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Cutaneous Acceptability And Hydratation of Topical Products In Patients Undergoing Radiotherapy and Antineoplastic Treatment

Aceitabilidade cutânea e hidratação de produtos tópicos em pacientes submetidos a radioterapia e tratamento antineoplásico

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RESUMO

Background: New antineoplastic agents have increased the survival rate of cancer patients, however, the incidence of cutaneous skin toxicity, which leads to worsening in the quality of life and to the necessity of interrupting the treatment, continues presently. Natural agents, as Aloe vera and Calendula, have been suggested as potential ways of prevention and treatment for radiation dermatitis resulting from radiotherapy, providing better adhesion to the therapies and improving the wellbeing of the patients. **Purpose:** To evaluate the cutaneous acceptability and hydrating effect of four topical test products in patients undergoing radiotherapy and antineoplastic treatment. **Methods:** Both sex participants, undergoing oncological treatments, were included. Patients received a prescription to self-applied topical test products - A (Washcare), B (Moistcare), C (Extremecare) and D (Coolcare Mask) during 30 days. Products acceptability and skin hydration were evaluated considering the occurrence of skin adverse reaction, participants self-reported feelings of skin discomfort, dermatologist and instrumental skin hydration evaluation. **Results:** Thirty-three participants initiated and completed the study. None of them had skin reactions or discomfort in the area of application, and no adverse events were reported. Twenty-five participants (75.8%) reported improvement in skin hydration after using the test products, while eight participants (24.2%) observed the maintenance of hydration (p<0,005). **Conclusion:** The products evaluated showed improvement in skin condition in most patients, increased hydration and good skin acceptability in patients with skin toxicities caused by the cancer treatments.

Keywords: Calendula; Radiodermatitis; Aloe; Wounds and Injuries; Skin; Toxicity.

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INTRODUCTION

New antineoplastic agents have increased the survival rate of cancer patients, however the incidence of cutaneous skin toxicity, which leads to worsening in the quality of life and to the necessity of interrupting the treatment, continues present[1-5]. Appropriate management of the cutaneous toxicities is necessary to ensure the adhesion to the oncological therapies and improving the wellbeing of these patients[6].

About 85% of the participants treated with new antineoplastic agents develop acneiform lesions and 35% develop cutaneous xerosis[7], while 60% of the participants, in conventional chemotherapeutic treatment present some skin side-effect[8]. The monoclonal antibodies that inhibit the epidermal growth factor receptor – EGFR and the multi-kinase inhibitors (imatinib, dasatinib, nilotinib, sorafenib e sunitinib) are the new classes most related to skin toxicities. Taxanes (docetaxel, paclitaxel) also show an incidence of toxic skin effects such as xerosis, erythema and urticaria[9]. Hand-foot syndrome is a frequent toxic reaction related to some chemotherapeutic agents as doxorubicin, cytarabine, docetaxel and fluorouracil[10].

Radiotherapy, as well, is one of the main modalities for the treatment of tumors[11]. One of the most common effects from the treatment with ionizing radiation is the radiation dermatitis, affecting 90% of the participants, among which 85% present moderate to serious cutaneous reactions[12-14], resulting from the combination of a decrease in functional staminal cells, endothelial alterations, inflammation, necrosis and skin cells death. Intrinsic factors like age, general health, ethnic origin, coexisting diseases, UV exposure, hormonal status[15] and genetic factors[16], as well as extrinsic factors like dose, volume and number of fractions of radiation, radiosensitizers use, concomitant chemotherapy and the site of treatment, may lead to this skin condition[5,15,17-19]. Erythema, skin dryness, itching, discomfort, pain and warmth sensation are some of the reactions that affect the oncological patient[1,20] and that support the need of specific products for the skin of this patient. Head and neck and breast tumor treatments are most related to the appearance of radiodermitis[12-14].

