduction: Radiodermatitis is characterized by skin lesions resulting from exposure to ionizing radiation, affecting between 80-90% of patients undergoing radiotherapy in the head and neck region. **Objective:** To evaluate the effectiveness of using chamomile cream compared with calendula cream in preventing acute radiodermatitis in participants undergoing radiotherapy for head and neck cancer. **Method**: Randomized, double-blind, prospective clinical trial with quantitative analysis. 23 participants randomly assigned to the group that used chamomile cream (n=12) or to the calendula cream group (n=11) were evaluated. The skin in the irradiation field was evaluated in the first radiotherapy session, every five sessions and after 30 days after the end of the treatment, according to the criteria of the Radiation Therapy Oncology Group (RTOG). **Results:** Participants had radiodermatitis in all the assessments, from grades 1 to 3, except in the first assessment. The highest mean level was observed in both groups in the sixth assessment (2.10±0.73 in the chamomile and 2.37±0.51 in the calendula group, respectively). In the chamomile group, the highest degree of radiodermatitis was 3, in the fifth and sixth evaluations, while in the calendula, grade 3 was observed for the first time in the sixth evaluation, remaining until the eighth. There was no statistically significant difference in the groups evaluated. **Conclusion**: There was equivalence in the effectiveness of the use of chamomile cream compared with calendula cream in the prevention of acute radiodermatitis in patients with head and neck cancer undergoing radiotherapy.

Key words: radiodermatitis/prevention and control; head and neck neoplasms/radiotherapy; chamomile/drug effects; calendula/drug effects.

RESUMO

Introdução: A radiodermatite é caracterizada por lesões cutâneas decorrentes da exposição à radiação ionizante, acometendo entre 80%-90% dos pacientes submetidos à radioterapia na região da cabeça e pescoço. **Objetivo**: Avaliar a efetividade do uso do creme de camomila em relação ao creme de calêndula na prevenção da radiodermatite aguda em participantes submetidos à radioterapia para câncer de cabeça e pescoço. **Método:** Ensaio clínico randomizado, duplo-cego, prospectivo, com análise quantitativa. Foram avaliados 23 participantes, aleatoriamente designados para o grupo que fez uso do creme de camomila (n=12) ou para o grupo do creme de calêndula (n=11). A pele no campo de irradiação foi avaliada na primeira sessão de radioterapia, a cada cinco sessões, e após 30 dias do término do tratamento, de acordo com os critérios da *Radiation Therapy Oncology Group* (RTOG). **Resultados**: Os participantes apresentaram radiodermatite em todas as avaliações, do grau 1 ao 3, exceto na primeira avaliação. O nível médio mais elevado foi observado, em ambos os grupos, na sexta avaliação (2,10±0,73 no grupo do creme de camomila e 2,37±0,51 no de calêndula). No grupo camomila, o maior grau de radiodermatite foi o 3, na quinta e sexta avaliações; enquanto, no calêndula, o grau 3 foi observado pela primeira vez na sexta avaliação, permanecendo até a oitava. Não houve diferença estatisticamente significativa nos grupos avaliados. **Conclusão**: Houve equivalência na efetividade do uso do creme de camomila em relação ao creme calêndula na prevenção de radiodermatites agudas em pacientes com câncer de cabeça e pescoço em radioterapia.

Palavras chave: radiodermatite/prevenção e controle; neoplasias de cabeça e pescoço/radioterapia; camomila/efeitos dos fármacos; calendula/efeitos dos fármacos.

