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RANDOMIZED, OPEN-LABEL STUDY USING SKIN PROTECTOR IN ACRYLIC TERPOLYMER-BASED SPRAY *VERSUS* STANDARD MOISTURIZER IN THE PREVENTION OF ACUTE RADIODERMATITIS IN PATIENTS WITH ANAL CANAL AND RECTAL CANCER

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Abstract

SIMÕES, Fabiana Verdan. **An open randomized study using a skin protector spray made of acrylic terpolymers versus and standardized moisturizer in preventing acute radiodermatitis in patients with anal and rectal cancer.** Supervisor: Professor Rafael Celestino da Silva, PhD. Co-supervisor: Professor Beatriz Guitton Renaud Baptista de Oliveira, PhD. Rio de Janeiro-RJ, Brazil, 2019.

Patients' ongoing anal and rectal cancer radiotherapy exhibit a high prevalence of radiodermatitis with moist desquamation, impairing clinical, economic, and social outcomes. Clinical trials targeting product efficacy in preventing radiodermatitis are lacking in the current literature. These products could contribute to diminishing adverse effects, reducing equipment idle time by therapy interruption, and increasing the cure rate. Our goal is to evaluate the effectiveness of cutaneous spray based on acrylic terpolymers in preventing radiodermatitis with moist desquamation in patients with rectal or anal cancer. Spray effectiveness will be defied against a standardized moisturizer in the institution made of *Calendula officinalis L.* and *Aloe barbadensis* extracts. An open, single-blind, randomized clinical study will be conducted in a single institution, reference in national treatment in oncological diseases. Patients will be randomized into two groups: (i) experimental, using cutaneous protector spray; and (ii) control, using moisturizer Dnativ Revita Derm. RTOC's scale will be used for evaluating skin condition. Data will be collected in forms, which considered: (i) the primary outcome of radiodermatitis with moist desquamation occurrence; and (ii) the secondary outcome of radiotherapy interruption caused by radiodermatitis occurrence and severity, and product adverse effects. Analyses will be performed by intention to treat and per protocol, using descriptive, analytical, and inferential statistics, with a significance level of ≤ 0.10 (α). Research was approved by the Ethics committee under approval nº 5.322.985.

Keywords: Anal Neoplasm. Oncological Nursing. Radiodermatitis. Radiotherapy. Rectal Neoplasm.

SUMMARY

1 HYPOTHESES

Null hypothesis (H0): The incidence of radiodermatitis with wet desquamation with the skin protector in spray is greater than or equal to the incidence of radiodermatitis with wet desquamation in the control group.

Alternative hypothesis (H1): The incidence of radiodermatitis with wet desquamation with the skin protector in spray is lower than the incidence of radiodermatitis with wet desquamation in the control group.

2 OBJECTIVES

2.1 PRIMARY OBJECTIVE

To analyze the effectiveness of the skin protector in spray based on acrylic terpolymer in the prevention of radiodermatitis with wet desquamation in patients with anal canal and rectal cancer compared to a standardized moisturizer in the institution based on *Calendula officinalis L.* and *Aloe barbadensis*.

2.2 SECONDARY OBJECTIVES

- Characterize the sociodemographic, clinical-pathological, nutritional profile, acute skin radiotoxicity score of patients with anal canal and rectal cancer on radiotherapy;
- Measure the incidence of radiodermatitis with wet desquamation;
- Measure treatment interruptions due to radiodermatitis severity in patients discontinued from the use of the studied products;
- Measure the time of occurrence of wet desquamation in the experimental and control groups;
- Determine the risk factors for the occurrence of radiodermatitis with wet desquamation in patients with anal canal and rectal cancer;
- Describe adverse events to products.

3 RESEARCH PROTOCOL

3.1 TYPE OF STUDY

This is a randomized, open-label, single-blind clinical trial, with acronym PROT. The products of the intervention and control groups studied will be:

- Intervention: The experimental product is the 3M™ Cavilon™ Spray Skin Protector, which titles its product as "No Sting Protective Film". It has the following chemical composition: Hexamethyldisyloxane, acrylic terpolymer, isooctane, polyphenylmethylsiloxane copolymer.
- Control: The comparator agent is the moisturizer Dnativ Revita Derm® gel cream with echosomes, from the brand Triasil Indústria Química e Farmaceutica Ltda, composed of: Vitamins A, E, provitamin C, the purified and stabilized active fraction of *Aloe barbadensis*, ceramides and *Calendula officinalis L*. Agreed at the local institution of the study for use in the prevention of radiodermatitis.