For the guarantee of acceptability and effective improvement in participants skin hydration in oncological treatment, the cutaneous acceptability of the products indicated for this participant needs to be verified, because their skin is much more sensitive and so require more attention. When choosing the formulations, they need to have a higher hydration power and higher security about the ingredients. Studies demonstrate that the use of preservative systems, common in dermatological products (parabens, for example), and the use of moisturizing ingredients like urea, may impair the skin already lesioned[21].

Taking these concerns in consideration, acceptability trials aim to confirm the absence of irritation risk and to recognize possible discomforts associated with the product application, due to the potential for adverse reactions[22,23].

Studies have demonstrated the use of natural agents, as *Aloe vera*[24-26] and *Calendula*[27], as a potential way of prevention and/or treatment for radiation dermatitis.

Calendula, a natural agent with antioxidants properties, is also studied as a potential treatment for radiation dermatitis[28]. Pommier *et al*. (2004) demonstrated less radiation dermatitis in breast cancer patients submitted to radiotherapy when comparing to the use of trolamine. Besides that, the interruptions in treatment were lower among these participants using *Calendula*[27].

Skin cleaning and hydration of injured skin are critical during chemotherapy and radiotherapy, so products like lotions and creams are recommended, but clear evidence about the best and most effective option is still lacking[29]. The products of our study - containing *Aloe vera* and *Calendula*, besides other moisturizing ingredients - were developed to attend the specific hydration requirements of these patients in oncological treatment.

Since the literature has insufficient data about effective interventions for cutaneous lesions, our study aims to assess the cutaneous acceptability, tolerability rate and moisturizing effect of non-pharmacological topical products containing *Aloe vera*, *Calendula* and antioxidants in oncological patients.

METHODS AND MATERIALS-

Study design and participants

This was a prospective, open-label, single group, 4-week and single-center clinical study evaluating the cutaneous acceptability and moisturizing effect of a topically cosmetic in subjects undergoing radiotherapy and antineoplastic treatment. The primary purpose was supportive care by monitoring adverse events (AEs) and cutaneous discomfort related to normal usage by oncological patients.

The study was conducted at Kenji Toyota Research Institute, Brazil, in accordance with the Declaration of Helsinki, international guidelines for Good Clinical Practice, and the National Health Council (CNS) Resolution 466/12. The study was approved by the Institutional Ethics Committee, and all participants provided written informed consent prior to participation.

We enrolled a group of 33 research participants of both sexes, aged from 31 to 76 years (median age 53.5), with diagnosis of cancer and receiving antineoplastic treatment with capecitabine, imatinib, sunitinib, doxorubicin, cetuximab and liposomal doxorubicin or radiotherapy. Patients skin phototype were classified from of I-VI according to the Fitzpatrick scale[30]. According to the Fitzpatrick scale phototypes I (white skin,

burns easily, never tans), phototype II (white skin, burns easily, tans minimally), prototype III (white skin, burns moderately, tans moderately) and phototype III (beige-olive skin, burns minimally, tans moderately and easily)[8] (Table 1). Regarding the phototype classification of the sample, we found that it corresponds to the distribution observed in the Brazilian population, according to the IBGE.[31].

The common characteristic among the participants that justified the inclusion was the presence of skin side effects related to the toxicity of antineoplastic and radiotherapy treatments that they were receiving.

The exclusion criteria were: burn wound exudate; a history of allergic reactions to the components of the product tested; surgical procedures within 30 days prior to screening; local infection; topical medications or cream in the areas of product application within seven days prior to recruitment.

Study procedures

Participants who were on systemic antineoplastic treatment received prescription of three products specifically formulated for cancer skin care management containing Aloe vera, calendula and antioxidants which does not contain parabens:

- Product A (Washcare), a cleaning foam used in place of soap to clean the entire body. Participants were instructed to wash their whole body while bathing with the product replacing the soap.
- Product B (Moistcare), a moisturizing lotion for the whole body. Participants were instructed to apply body lotion twice a day, one after the bath, the other as suitable.
- Product C (Extremecare), a concentrated moisturizing cream to be used in more dry areas. Participants were instructed to apply the cream in hands, feet, knees and elbows.