RESUMEN

Introducción: La radiodermatitis se caracteriza por lesiones cutáneas derivadas de la exposición a radiaciones ionizantes, que afectan entre el 80 y el 90% de los pacientes sometidos a radioterapia en la región de cabeza y cuello. **Objetivo:** Evaluar la efectividad del uso de la crema de manzanilla en relación con la crema de caléndula para prevenir la radiodermatitis aguda en participantes sometidos a radioterapia para el cáncer de cabeza y cuello. **Método:** Ensayo clínico prospectivo, aleatorizado, doble ciego con análisis cuantitativo. Se evaluaron 23 participantes, asignados aleatoriamente al grupo que usó la crema de manzanilla (n=12) o al grupo crema de caléndula (n=11). La piel en el campo de irradiación se evaluó en la primera sesión de radioterapia, cada cinco sesiones y a los 30 días de finalizado el tratamiento, según los criterios del Grupo de Oncología Radioterápica (RTOG). **Resultados:** Los participantes presentaron radiodermatitis en todas las evaluaciones, desde el 1º al 3º grado, excepto en la primera evaluación. El nivel medio más alto se observó, en ambos grupos, en la sexta evaluación (2,10±0,73 en el grupo manzanilla y 2,37±0,51 en el de caléndula). En el grupo manzanilla, el mayor grado de radiodermatitis fue 3, en la quinta y sexta evaluaciones, mientras que en la caléndula se observó por primera vez grado 3 en la sexta evaluación, permaneciendo hasta la octava. No hubo diferencia estadísticamente significativa en los grupos evaluados. **Conclusión:** Hubo equivalencia en la efectividad del uso de crema de manzanilla en relación con la crema de caléndula en la prevención de la radiodermatitis aguda en pacientes con cáncer de cabeza y cuello sometidos a radioterapia.

Palabras clave: radiodermatitis/prevención y control; neoplasias de cabeza y cuello/radioterapia; manzanilla/efectos de los fármacos; calendula/efectos de los fármacos.

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INTRODUCTION

Radiodermatitis is characterized by skin lesions resulting from ionizing radiation[1]. Radiodermatitis, radiodermatis, radiation-induced skin lesions or radiation dermatitis are reported by 95% of the patients with cancer submitted to radiotherapy[2] and affect nearly 80% to 90% of the patients submitted to radiotherapy of head and neck[3].

Several factors may potentially affect skin toxicity during radiotherapy. Patient related factors depend on age, comorbid conditions, skin phototype, genetic and nutritional predisposition and Body Mass Index (BMI) determined by the division of the individual's weight by the square of the height. Radiotherapy-related factors comprehend total dose, fractionation, energy and volume of radiation fractions, treatment site and concomitant chemotherapy[4].

Skin lesions can vary from mild erythema to severe complications as acute or chronic ulceration, and necrosis. Radiodermatitis either occurs early on in the treatment period or appears months or up to five to ten years after the end of the radiotherapy[5]. Despite recent technological advances of radiotherapy which hardly affect healthy tissues, the skin is irradiated with inevitable reactions in most of the treatments[6].

Mild erythema is typically the first clinically apparent skin change after breast radiation. However, the most conventional skin reaction occurs approximately 10-14 days after initiation of treatment and often will progressively worsen throughout the course of the treatment[7]. Skin hyperpigmentation often occurs 2-3 weeks after treatment initiation, particularly in patients with increased melanin content and can last for several months. Epilation can also occur if there are hair follicles in the irradiated field[7].

Dry desquamation is typical of high radiation doses and consists of desquamation of dry and squamous skin. Moist desquamation is the result of destruction and the desquamation of dermal layers presents as serous fluid drainage and likely very painful for the patient[7].

Radiodermatitis can damage the quality-of-life of the patient and compromise the efficacy of the treatment if interruption occurs while the lesion heals and delaying the treatment[8]. So far, there is no consensus or a universal standard of care to prevent or treat radiodermatitis during radiotherapy and radiation oncologists use their own clinical experiences to intervene[5].

Chamomile and calendula-based compounds are some of the topic products adopted to prevent radiodermatitis in patients submitted to radiotherapy[4,9].

Chamomile (*Chamomilla recutita*) is a medicinal plant of the *Asteraceae* family, typically used due to its antioxidant, antimicrobial, antidepressant, anti-inflammatory, antidiarrheal, hepatoprotective and antidiabetic properties. It still helps in the angiogenesis and treatment of several skin lesions[10].

On its turn, calendula (*Calendula officinalis*), also a medicinal plant of the *Asteraceae* family has antiallergic, antiphlogistic, antiedema, virucidal, bactericidal, fungistatic, antiulcerative, antiseptic properties, restorative of the skin, soothing and refreshing[11]. Its topical use is recommended for anti-inflammatory and healing therapeutic actions[9].

Due to the scarcity of scientific evidence in the literature, this study is justified whose objective is to evaluate the efficacy of topical products in preventing dermatitis; this is a side effect that can be prevented or minimized through follow-up of patients by nursing professionals who offer information and guidelines, evaluate the area irradiated and toxicity of the tissues through evaluation scales, indicate products to treat the lesions matched to the skin reactions, identify physical, psychological and socioeconomic needs, referring the patient to the multiprofessional team[12].