The primary outcome to be measured is the incidence of wet desquamation in the experimental and control groups during RT; and the secondary outcomes: the occurrence of adverse events pruritus and pain in the use of the products; occurrence of temporary interruption of radiotherapy by radiodermatitis; occurrence of radiodermatitis in severe degrees (3 or 4).

3.2 FIELD OF RESEARCH

The research will be developed at the Hospital do Câncer I - HCI/INCA with the collaboration of the following services: Radiotherapy, Clinical Research and Clinical Oncology. In the institution, the RT outpatient clinic has five equipment/devices for the treatment of teletherapy, three Linear Accelerators and two Cobalt devices (of which, one is not functioning), as well as a brachytherapy device. The periods of operation are morning, afternoon and night.

The Radiotherapy Outpatient Clinic team is composed of nurses, physicians, physicists, nursing technicians and auxiliaries, and RT technicians. The nursing team is composed of nine nurses and seven mid-level nursing professionals who rotate between teletherapy and brachytherapy services. The RT outpatient clinic also has the support of the hospital team with the following professionals: engineers, dentists, social workers, nutritionists, psychologists, physiotherapists and speech therapists.

The flow of the patient in the RT sector at the study site begins with the consultation with a radio-oncologist, scheduled through the Regulation System of

the State of Rio de Janeiro. The patient is referred from his clinic of origin, when internal, or from a public health institution, when external, to INCA for RT.

On the day of the first medical appointment, the radio-oncologist performs anamnesis, physical examination and analyzes the examinations brought by the patient. When RT is indicated, the patient and family members receive guidance on the procedure, side effects, expected benefit and the patient's informed consent for treatment is obtained. In addition, the patient is instructed about the scheduling of the tomography and the care of preparation for this examination. Tomography aims to acquire images for the design of the structures and planning of RT in relation to the treatment dose and the calculations of dose distribution by the physicist.

From these procedures, the therapeutic planning form is released by the physicist and the patient is scheduled for simulation, by means of conventional simulators (2D) or CT scanners (3D), in order to determine the position of the treatment, target volume, field geometry, with adjustments in the demarcations, among other relevant information to be obtained. The beginning of the treatment occurs on the same day or up to five days later, according to the availability of vacancy in the treatment device.

3.3 PARTICIPANTS, INCLUSION CRITERIA, EXCLUSION AND DISCONTINUITY

To capture the participants, the primary researcher will search weekly for patients with anal canal and rectal cancer scheduled by the State Regulation System (SER) for care at the Radiotherapy Outpatient Clinic of HCI/INCA. A spreadsheet will be created to control the dates scheduled for the first-time appointment with the radio-oncologist, CT scanner, conventional simulator, and beginning of treatment.

The cooperation of the medical team will be requested to fill out a preliminary form containing the inclusion and exclusion criteria of the research on the day of the first consultation with the patient. The form contain the following data: diagnosis, age, indication of treatment, type of fractionation (conventional or hypofractionation), device proposed for treatment, proposed technique, if there was a previous history of RT in the same field of treatment.

Thus, eligible patients will be referred to the Nursing Consultation (CE) for screening the research, carried out on the same day of medical care or until the date scheduled for tomography. In the CE, the inclusion and exclusion criteria of the research will be evaluated, which are:

- Inclusion criteria: patients with anal canal and rectal cancer with indication for RT and conventional fractionation of treatment in Linear Accelerator (< 250cGy/day); age > or = 18 years; no previous history of RT in the same field/treatment site (reradiation).
- Exclusion criteria: patients with pre-existing dermatitis at the irradiated site that hindered the evaluation of the skin, previous report of allergic reaction to any products used in the research.