Participants who were undergoing radiotherapy, in addition to these three products, also used product D (Coolcare Mask), a gel associated spray, which forms a mask on the skin used to refresh and moisturize the radiation area. Participants were instructed to apply the product twice a day, one after radiotherapy sessions.

A clinical study to prove safety of use of each product was developed previously according to the Guide for the Safety Evaluation of Cosmetic Products of ANVISA Study Assessments.

The study comprised two scheduled clinic visits, at the beginning and after 30 days. At day 0, participants were submitted to a dermatological evaluation and measurement of skin hydration. At the same day, they answered a clinical investigation instrument, received the study products and a diary to record the date and time of each product application in order to monitoring adherence, adverse events (AEs) and cutaneous discomfort related to usage. Participants were contacted by telephone to access level of adherence and answer possible doubts after 15 days. At the 4-week follow-up visit, participants returned to the research center and completed the dermatological evaluation data, an instrumental measurement of skin hydration and questionnaire of cosmetic apreciability in the native language of participants.

To improve quality of data, the participants were asked to inform the investigator about any new medication use outside of traditional oncological treatment; not to apply any similar product in the

Table 1. Fitzpatrick scale phototypes[32]

Fitzpatrick scale phototypes						
Phototype	**Sunburn and tanning history (defines the phototype)**	**Immediate pigment darkening**	**Delayde tanning**	**Constitutive color (unexposed buttock skin)**	**UV-A-MED (mJ/cm²)**	**UV-B MED (mJ/cm²)**
I	Burn easily, never tans	None	None	Ivory white	20-35	15-30
II	Burns easily, tans minimally with difficult	Weak (+/-to+)	Minimal do weak (+/-to+)	White	30-45	25-40
III	Burns moderately, tans moderately and uniformly tsurns	Definite +	Low +	White	40-55	30-50
IV	minimally, tans moderately and	Moderate ++	Moderate ++	Beige-olive, lightly tanned	50-80	40-60
V	Rarely burns, tans profusely	Intense brown) +++	Table 1 Strong, intense, brown +++	Moderate brown tanned	70-100	60-90
VI	Never burns, tans profusely	Intense (dark brown) +++	Strong, intense, brown +++	Dark brown or black	100	90-150

study area; not to use topical or systemic antiallergic or anti-inflammatory medication; expose themselves to excessive sunlight/artificial tanning beds; not to use tea, compress, shampoo and soap; and not to participate of other study.

Study Assessment

Assessment of skin was performed by the dermatologist at day 0 and day 30.

Cutaneous Acceptability of the study products were investigator-assessed based on occurrence of adverse events and feelings of cutaneous discomfort self- recorded by participants in their treatment diaries (dryness, prickling, itching, and stinging), and causality defined by World Health Organization (WHO)[33] and skin adverse reactions graded for severity according to International Contact Dermatitis Research Group (ICDRG) scale which evaluate the appearance of erythema, edema, and skin desquamation[34]. The intensity of the reaction was classified as: 0, no reaction; 1, mild/ good reaction; 2, moderate reaction; and 3, severe/ bad reaction.

Skin Hydration was performed by dermatologist and instrumental evaluation. Dermatologist evaluated skin hydration at day 0 using a two-point scale: Good (adequate hydration) and Bad (dryness, lack of elasticity and / or desquamation) and after use test products (day 30). Hydration improvement was evaluated using a three-point scale: Excellent (high hydration, good elasticity, no desquamation); Good (skin clinical aspect with mild improve); and no alteration (skin presented the same condition before use of test products). Instrumental skin hydration was made by a multiple probe Corneometer (Courage & Khazaka, Cologne, Germany), by placing the probe on to the skin surface. The measure was carried out under standard conditions of temperature and humidity (T°= 20°C, humidity 40-60%) and after a rest period of 20 minutes. The results covered a range of non-hydrated skin (<30 uc), hydrated skin (30-45 uc), sufficiently hydrated skin (>45 uc).