In addition, the study evaluated and compared the effect of the use of chamomile and calendula-based creams to prevent radiodermatitis in patients submitted to radiotherapy for head and neck cancer (HNC), promoting effective and quality care and implementing evidences-based technological innovations.

The hypothesis is that both topics (chamomile and calendula) have positive and similar effects in preventing radiodermatitis.

METHOD

A double-blind randomized clinical trial was developed, this strategy is meant to avoid conscious or unconscious interference on the results of the trial by the participant and the principal investigator responsible for the study because the topic utilized is unknown.

The study was registered at the platform of "*Registro Brasileiro de Ensaios Clínicos* (ReBEC)" numberRBR-98myd6 and matched to the recommendations of the Consolidated Standards of Reporting Trials (CONSORT).

The research complied with the Directive 466/12[13] of the National Health Council which rules the ethics of studies conducted in Brazil, was approved by "*Hospital de Clínicas da Universidade Federal do Triângulo Mineiro (HC-UFTM)*" and "*Hospital Doutor Hélio Angotti (HHA)*" and by the Institutional Review Board (IRB) of HC-UFTM report number 3.796.696 (CAAE: 2526 1219.0.0000.8667).

All the participants read, understood and signed the Informed Consent Form (ICF) and consented voluntarily to join the study.

The investigator of the radiotherapy services of HC/UFTM and of HHA, both in the city of Uberaba, Minas

Gerais, Brazil, contacted the study participants from February 27 to December 4, 2020.

The inclusion criteria were patients consulted at SUS in both institutions, males and females, age equal or older than 18 years, diagnosed with HNC in treatment with exclusive radiotherapy or concomitant with chemotherapy. Those with history of radiotherapy in the same area of treatment and previous report of allergic reaction while using one of the topical products prescribed during the study (chamomile or calendula) were excluded.

In the first stage, two groups were created and randomly selected by the software Microsoft Excel®: one would receive the topical chamomile and the other, the topical calendula.

In the stage two, the participants were randomly assigned to either group (chamomile or calendula) from simple random sample through the software Microsoft Excel®, with equal odds of being assigned to group one or two.

In both stages, blinding was adopted to ensure that the participant and the investigator-evaluator were unaware of either one of the two groups, chamomile or calendula.

When joining the study, the participants were assigned a code according to the group to which they were assigned (T1-Chamomile and T2-Calendula). Only the pharmacist of record and the study coordinator were aware and it was disclosed to the other team members after the final evaluation of the last participant.

All the patients consulted in both services (HC-UFTM e HHA) who met the inclusion criteria and none of the exclusion criteria during one year in retrospect were thought as potential participants of the study sample. Based in the history of the services, nearly 50 participants were estimated to be potentially evaluated in the study period. This number was not reached due to the necessity of closing the data collection according to the study schedule which was part of a Master thesis.

Both topical products were manufactured by a pharmacy with regular register at the National Registry of Legal Entities (CNPJ) and by a pharmacist registered at the Regional Pharmacy Council of Minas Gerais (CRF-MG). The chamomile and calendula glycolic extracts were obtained from pharmaceutical industries registered at the National Registry of Legal Entities (CNPJ). The production costs of both topicals was covered by the investigator's resources.

Essences to mask the smell of the creams were not used because they could cause allergies and discomforts as nausea and vomits. Visible differences of smell in both topical were undetected after a pilot-manipulation, the stability of the creams produced was kept for 120 days from the date of fabrication.

The contents of the creams were:

- chamomile cream = 10%; silicon cream pH = 5.5; and *qsp* = 100 grams;
- calendula cream = 10%; silicon cream pH = 5.5; and *qsp* = 100 grams.

In the first session of radiotherapy, at every five sessions and 30 days after the end, the data about the history of disease, socioeconomic, demographic, clinic, nutritional characteristics, skin exam and adverse events were collected and recorded by the investigator-evaluator.

The investigator handed over the chamomile or calendula cream cost-free to the study participants . They were guided to apply topically a thin layer of the cream on the area of the treatment three times a day with clean hands from the first to the last days of radiotherapy sessions and to continue the applications for more 30 days after the end of the radiotherapy.