Based on the evaluation of these criteria, the research will be presented, the objectives will be explained and the Informed Consent Form (ICF) will be delivered, with reading and clarification of doubts by the researcher or his team.

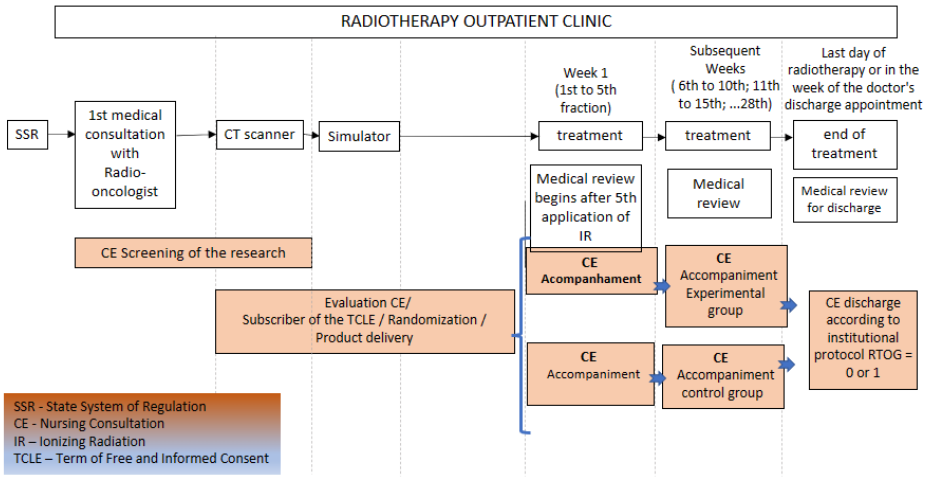
When the patients agree to participate, the ICF will be signed on the day scheduled for the FB of evaluation, which could can until the first day of radiotherapy treatment. In the evaluation FB, after signing the ICF, the patients will be randomized into two groups: experimental, with the use of the skin protector in spray, and control, with the use of the moisturizer Dnativ Revita Derm®.

The following discontinuity criteria for intervention will be considered: observation of wet desquamation during RT; non-adherence to the research protocol; observation of an autoimmune disease lesion in the treatment area that would hinder skin evaluation; loss of follow-up; Death; and at the discretion of the investigator, for factors that could compromise the results of the research.

These criteria will be evaluated after randomization, during the follow-up FB. Discontinued patients will be followed weekly at the consultation from the date of discontinuity and treated according to the algorithm of patients who radiate the pelvis of the Care Protocol for Radiodermatitis of the Institution, until they reach the criteria for discharge from the CE on the day of the end of the RT or after that day (INCA, 2018). The discharge criterion is the evaluation of the skin with grade 0 or 1 toxicity rating by the RTOG. This follow-up of the participants in the research after the outcome aim to evaluate the incidence of radiodermatitis by RTOG and treatment interruptions.

The criteria for discontinuity of the research will be: withdrawal of the ICF, change by the physician from the treatment planning for hypofractionation, and at the discretion of the investigator. The discontinued patients will be followed up at the nursing consultation and followed the Care Protocol for Radiodermatitis of the Institution (INCA, 2018). Figure 1 records the research procedures.

Figure 1. Patient journey at the Radiotherapy Outpatient Clinic and research procedures. Rio de Janeiro, RJ, Brazil, 2019.



Source: The authors.

3.3.1 Sample size calculation and randomization

To define the sample size, the researchers relied on previous research carried out in an exploratory way in the same institution surveyed with a sample of 112 patients with anal canal and rectal cancer treated within one year, to evaluate the occurrence of radiodermatitis with wet desquamation in patients submitted to RT with Linear Accelerator and who used the product Dnativ Revita Derm® for the prevention of radiodermatitis. In this observational study, a prevalence of wet desquamation was obtained and, consequently, a prevention response to the event of 35% (to be published).

Another intervention study on the subject used the expected percentage of reduction of the event or improvement of the response of 30% (GRAHAM *et al.*, 2004). In contrast, in another clinical trial in which the investigational product

was *Calendula officinalis L., the* expected percentage of reduction of the event was 20% (POMMIER, 2004).