Cosmetic Appreciability/Tolerability was verified, using a targeted questionnaire answered by the participants after the product's application. A specific questionnaire was administered for each test product (Washcare, Moistcare, Extremecare, Coolcare Mask). In general, the participants were asked about the improvement of the hydration, appearance, dryness relief or soothed (Table 2).

Statistical Analysis

Thirty-three participants were enrolled and complete the study. The analysis conducted followed the described parameter values at baseline time (T0), before using the test products, and 30 days after the application (T30). The quantitative variables were represented by mean, standard deviation, minimum, median, maximum and number of valid participants. The qualitative variables were represented by simple frequency and percentage. The Binomial test for proportion comparison in a single sample was used in order to compare the responses before (T0) and after (T30) in relation to the improvement of hydration and hydration maintained in the dermatological evaluation.

To compare the measures T0 and T30 quantitatively in instrumental measures of hydration, we used the

Table 2. General skin care management tolerability questionnaire.

Questionnaire
1) What soap, lotions and/or creams have you tried in the past 3 months?
2) Compared to other moisturizers products you have tried which statement best describes how well you tolerated this product: a- I tolerate this product extremely well, much better than other products I have tried. b- This product was well tolerated, better than most I have tried c- I tolerate this product about the same as others I have tried d- I did not tolerate this product as well as others I have tried e- This product was poorly tolerated on my skin
3) Compared to other products you have tried, which statement best describes the hydration or overall appearance or dryness relief or soothed of this product: a- Much better than the others I have tried b- Somewhat better than the others I have tried c- The same as the other products I have tried d- Not quite as others I have tried e- Much less than others I have tried
4) How would you rate your overall experience with products? a- very good b- good c- average d- bad e- very bad
5) Please list any additional comments regard test products

paired sample t-Student test. It was considered a significance level of 5% ($p \leq 0.05$). Only data from subjects adherent with study product use were used in the analyses, and all 33 subjects were adherent with study product use. Instrument categories that had less than three responses were grouped for the statistical test.

All procedures performed in studies involving human participants were conducted in accordance with the ethical principles founded in the 1964 Helsinki declaration and its later amendments or comparable ethical standards and Good Clinical Practice Guidelines and in accordance to Brazilian Ethical normative, in special, Resolution no 466/2012, of the National Council of Health, from the Ministry of Health. The study was approved by the Research Ethics Committee of the Faculdade de Medicina do ABC (FMABC) (Reference number: 70638517.4.0000.0082). Informed consent was obtained from all individual participants included in the study.

RESULTS

Thirty-three patients were included, 24 women (72%) and 9 men (28%), with an average age of 52 years (range: 31 - 76 years). From the sample evaluated, 48% (16 patients) had a diagnosis of breast cancer, 21% (7 patients) had rectal cancer, and the remainder had various neoplasms (larynx, esophagus, plasmacytoma, skin, osteosarcoma, and thymoma). From the 33 patients evaluated, 26 (78%) had cutaneous xerosis, 11 (33%) radiodermatitis, 7 hand-foot syndrome (21%) and 6 (18%) acneiform eruptions. The vast majority had phototype IV (22 - 66%), while 8 had phototype III (24%). Two patients had phototype V and 1, phototype II. From these, only 2 patients were undergoing radiotherapy alone (1 breast cancer patient and 1 skin cancer patient) and 20 patients received combination therapy. (Table 3)

Table 3. Patient Characteristics.