The development of radiodermatitis was evaluated according to the level of toxicity following the criteria of the Radiation Therapy Oncology Group (RTOG) of the European Organisation for Research and Treatment of Cancer (EORTC)[14], and within the scale: grade 0 – no reaction, intact skin; grade 1 – mild erythema, epilation and/or dry desquamation; grade 2 – painful erythema, wet desquamation and/or moderate edema; grade 3 – confluent moist desquamation and/or important edema; grade 4 – ulceration, hemorrhage and/or necrosis.

The participants who developed some grade of radiodermatitis and needed local treatment continued using these products (chamomile or calendula) in areas of intact skin, and another topical prescribed by the radiology oncologists was included only where dry or moist desquamation occurred.

The Visual Assessment Scale (VAS) was utilized to evaluate the intensity and the degree of pain reported by the participants in the area of the treatment, ranging from 0 to 10, being 0, the total absence of pain and 10, the maximum level the patient can bear[15].

In addition to the topical product (cream of chamomile or calendula) the participants were guided to avoid lotions, creams, powder or alcohol on the skin in the area of treatment and use only what has been prescribed by the radiology oncologist or nursing team. When showering, wash the skin with soap and lukewarm water and dry without friction and to not rub, scratch, scrub or brush and shave the irradiated skin.

Band-aid or dressing on the demarcated area is not recommended, except when the participant had skin ulceration requiring secondary protection. Extreme heat or cold (hot water bag or ice) and sun exposure should be avoided.

The data collected were submitted to descriptive analysis based in absolute and percent frequencies. The comparison between the groups was made with the chi-square test (Pearson and/or Yates) for the categorical variables and test *t* of Student for numerical variables.

The RTOG grading, the main outcome of the study, was analyzed for the groups through eight evaluations during radiotherapy and 30 days after the end of the treatment based in the analysis of the variance for repeated measures and two-way Tukey test comparisons[16,17]. The software Statistical Package for Social Science (SPSS), version 20.0.0 was adopted for all the analyzes with level of significance of 5% (p=0.05).

RESULTS

36 participants were enrolled in the study, 20 in the group chamomile and 16 in the group calendula. Due to losses and exclusions during the study, only 23 participants remained to be analyzed for lesions according to RTOG grading, 12 in the chamomile and 11 in calendula as shown in the flowchart CONSORT in Figure 1.

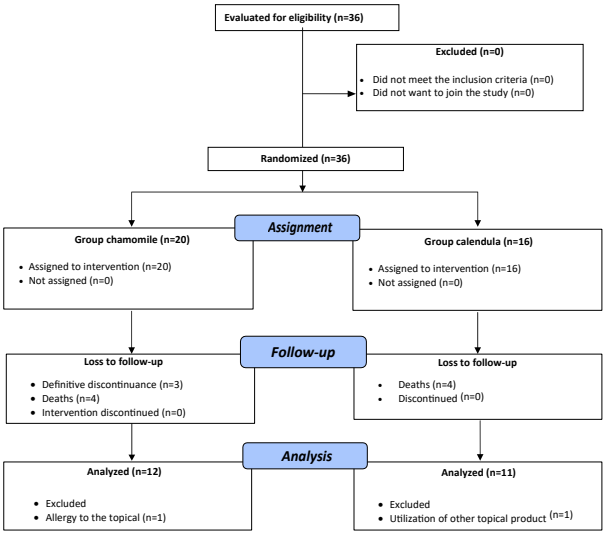

Figure 1. Flowchart CONSORT of selection and enrollment of participants

The sociodemographic, epidemiological and clinical characteristics of the participants were statistically similar between the groups (chamomile and calendula) showing they are comparable.

Of the participants, 25 were consulted at HHA (69.4%), 25 were males (69.4%), 21 were of Brown race (58.3%), 23 did not complete elementary school (63.9%), 26 had family income (72.2%) from one to two minimum wages ; 23 were retired (59.0%), 17 were married (47.2%), 14 were in the age range of 60-69 years (38.9%); 10 had BMI between 18.5 to 24.9% kg/m^2 (34.5%); 23 quit smoking (63.9%); 30 smoked for more than 20 years (88.2%); 25 quit alcohol drinking (69.4%); 28 drank alcohol for more than 20 years (87.5%).

The clinical characteristics revealed that 12 had larynx cancer (32.4%), 19 were in stage IV (52.8%) and 29 submitted to radiotherapy concomitant with chemotherapy (80.6%).