Considering those efficacy and effectiveness studies, it is expected, in this study, that with the use of the skin protector in spray there would be a difference in response 30% better than the control product Dnativ Revita Derm®. With the application of the Fleming method for the sample calculation, in which 0.35 referred to the expected response and 0.30 referred to the improvement of the response with the experimental product, the formula was calculated: (0.35 + (0.30 x 0.35) = 0.455). Thus, the expected response was ≥ 45.50% for patients using the skin protector in spray, an experimental product (A'HERN, 2001; FLEMING, 1982).

With an alpha error of 0.10 and a power of 80%, the calculated sample size was 112 participants, with 56 in each study group. Considering a follow-up loss of 10%, the estimated final size was 124 patients, with 62 in each group. Data collection will begin in December 2020, with a forecast of completion in January 2022.

The randomization in the experimental and control groups will be performed by three nurses trained during the CE evaluation by permuted blocks, through a module of the REDCap (*Research Electronic Data Capture*) application, available at the study institution. The randomization list will be hidden by the software itself. Blinding will occur in the stage of skin evaluation, in which the nurse responsible for this evaluation will not know which group the participant was part of, as well as in the stage of statistical analyses. Due to the different sensory characteristics of the products chosen as intervention and control, it is not possible to blind the research participants, which justifies the categorization of the study as single-blind, by blinding the evaluation of the outcome.

3.4 EXPERIMENTAL PROTOCOL AND CONTROL

After randomization, in the evaluation FB, the application of the experimental and control products will follow the steps shown in Table 1.

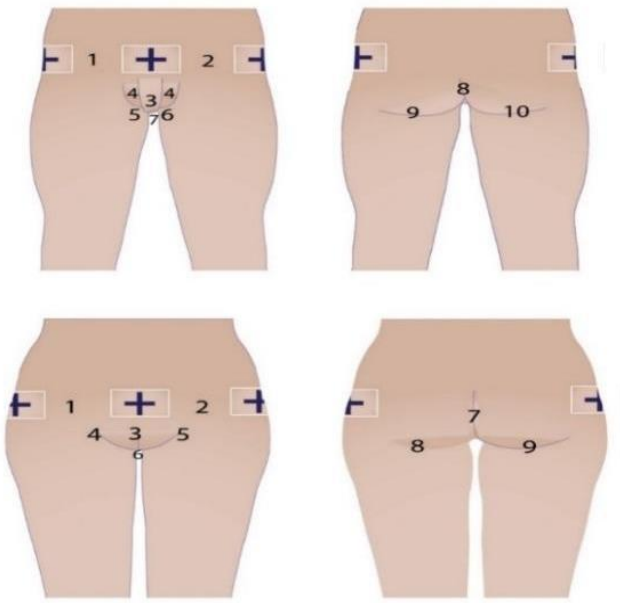
The use of experimental and control products will occur until the end of the study (incidence of wet desquamation) or when the nursing discharge consultation is reached.

Table 1. Mode of application of the experimental and control products**.**

Products	**Mode of application**
Experiment: Skin protector in spray	The first application occurs in the evaluation nursing consultation, with demonstration of the use by the nurse and training of the participant/family member. The product should be applied with one to two sprays in each numbered area of Figure 2 from the 1st day until the last day of RT or in the high FB. The orientation is to apply every day, once, post-irradiation, including weekends and holidays at home, after intimate hygiene, drying the area for application of the product. After applying the product, it is allowed to dry for 90 seconds before putting on the underwear.
Control: Moisturizing cream gel	The first application occurs in the evaluation nursing consultation, with demonstration of application by the nurse and training of the participant/family member. The product should be applied at least twice a day, being reapplied to each intimate hygiene in all numbered areas of Figure 2 from the 1st day until the last day of RT or in the CE of discharge. The application should be done with circular and gentle movements until the absorption of the product in the skin, with intimate hygiene without application of the product before performing the RT. During the treatment session the skin should be clean.
Intimate hygiene products	Participants in both groups will receive intimate hygiene products for home care (Intimate liquid soap and wet wipes). Intimate hygiene after physiological eliminations should be performed with intimate liquid soap with slightly acidified pH and, outside the home, with wipes moistened without alcohol, parabens and sulfates.