Average Age		**52 years old**
Sex	Male	9
	Female	24
Phototype	II	1 (3%)
	III	8 (24%)
	IV	22 (66%)
	V	2 (6%)
Primary Tumor	Breast	16 (48%)
	Rectum	7 (21%)
	Other tumors	10 (30%)
Signals and Symptons	Xerosis	26 (78%)
	Radiodermatitis	11 (33%)
	Hand-foot syndrome	7 (21%)
	Skin rashes	6 (18%)

Cutaneous Acceptability

All participants completed the study and presented adequate adherence requirement for inclusion in the analysis of study products acceptability. After 30 days of test products use, there were no adverse events reported and no record of the appearance of lesions, symptoms or signs of skin irritation as erythema, pruritus, fervour, desiccation, papule, vesicle, blister, crust, edema or dyschromia in any participant. None of the 33 participants reported cutaneous discomfort in the area of application. The most common affected areas were arms (27%) and legs (21%), followed by face (18%) and breast (15%). (Table 4).

Skin Hydration

Twenty-five participants of these study (75.8%) improved skin hydration after use of test products while eight participants (24.2%) maintained skin hydration between day 0 and day 30. None of them related decrease of hydration. Regarding the instrumental analysis of hydration using the corneometer, the value at start and end of therapy showed a quantitative increase of hydration measure after 30 days (16,5%) (Table 5).

Cutaneous Appreciability

Those participants who underwent **antineoplastic treatment** received product A (Washcare - cleaning foam), product B (Moisturizing - lotion) and product C (Extremecare - moisturizing cream). They were able to evaluate the quality of the product as Very Good, Good, Average, Bad or Very Bad, but none of the participants reported their experience use with test products as Bad or Very Bad and then, for the analysis of the data, the answers were compared Very Good or Good versus Average. Of the 33 participants who participated in the antineoplastic treatment, the clear majority demonstrated Good and Very Good overall experience after use of product A (31- 93.9%) and product C (32 – 97%) and few of them related Average experiences with those products, 6.1% and 3% respectively. Product B had 100% of acceptability (Very Good and Good) in those participants. The difference between the responses (Very Good or Good versus Average) was significant ($p < 0.001$) for all products (Figure1A).

Skin apreciability was evaluated in patients **undergoing radiotherapy** for products A, B and C and also D (Coolcare Mask gel solution). Of the 21 participants who participated in the radiotherapy treatment, all of them related Very Good and Good experience of use of products A, B and C. The evaluation of product D (Coolcare Mask) was Very Good or Good for 20 participants (95.2%) and Average or Bad for one participant (4.8%) (Figure1B).

According to the results of Table 6, at the significance level of 5%, all products showed a much better or better tolerance percentage compared to the same category products that they used previously.

Table 4. Cutaneous acceptability of test products: absolute number and frequency of skin adverse reactions and reports of discomfort

Classification by dermatologist				
Reactions	**Very good (0 – no reaction)**	**Good (1- mild)**	**Average (2- moderate)**	**Bad (3- severe)**
Erythema, Pruritus, Fervour, Desiccation, Cutaneous Discomfort [a]	33 (100%)	0 (0%)	0 (0%)	0 (0%)
Reactions	**Good**	**Average**	**Bad**	
Papule, Vesicle, Blister, Crust, Edema And Dyschromia[b]	33 (100%)	0 (0%)	0 (0%)	
Reports by participants				
Reactions	Participants n (%)	Reactions	Participants n (%)	
Redness	0 (0%)	Tenderness	0 (0%)	
Dryness	0 (0%)	Flaking	0 (0%)	
Prickling	0 (0%)	Tightness	0 (0%)	
Stinging	0 (0%)	Throbbing	0 (0%)	
Itching	0 (0%)	Bumpiness	0 (0%)	
Hotness	0 (0%)	Other	0 (0%)	
Area Of Application				
Area	Participants n (%)	Area	Participants n (%)	
Neck	1 (3.03%)	Feet	1 (3.03%)	
Back	2 (6.06%)	Chest	2 (6.06%)	
Face	6 (18.18%)	Legs	7 (21.21%)	
Breast	5 (15.15%)	Arms	9 (27.27%)	

Table 5. Hydration skin improvement after 30 days of test products use.