The grade of acute radiodermatitis according to RTOG evaluated at each assessment for patients in follow-up for both groups during radiotherapy is summarized in Table 1. In all the evaluations, it was detected mild erythema, epilation and/or dry desquamation, which is the lowest grade of lesions for both groups and the highest grade of lesions – confluent, moist desquamation and/or important edema (RTOG=3) was found in the group chamomile in the fifth evaluation remaining up to the sixth and in the group calendula, for the first time in the sixth evaluation, continuing up to the eighth (Table 1).

Only 12 participants of the group chamomile and 11 in the group calendula who submitted to all skin evaluations from the first up to 30 days after the end of the radiotherapy were compared in relation to the grade of radiodermatitis. Both groups presented some grade of radiodermatitis (1≤RTOG≤3). The mean grade of RTOG peaked in the sixth evaluation, being significantly similar between the two groups in all the evaluations (p>0.005) from the first up to 30 days after the end of the radiotherapy (Table 2).

There were participants who presented some grade of radiodermatitis with prescription of another topical product. In these cases, they were applied only in the lesion area or desquamation, continuing with the chamomile and calendula cream in the rest of the intact skin. In the group chamomile, the participants initiated the use of another topical product from the fifth evaluation (2; 14.3%), while in the group calendula, they initiated from the second evaluation (1; 6.7%). The great number of participants who used another topical product in the group chamomile was found in the sixth evaluation (3; 23.1%) and in the seventh, in the group calendula (6; 50.0%).

As secondary outcome, the pain in the area of treatment was evaluated based in VAS for the participants in follow-up in each one of the evaluations. It was found variation from zero (no pain) to ten (maximum intensity of pain) for both groups. Considering only the participants who were pain-checked along the evaluations in each group, totaling 12 in the group chamomile and 11 in the group calendula, no significant differences were detected in mean grades of the scores of pain in both groups in all the evaluations (p>0.05).

Table 1. Descriptive summary of toxicity grading (ROTG) of the participant's skin followed up in each evaluation

RTOG										
	Chamomile					Calendula				
Grading	N	Minimum	Mean	Maximum	SD	N	Minimum	Mean	Maximum	SD
I	20	1.0	1.0	1.0	0.0	16	1.0	1.0	1.0	0.0
II	19	1.0	1.0	1.0	0.0	15	1.0	1.1	2.0	0.3
III	17	1.0	1.0	1.0	0.0	15	1.0	1.1	2.0	0.4
IV	16	1.0	1.3	2.0	0.5	14	1.0	1.3	2.0	0.5
V	15	1.0	1.9	3.0	0.5	14	1.0	1.4	2.0	0.5
VI	14	1.0	2.1	3.0	0.6	12	1.0	2.2	3.0	0.6
VII	11	1.0	1.8	2.0	0.4	11	1.0	2.2	3.0	0.6
VIII	10	1.0	1.4	2.0	0.5	9	1.0	1.7	3.0	0.7
30 days*	12	1.0	1.1	2.0	0.3	11	1.0	1.1	2.0	0.3

Captions: RTOG = Radiation Therapy Oncology Group; SD = Standard Deviation.
(*) 30 days after the end of the radiotherapy.

Table 2. Descriptive and comparative summary of toxicity grading (RTOG) of the participant's skin in each evaluation (n=23)

RTOG					
	Group Chamomile (n=12)		Group Calendula (n=11)		p-value*
Grading	Mean	SD	Mean	SD	Chamomile *versus* calendula
I	-	-	-	-	-
II	1.00	0.00	1.12	0.35	1.000
III	1.00	0.00	1.12	0.35	1.000
IV	1.40	0.51	1.25	0.46	0.999
V	1.80	0.42	1.62	0.51	0.999
VI	2.10	0.73	2.37	0.51	0.998
VII	1.80	0.42	2.12	0.64	0.991
VIII	1.40	0.51	1.62	0.74	0.999
30 days**	1.10	0.31	1.00	0.00	1.000

Captions: RTOG = Radiation Therapy Oncology Group; SD = Standard deviation.
(*) Anova-F with repeated measures followed by Tukey test.
(**) 30 days after the end of the treatment.

In the group chamomile, the mean grade of the pain peaked in the third and eighth evaluations (4.6; 4.3; respectively) and in the group calendula in the fourth and eighth evaluations (4.5; 4.5; respectively) as shown in Table 3.