The numberings in Figure 2 show the regions of application of the products. In the male pelvis: 1 and 2 - represent the sides of the suprapubic region; 3 - penis; 4 - scrotal sac; 5 and 6 - groin; 7- perineum; 8 - intergluteal regions, including anus; 9 and 10 - lower fold of the buttock. In the female pelvis: 1 and 2 - represent the sides of the suprapubic region; 3 - vulva; 4 and 5 - groin; 6 - perineum; 7- intergluteal region; 8 and 9-fold lower buttock. After the orientations, the research participants will receive a guide leaflet on the application of the products.

Figure 2. Demonstration areas for application of experimental and control products in the male and female pelvis with radiotherapy markings, anterior and posterior regions. Rio de Janeiro, RJ, Brazil, 2019.



Source: BEECKMAN *ET AL,* 2015. Adapted by the author. Brazil, Rio de Janeiro, 2019.

Each research participant will be instructed about the Assistance Protocol for Institutional Radiodermatitis regarding education for patients who perform irradiation of the pelvis region. The guidelines are: drink at least two liters of fluids a day or follow medical advice; at night, at least, avoid wearing underwear (panties or underwear); wear cotton underwear, avoiding synthetic product; do not scratch the irradiated area; keep nails trimmed and clean to prevent injuries during sleep by scratching; avoid heat sources in everyday life; do not smoke ingest alcoholic beverages during RT; in case of diarrhea seek medical review and come to the extra nursing consultation; do not use the force of the water jet directly on the irradiated skin, washing gently. Avoid hot and prolonged baths, scented and colorful soaps, giving preference to neutral or slightly acidified soap; not to shave with blade or wax (pubis, groin), being allowed the use of electric razor for not harming the skin (INCA, 2018).

5.4.1 Training of the research and radiotherapy team

The research team is composed of six nurses, a Scientific Initiation student from the Anna Nery School of Nursing (EEAN) and a radio-oncologist. Both

participated in the Good Clinical Practices Course and, according to their attributions, conducted additional training on the following topics with the main investigator: Evaluation of the patient's skin in RT; Good Clinical Practices at PROT; ICF; Adverse events; PROT Procedures; REDCap application. All classes and trainings had an attendance list and receipt of a declaration of participation. In the course of the research, other meetings with the team can be held if necessary to align the procedures, according to the evolution of their operational stages.

Guidance will also be given on the PROT research and its stages to the physicians of the Radiotherapy Service of the institution, based on the dialogue with the head of the service. The nurses and nursing technicians of the Radiotherapy Outpatient Clinic will receive training addressing the following subjects: Research objectives, operating procedures, violation of protocol, statistical analysis, adverse events and collaboration during the intervention period. The radiotherapy technicians of the service will receive a document with information pertinent to the accomplishment of the research.

3.5 DATA COLLECTION

It is expected that the data collection will occur from December 2020 to January 2022. Data collection will be performed using the following instruments:

a) Initial evaluation form - applied in the evaluation nursing consultation, including the sociodemographic variables: age, sex, origin, education, marital status, life habits: alcoholism and smoking; the clinical and treatment variables: weight, height, BMI, oncological diagnosis, comorbidities, performance status *Easter Cooperative Oncology Group* (which assesses functional capacity), tumor staging, histological type, total and daily irradiated dose (in centigrays – cGy), number of RT sessions, concomitant chemotherapy, presence of incontinence (type, frequency and amount of loss), presence of anal or vaginal exudate (frequency); information on water intake and exposure to heat sources; and evaluation of the skin in the area to be treated.

b) Subsequent evaluation form - applied weekly in the follow-up nursing consultations, with clinical variables: adverse events related to the products or those that potentially interfered in the outcome of the study; presence and

classification of radiodermatitis according to the original RTOG scale (COX; STETZ; PAJAK; 1995); and temporary interruption of treatment with number of days interrupted, fraction of RT and reason. In addition, the lot and quantity of each experimental product and control delivered will be recorded; and checked for care guidelines on treatment.

c) Evaluation form of the irradiated field – that will be completed by the member of the team responsible for the evaluation of the skin in the follow-up consultations, with data on the characteristics of the skin and classification of radiodermatitis according to the RTOG scale.