Improvement of hydration	**Total**	**%**	**P-value**
Dermatologist Evaluation - One-Sample Proportion Test using binomial distributions			
No (Unchanged)	8	24.2%	< 0.005
Yes	25	75.8%	
Total	33	100.0%	
Instrumental assessment (Quantitative data) - Paired sample t-Student test			
	D0 Hydration	D30 Hydration	P-value
Mean (Standard deviation)	51,09 (17,32)	59,55 (12,69)	< 0.001
Median (Minimum and maximum)	52,9 (15,2 - 82,4)	57,7 (33 - 90,2)	
Total	33	33	

Treatment \Interruptions

No interruptions in the radiation treatment were observed, due to skin conditions, to the patients included in this study. All patients finished their radiation schedule within the period of time prescribed by the radiation oncologist.

DISCUSSION

This study allow us to observe that patients who were part of the study sample and who were under chemotherapy or radiotherapy and have developed any cutaneous reactions related to these therapies have presented high acceptability of the following skin care products Washcare, Moistcare, Extremacare and Coolcare Mask, avoiding eventual interruptions of the prescribed protocols potencially resulting in a better prognosis[35,36]. We also noted that most patients (approximately 75%) reported improvements in skin hydration status - that is, the opposite of what would be expected; as, as reported, antineoplastics were not discontinued, which could theoretically make the skin situation even worse.

In our study, the sample consisted of 48% (16 patients) with breast cancer, receiving local radiotherapy after

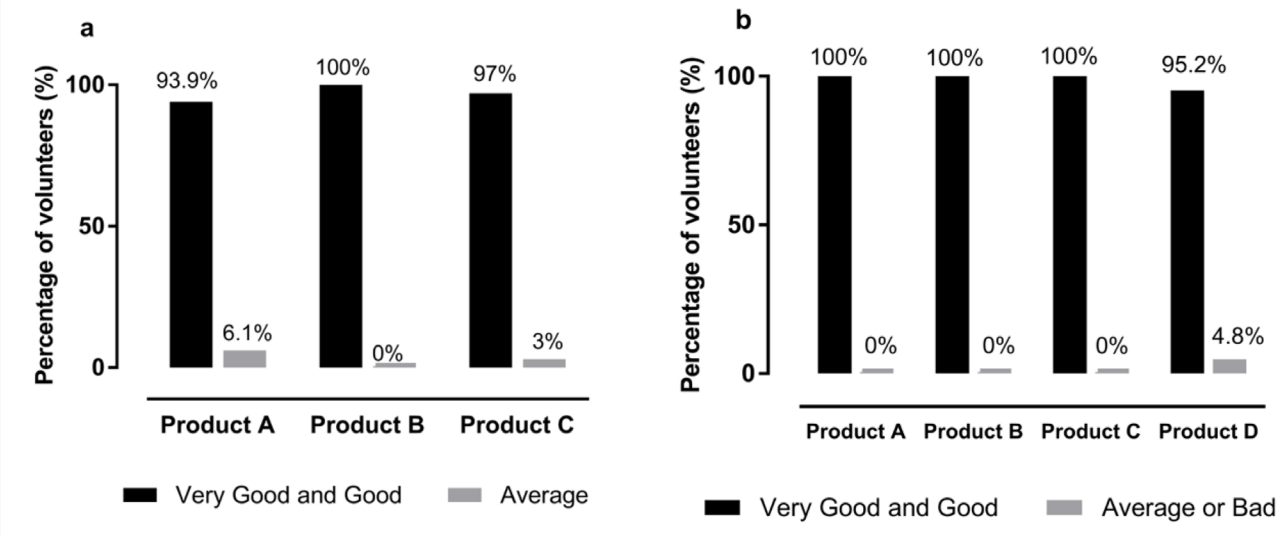

Figure 1. Cancer skin care products: overall experience. Graphical representation of the use experience of products during antineoplastic treatment (33 participants) (**a**) and radiotherapy treatment (21 participants) (**b**). Solid bars represent "very good and good" experience and gray bars represent "average or bad" experience. Test products - product A (Washcare), B (Moisturizer), C (Extremecare) and D (Coolcare Mask).