DISCUSSION

In an exploratory study conducted by the National Cancer Institute José Alencar Gomes da Silva (INCA), 99.6% of the patients had some grade of radiodermatitis: 64.7%, grade 1, 23.4%, grade 2 and 11.4% grade 3. Only one (0.6%) did not present radiodermatitis during radiotherapy[12].

For patients with HNC the development of dermatitis is common, it can occur in approximately 80-90% of this population because the skin in this region is more sensitive with creases which favor humidity and frequent friction becoming more fragile[3].

These patients can be exposed to an extremely aggressive, debilitating condition associated with pain, weight loss and may have the body image altered, even for a certain period, and radiodermatitis[18] is one of the causes. This condition can be minimized through guidelines about skin care, weekly follow-up of the irradiated area, topical solution to be applied during radiotherapy, with early intervention for any type of lesion that onsets[11].

Table 3. Descriptive and comparative summary of complaints of pain in the local of the treatment (VAS) of the participants in follow-up according to the group and evaluation (n=23)

	PAIN				
	Chamomile (n=12)		Calendula (n=11)		p-value*
Grading	Mean	SE	Mean	SE	Chamomile *versus* calendula
I	3.20	0.99	3.75	1.10	-
II	3.20	0.89	3.37	1.00	1.000
III	4.60	0.95	3.75	1.06	1.000
IV	4.20	0.89	4.50	0.99	1.000
V	2.80	0.94	4.00	1.05	1.000
VI	2.20	0.97	4.00	1.08	1.000
VII	2.80	1.13	3.62	1.26	1.000
VIII	4.30	1.04	4.50	1.17	1.000
30 days**	2.70	1.07	3.00	1.20	1.000

Caption: VAS = Visual analogue scale; SE = Standard error.
(*) Anova-F with repeated measures followed by Tukey test.
(**) 30 days after the end of the radiotherapy.

Both chamomile and calendula are two medicinal plants knowingly effective not only in skin lesions but for other diseases as well and widely prescribed[19-23].

In the present study, it was found in all evaluations for both groups (chamomile and calendula), except in the first, that some grade of radiodermatitis occurred, from a mild erythema, epilation and/or dry desquamation (RTOG=1) up to a confluent, moist desquamation and/or important edema (RTOG=3), being this the maximum grade detected in the group chamomile in the fifth evaluation continuing up to the sixth and in the group calendula, it was found for the first time in the sixth and remaining up to the eighth evaluation. No significant difference of the grade of radiodermatitis was found in both groups, however, the highest mean score of radiodermatitis (RTOG) in the two groups was detected in the sixth evaluation with 2.10 (SE = 0.21) in the group chamomile (10% cream chamomile; silicon cream PH=5.5 and *qsp*=100 grams) and 2.37 (SE=0.23) in the group calendula (10% of cream calendula; silicon cream PH=5.5 and *qsp*=100 grams). In the group chamomile, the participants initiated another topical to treat lesions from the fifth evaluation and in the group calendula, from the second evaluation. None of the participants developed ulceration, hemorrhage and/or necrosis, the highest grade of radiodermatitis (RTOG=4).

A randomized clinical trial[1] concluded that chamomile gel containing 8.35% was safe when compared to 2.5% and 5.0% concentrations to prevent radiodermatitis in patients in radiotherapy for HNC and higher concentrations of chamomile explained the delay in developing erythema. In addition, comparing the patients who used chamomile with those utilizing urea, it was noticed that for both groups, the beginning of development of radiodermatitis (RTOG=1) occurred in the final of the first week and all presented grade 1 in the end of the study and grades 3 and 4 were not detected in the participants[1].

In a controlled double-blind randomized clinical trial with 51 patients with HNC in radiotherapy[9], calendula, widely applied and recommended to treat radiodermatitis presented better therapeutic response than essential fatty acids to prevent and treat this disease[11]. Its oily and alcoholic extracts have anti-inflammatory, antibacterial, angiogenic and fibroblastic properties also utilized to treat several other types of skin lesions as bruises, burns, leg ulcers, inflammation of mucosa membranes of the mouth, throat and vagina[21].

In a systematic literature review[4] comparing the effects of pharmacological to non-pharmacological topicals in radiodermatitis, it was found that no difference exist among them. Trolamine, *Aloe vera*, allantoin, Lianbai liquid sucralfate, Na-sucrose Octasulfate, oil, hyaluronic acid and dexpanthenol were utilized as pharmacologic topicals. Non-pharmacological topicals controls included regular care and routines of the institution, aqueous cream, neutral soap, water-thermal gel and placebo. Even with the variety of the interventions evaluated, the results encountered did not suggest evidences of benefits of the use of any of these interventions for acute dermatitis.