The evaluation of the participant's skin in the region of application of RT will be made in the first evaluation consultation and during the treatment in the follow-up nursing consultations, until the discharge from the nurse, in order to observe the evolution and the presence of toxicity. Follow-up nursing consultations will occur once a week or even twice, in cases where it is need. The nursing discharge occurs at the last RT application or after, according to the evaluation of the skin within grades 0 or 1 by the RTOG (COX; STETZ; PAJAK; 1995).

A photograph of the skin region evaluated as an illustrative documentary record, of a nature not mandatory by nurses in the FB, will be taken. When authorized, the photographic record will be taken with a camera of at least 8 megapixels, focusing at 90º of the irradiated area, and at a distance of approximately 30 cm. No photograph will be taken in cases when there is some visual element of identification of the patient.

The consultations will be done by the main researcher and two nurses, one from the RT service and the other former nursing resident of the Institution. The skin will be evaluated by two nurses from the research team trained by the main researcher. In addition to this evaluation, during the follow-up in the consultations the observation of complaints and reports about the treatment will be made.

To evaluate adverse events, the *Common Terminology Criteria for Adverse Events (*CTCAE) version 5.0 scale will be applied. All records of adverse events in medical records will be evaluated and signed by a nurse from the research team and a physician from the RT service in the research field.

An electronic clinical record (eCRF) was created through the REDCap application to record the collected data. This application is already licensed for use in the researched institution, and the system security procedures followed the standard operating procedures of the Informatics Division of the institution.

This clinical form was customized by the data managers of the Clinical Research area of the institution according to the research instruments. The collection of clinical data and its insertion in the eCRF will be performed by the responsible researcher or by another nurse member of the previously trained research team.

3.6 DESCRIPTION OF THE VARIABLES STUDIED

The analyses willbe performed by Intention to Treat (ITT) and by protocol (PP).

3.6.1 Exposure variables

a) Intent-to-treat treatment (ITT)

The treatment, use of the experimental product, by ITT is considered the appropriate analysis to test "superiority" in randomized clinical trials, that is, when a new tested treatment is considered better than the standard. It is characterized by including all individuals in the groups that were initially allocated, that is, regardless of adherence, protocol deviation, withdrawal or treatment change are analyzed according to their original allocation group, avoiding confusion bias (SEDGWICK, 2015).

b) Protocol treatment (PP)

Treatment by protocol is characterized by the analysis that considers the exclusion of patients' non-adherent to the research protocol (SEDGWICK, 2015).

3.6.2 Outcome variables

a) Incidence of wet desquamation by intention to treat;

b) Incidence of wet desquamation by protocol;

c) Occurrence of temporary interruption of RT by radiodermatitis;

d) Occurrence of radiodermatitis severity: severe radiodermatitis was defined from grade 3, due to the institutional nursing routine of the research field

to send an opinion to the radio-oncologist for evaluation on temporary interruption of RT in the observation of this degree. Thus, the degrees of RTOG were categorized into "grades 0 or 1 or 2" (which corresponded to those without radiodermatitis and mild/moderate degrees) and "grades 3 or 4" (severe degrees).

3.6.3 Covariables

a) Sociodemographic variables:

- Origin: divided into internal strata (coming from sectors of the research field institution itself) and external (forwarded by the Regulation System to the Institution research field only for the treatment of RT);

- Age: categorized into age groups based on the median obtained;

- Gender: male and female;

- Skin color: the strata: black, brown, indigenous will be grouped as "non-white" and compared with those declared "white";

- Education: the strata of complete, secondary and higher education are categorized as "with instruction" and the "uneducated" is the strata without schooling and incomplete elementary school;

- Marital status: married strata and stable union are categorized into "lives with the partner", while single, divorced, and widowed are grouped into "does not live with a partner";

- Life habits: smoking and alcoholism.

b) Clinical variables:

- Body Mass Index (BMI): the BMI variable will be analyzed by ranges, thinness, normal, overweight and obesity (grade I to III). According to the BMI classification by the WHO, thinness (<18.5 Kg/m2), normal (between 18.5 and 24.9 Kg/m2), overweight (between 25 and 29.9 Kg/m2), grade 1 obesity (between 30 and 34.9 Kg/m2), grade II obesity (between 35 and 39.9 Kg/m2), grade III obesity (40 Kg/m2) (WHO, 2000);

- ECOG: the variable PS-ECOG (*Performance Status* Easter Cooperative Oncology Group) will be categorized into strata 0 or 1 (0-1) and 2 or 3 (2-3). The definition of the ECOG performance status scores are: 0 - Completely active; able to carry out all its activities without restriction; 1 - Restriction to strict physical activities; is capable of light work and of a sedentary nature; 2 - Able to perform

all self-care, but unable to perform any work activity standing approximately 50% of the hours in which the patient is awake; 3 - Able to perform only limited self-care, confined to the bed or chair more than 50% of the hours in which the patient is awake; 4 - Completely unable to perform basic self-care, totally confined to the bed or chair (NEEMAN *et al*., 2017);

- Comorbidities;

- Diagnosis: will be categorized according to the International Classification of Diseases (ICD), namely: C.20 - malignant neoplasm of the rectum, C.21 - neoplasm of the anus and anal canal and C.21.8 - neoplasm of the rectum, anus and anal canal with invasive lesion;

- Staging: tumor stage will be categorized as "stage I or II" and "stage III or IV". Data without information will be considered omitted;

- Histological type: the strata are adenocarcinoma and squamous cell carcinoma;

- Skin hydration: the strata are hydrated and dehydrated skin. The evaluation will be made from the observation by the researcher of the irradiated area in a generalized way, not focused exclusively on the areas that presented signs of radiodermatitis.

c) Variables on RT:

- Total dose and number of fractions: they will be categorized into ranges according to the cutoff based on the median. In the case of the dose, the median cutoff of the ranges must coincide with the maximum dose prescribed for rectal cancer cited in the literature (45-50.5 Gy);

- Treatment technique: IMRT and VMAT will be grouped in a single stratum "IMRT/VMAT", because they are techniques that modulate the radiation beam and compared with the 3D stratum;

- Concomitant treatment: The exclusive RT and combined RT strata (i.e., with chemotherapy);

- Temporary interruption of radiotherapy: the interrupted days of treatment will not be counted continuously, but due to absence on the day of treatment, not including holidays and weekends. In the reasons for treatment interruption, the strata will be considered as non-adherence and classified according to the WHO into five factors: socioeconomic (poverty, low educational level, lack of effective social support networks, unstable living conditions, long distance to the treatment

center, high cost of transportation); related to the team and the health system (device under maintenance, lack of communication of the team, such as, for example, about the return of operation of the device); disease-related (severity of symptoms, rate of progression); patient-related (forgetfulness, anxiety about adverse effects); treatment-related (adverse events after chemotherapy or radiotherapy, such as radiodermatitis and diarrhea) (WHO, 2003). These factors will be investigated in the nursing follow-up consultation;

- Adverse events identified according to the CTCAE scale: in the variables diarrhea and fecal incontinence, colostomized patients will be considered omitted.

d) Variables on body fluid losses:

- Loss of body fluids and type of intimate protection against these losses: body fluid losses will be considered rectal or vaginal bleeding, fecal and/or urinary incontinences and outflow of exudates via rectal or vaginal. The frequency of these losses will be classified as once a week or less; two or three times a week; once a day; several times a day (occasional losses of more than once a day); and constant losses (when there was difficulty in evaluating the skin on physical examination by the uninterrupted outflow of feces or exudates.)

e) Variables about sensations in the use of the studied products: the strata are relief, discomfort and burning;

f) Variables about skin conditions:

- Classification of the degrees of radiodermatitis by RTOG.

3.7 STATISTICAL PROCESSING OF DATA

After organization of the database and double checking, the data will be processed in the IBM SPSS software, version 23. Descriptive statistics will be applied to analyze the sociodemographic, clinical and RT-related variables of the total sample of participants and for the "experimental" and "control" groups. The analyses of quantitative variables will be performed using descriptive statistics, with calculation of mean, median and standard deviation (SD). Qualitative variables will be analyzed based on absolute (n) and relative (%) frequency.