Table 6. Product tolerance of Use 30-days follow-up in One-Sample Proportion Test using binomial distributions

Tolerance	Total (%)	p-value
Compared to other soaps you have tried which statement best describes how well you tolerated the Product A:		
Extremely well or well	26 (78,8)	
The same or poor tolerate	7 (21,2)	< 0,001
Total	33 (100)	
Compared to other lotions you have tried which statement best describes how well you tolerated the Product B:		
Extremely well or well	29 (87,9)	
The same or poor tolerate	4 (12,1)	< 0,001
Total	33 (100)	
Compared to other creams you have tried which statement best describes how well you tolerated the Product C:		
Extremely well or well	28 (84,8)	
The same or poor tolerate	5 (15,2)	< 0,001
Total	33 (100)	
Compared to other product for skin relief, you have tried which statement best describes how well you tolerated the Product D:		
Extremely well or well	19 (90,4)	
The same or poor tolerate	2 (9,6)	< 0,001
Total	21 (100)	

the end of systemic treatment or systemic treatment for metastatic pathology. Of the antineoplastic treatments used, the most common were docetaxel and doxorubicin, but there were also patients using capecitabine, trastuzumab, pertuzumab, lapatinib, palbocyclib and ribocyclib. From the 21% (7 patients) with rectal cancer, 2 had chemotherapy associated with radiotherapy and the antineoplastic drugs used were taxol, imatinib, bevacizumab, cetuximab. Among the other patients, there was use of systemic therapy with sunitinib and sorafenib.

Therefore, the sample consisted of patients at high risk of developing skin lesions related to skin toxicity secondary to drug use[9].

Chemotherapeutic agents, despite the benefits, have significant side effects to the skin, including dryness, follicular rash, pruritus and pain[7,37]. The radiation therapy also affects the skin of oncological patients in a considerable way. A radiotherapy-treated skin often presents radiation dermatitis, with an acute phase characterized by erythema and edema, which may progress to desquamation and irritation[29]. In

the chronic phase of radiation dermatitis, epidermis and dermis become thin or atrophied, with loss of sebaceous glands, hair follicles and changes in texture[38,39]. These reactions support the need for products – creams or lotions - specially developed for the skin of these patients.

Several studies have been conducted focusing on the use of *Aloe vera* for prevention or treatment of radiation dermatitis[26]. A clinical trial compared 73 radiotherapy patients for the use of Aloe vera. At low doses of radiation, no considerable differences were observed (< or = 27 Gy). However, the occurrence of radiation dermatitis was lower at higher radiation doses in the group using *Aloe vera* plus mild soap in comparison to another one using mild soap alone, which indicates a protective effect of *Aloe vera*[25]. Another trial evaluated 60 participants submitted to radiotherapy and the use of *Aloe vera* lotion. When compared to areas which had not received lotion, the area which received *Aloe vera* presented less radiation dermatitis, with the statistically significant difference between the areas from the fourth week of treatment (p<0,001). A considerable difference could be seen when the patients had received a high radiation dose, about weeks 5 and 6 of radiotherapy[26].

In opposition to these trials, another one found that *Aloe vera* gel did not protect against radiation dermatitis with a minimum radiation dose of 50 Gy[40]. There are many variables that may influence the effect of skin products - phototype, age, previous therapies[6] and also the dose[17] – and a review about the use of Aloe vera for the prevention of radiation dermatitis demonstrated that many methodology problems were found, such as difficulties in providing adequate blinding. Considering those factors, the authors concluded that there are not enough evidence to indicate *Aloe vera* for prevention or treatment of radiation skin reactions[41].