However, despite some barriers that have been investigated[24,25], there is still no consensus or universal standard of care to prevent or treat radiodermatitis during radiotherapy; many dressings are being utilized in clinical trials to identify possible topicals to help the clinical practice.

When dry or moist desquamation occurs, the main measures are aimed to keep the skin dry and clean, protected from infection and manage pain. Some of the most frequently used dressings include hydrocolloid or hydrogel and silver-based ointments which provide a barrier, soothing and refreshing effect which improves comfort[26].

Thus, the treatment of each grade of radiodermatitis requires strict evaluation by the nursing team and the radiology oncologist to control the pain of the irradiated area, prevention of infection to avoid future discontinuation of the treatment and damages to the patient[12].

Skin toxicities when severe can cause discontinuation of the radiotherapy treatment and if prolonged for one week or more, the patient's prognosis worsens as well as local control and survivorship. Thus, it is necessary to attempt to postpone grade 2 radiodermatitis to prevent toxicity-related interruptions[27].

Pain in the region of the treatment is a typical complaint in some moment during radiotherapy[28].

Pain impacts negatively the quality-of-life of the oncologic patient, mainly those with disease progression. Oncologic pain can provoke, in addition to physical manifestations, negative psychosocial effects[29]. Nearly 70% of the patients with cancer report pain and patients with HNC may have more prevalence of the pain[30]. In that line, the individualized evaluation with anamnesis and physical exam is important for improved prescription of the treatment, possibly bringing relief and comfort to the oncologic patient[29].

It was found a variation from zero (absence of pain) to ten (maximum intensity of pain) for both groups (chamomile and calendula) according to VAS. For the group of chamomile, the mean grade of pain peaked in the third and eighth evaluations (4.6; 4.3, respectively) and in the group calendula, in the fourth and eighth evaluations (4.5; 4.5, respectively) without significant difference between them (p>=0.05). The pain reported was specific of the region submitted to the radiotherapy (anatomic region of the tumor) regardless of the topical utilized, being also associated with the context of the disease.

The number of the participants was limited because of the historical series of consultation in both institutions and only those who matched the inclusion and exclusion criteria and who voluntarily accepted to join were enrolled. There were loss to follow-up and deaths inherent to not submitting to the oncologic treatment. No other self-reported complaints were investigated and neither changes of self-image. Other obstacles to expand the sample, diversify other types of solutions and test different concentrations were the cost of production of the topicals and continuation of the studies because of the structure of the services.

A positive aspect was the strict methodological approach based in a double-blind, randomized clinical trial, avoiding any conscious or unconscious interference on the study results.

Multicenter studies involving services of other states and regions of the country and sufficient fund raising can be an alternative to continue the studies to evaluate the effect of topical products in preventing radiodermatitis. It can be applied not only in participants with HNC but also in other areas of treatment, with other topicals of different costs since so far no standard validated protocol exist, leaving the clinical decision to be taken based in the best experience of radio oncologists teams.

CONCLUSION

Radiodermatitis is a side effect of radiotherapy. It was detected in all the participants of both groups (chamomile and calendula) during the radiotherapy treatment, presence of some grade of radiodermatitis since the mildest erythema, epilation and/or dry desquamation (RTOG=1) up to confluent, moist desquamation and/or important edema (RTOG=3). Both in the chamomile and calendula groups the participants skin did not remain intact, however, the topicals utilized were able to avoid ulceration, hemorrhage and/or necrosis (RTOG=4).

Regardless of the occurrence of the highest grading of radiodermatitis (RTOG=3) in the group calendula in the sixth evaluation and similar grading (RTOG=3) in the group chamomile in the fifth evaluation, it was found statistic similarity in the effectiveness of the use of the two topicals.

Other primary studies involving variations of coverage, participants from other country regions and sufficient financial funding are some of the aspects to investigate the effectiveness of topical barriers in preventing radiodermatitis in patients submitted to radiotherapy.

CONTRIBUTIONS

All the authors contributed to the study design/concept, acquisition, analysis and interpretation of the data, wording and critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

FUNDING SOURCES

None.

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Recebido em 6/5/2021
Aprovado em 1/6/2021

Scientific-Editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777