In the bivariate analyses that included qualitative variables, Pearson's chi-square test, Fisher's exact test, and the odds ratio will be applied. The latter been applied only to the associations that can be significant to the chi-square test or

Fisher's exact test. Still in relation to the odds ratio, we chose to add the correction of 1 participant for those variables whose total of exposed or not exposed was equal to zero. In quantitative variables, the Kolmogorov-Smirnov test will be initially performed to determine whether the sample obeyed the normal distribution. A significance level of 10% ($p<0.10$) will be assumed for all bivariate analyses.

To test the hypothesis of association between exposure and outcome, binary logistic regression based on the odds ratio, with 90% confidence intervals (90% CI), will be conducted. The composition of the multivariate model will be elaborated in two stages. First, the association between the covariates and the exposure and outcome variables studied will be tested. All the variables that, in the bivariate analyses, will present the p-value ≤0.10 and that, according to the literature, are known to be associated with the outcome and/or exposure studied will be listed to compose the multivariate model. Finally, the variables will be inserted into the model by the *enter* method, with the first input block dedicated to sociodemographic variables and the second block referring to clinical or health variables.

Finally, two risk measures will be adopted. One of them is the estimated survival analysis by the Kaplan-Meier method and the log-rank test. The objective is to verify the differences between the experimental and control groups as a function of the time between the beginning of the experimental treatment with the terpolymer-based skin protector (exposure) and the occurrence of wet desquamation (outcome) based on their survival curves. The logrank test will be conducted to compare the two curves, considering as significant the results with p-value ≤ 0.10.

The second measure is the absolute risk reduction (RAR), which expresses the reduction in the risk of getting sick in the group that underwent the intervention in relation to the control group. The RAR calculation iss based on the difference between the incidence of the event in the control groups (Ic) and the incidence in the experimental group (Ie). Thus, RAR = Ic – Ie.

3.8 ETHICAL ASPECTS

The protocol was designed and conducted according to consensus of good clinical practices, and the team conducted training of the Good Clinical Practices Course promoted by the Clinical Research sector of the institution studied. The research project was approved by the Research Ethics Committee from the proposing institution, Anna Nery School of Nursing, Federal University of Rio de Janeiro (EEAN/UFRJ) under Opinion No. 5.322.985, CAAE registration No. 19153319.6.3001.5274.

The confidentiality of the participants will be respected through their numerical coding based on the evaluation nursing consultation. This identification number will be associated with the number of medical records in the institution, the initials of the patient's name and his date of birth, and will be recorded in a spreadsheet under the responsibility of the main researcher.

Participants will be informed on the nature of the treatment, the products under study, the research objectives and procedures, the confidentiality of the data and the possible benefits and risks of the research. The risks related to the product under investigation are of allergic origin, such as itching and redness with plaques. If any subject has allergic reactions to the products, he will be referred to the medical review of RT for evaluation and treatment, with the provision of another product for the prevention of radiodermatitis in the nursing consultation, according to the Institutional Protocol.

The possible benefits of the use of the product under investigation, of skin protection from wet desquamation, will be highlighted in the participants' approach.

It will be emphasized that participation is voluntary and that it is allowed to refuse participation at any time, without prejudice to subsequent care in the institution. The participants who agree to participate will sign the Informed Consent Form (ICF). The procedure of delivery and signature of the ICF wil take place in accordance with the consensus of the International Conference on Harmonization for Good Clinical Practice, that is, the term will be signed and dated personally by the patient or the responsible representative of the patient.

The information produced in this research will be kept by the researcher for a period of five years after the end of the study, according to Resolution 466/12, and the documents filed at the INCA's Research Center (CPQ/INCA).

3.9 FINANCING

The main researcher declares that she has no conflicts of interest, and the choice of the brand of the product was an experiment guided by the fact that it had already been previously adopted in the local institution of the research, a period in which the empirical observations that originated the hypothesis tested in this research were possible. In addition, this product is already in use in the institution.

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