Besides *Aloe vera, Calendula* is said to be able to prevent oxidative stress, becoming a potential treatment for radiation dermatitis. *Calendula* extract contains polyphenols which act as antioxidants on the skin[28]. In a clinical trial with breast cancer patients submitted to radiotherapy, *Calendula* was compared to the use of trolamine. The appearance of radiation dermatitis and the treatment interruptions were lower among the participants using *Calendula* when compared to the participants using trolamine (41% vs 63% p<0,001)[27].

Some articles are still call attention about the use of products containing parabens and urea in injured skins – a common situation among participants of oncological treatments. Since 1960, there are a variety of controversies related to the use of parabens, for example. In injured skins, contact dermatitis related to the use of parabens was reported[42]. About urea, the absorption may be different when compared to an injured skin and a normal one. In normal skin, the absorption is about 9,5 ± 2,3%, while in an injured skin is 67,9 ± 5,6%[21]. The investigational products we used during this trial contained *Calendula* and *Aloe vera*, besides other moisturizing ingredients. None of them contained parabens, fragrances, pigments and/or urea.

In this study patients on antineoplastic treatment were instructed to apply B (Moistcare) and C (Extremecare) products twice daily and radiotherapy patients B (Moistcare), C (Extremecare) and D (Coolcare Mask) products twice a day. All patients were instructed to apply product A (Washcare) once a day while showering in place of soap. Because they are products with highly safe formulations, all patients had great tolerability with the use of the products, and none of them had any kind of skin reaction resulting from the use of the products and neither need to interrupt the cancer treatment.

The products have been shown to be effective in improving skin condition and increasing hydration in both dermatological and instrumental corneometer measurements in most patients. The good results obtained are related to the product formulation, which contains humectant, antioxidant and restorative components. It is possible that the improvement of the skin condition of the patients was influenced by the high adherence observed in the application of the products, since there was no comparison with the control group. But it is important to note that there are no similar reports in the literature of skin condition improvement of patients already undergoing cancer treatment, with dermatological involvement as described in table X (cite the table in which we describe the skin lesions of patients), which makes us think that the formulation of the product, with high skin compatibility, is very important in the observed results.

The development and grade of skin reaction after exposure to oncological treatments depends on both intrinsic and extrinsic factors as age, general health, phototype, coexisting diseases, volume and number of radiation exposure, stage of cancer development and site of treatment[15,17]. Even those parameters were not being considered in the study, the products increased skin hydration, evaluated by instrumental and dermatological clinical measures and had a great acceptance rate from the participants.

Considering we did not use blinding during our trial, we could not control the possible effect of investigator bias during the evaluation of the skin reactions. Nevertheless, the tolerability rates of all the investigational products were considered higher than the tolerability rates obtained using products of the same category (p<0,001 for products A, B, C and D).

The main limitation of this study is the fact that there was no control group, which makes more robust conclusions about the efficacy of the products studied difficult, but this evaluation will be made in other subsequent prospective studies already in progress.

CONCLUSION

According to our data, participants in oncological treatment (both antineoplastic treatment and radiotherapy) who made use of non-pharmacological topical products demonstrated a statistically significant improvement in skin hydration, determined by instrumental and dermatological clinical measures. Improvement of skin condition and increased hydration were regularly distributed in the samples, regardless of the type of treatment, previous lesion, gender or age of the patients. This result demonstrates that the products evaluated in the studied sample contributed to the improvement of skin condition and increased hydration of patients undergoing antineoplastic treatment and radiotherapy.

Considering that no participant presented or reported any cutaneous adverse effects when using the investigational products, we consider they present a good cutaneous acceptance and also may be indicate in order to alleviate dryness and lesions derived from oncological treatments.

AUTHOR'S CONTRIBUTION

Carlos D`App Santos Machado-Filho: Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Manuscript writing, Provision of study materials or patient

Odimila Kawahata Adriano Silva: Collection and assembly of data, Final approval of manuscript, Manuscript writing, Provision of study materials or patient

Silvia Regina Lamas: Data analysis and interpretation, Final approval of manuscript, Manuscript writing, Provision of study materials or patient

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