Optimal Topical Agent for Radiation Dermatitis During Breast Radiotherapy: A Pilot Study

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Background: Women receiving radiation to the breast will likely be recommended to use a topical cream to minimize and delay the development of radiation dermatitis. Although many topical products are commercially available and have been tested for safety and efficacy, few studies have compared various products to one another for superiority and cost effectiveness.

Objectives: The purpose of this pilot study was to compare three commonly used skin care products prospectively to one other in a homogenously controlled group of women undergoing whole breast irradiation to assess superiority in minimizing the common toxicity criteria grade of radiation dermatitis, effect on quality of life, and cost.

Methods: The authors conducted a systematic review to determine the three types of skin care products with the strongest evidence of minimizing radiation dermatitis. Patients were voluntarily enrolled and randomized to one of three possible skin care topical regimens. Patients completed a quality-of-life survey to assess their preference in topical skin care regimen. The cost of each arm’s topical product was assessed at the completion of patient participation.

Findings: No statistical difference was noted in the severity or occurrence of radiation dermatitis among the groups. In addition, no statistical difference was found among the three treatment arms in quality-of-life score changes, and no patients required a treatment interruption in their radiation or in the skin care product during treatment. A cost difference among the treatment arms was noted.

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About 231,840 new cases of invasive breast cancer will be diagnosed among women in the United States in 2015 (American Cancer Society, 2015). The majority of women with breast cancer receive some form of systemic therapy (e.g., hormonal therapy, chemotherapy). Local treatment for breast cancer includes either mastectomy, with or without reconstruction, or breast-conserving surgery (BCS) followed by whole-breast irradiation (WBI). High-level evidence shows that, for women with early-stage breast cancer (0–II), either mastectomy or BCS with WBI yield equivalent survival rates (National Comprehensive Cancer Network [NCCN], 2008).

Women with breast cancer experience a myriad of symptoms related to their treatments. This pilot feasibility study focused on exploring how different skin care agents used in radiation treatment fields may delay and/or minimize the severity of radiation-induced dermatitis (RID) related to WBI delivered after BCS. About 90%–100% of women receiving WBI postlumpectomy experience some degree of radiation dermatitis, ranging from mild grade 1 (faint erythema and/or dry desquamation) to
severe grade 4 dermatitis (skin necrosis and/or full thickness ulceration) (Berardesca, 2004; Bostrom, Lindman, Swartling, Berne, & Bergh, 2001; Fenig et al., 2001; Harper, Franklin, Jenrette, & Aguero, 2004; Schmuth et al., 2002).

RID can affect treatment schedules because many radiation oncologists elect to interrupt patients’ treatments (dose delay) to allow skin recovery and minimize the progression of radiation dermatitis. Interventions in treatments increase the risk of tumor cell repopulation and reduce the anticancer effect of radiotherapy. In addition, women may experience distress related to the pain and discomfort associated with RID, making skin care an important concern. Unfortunately, limited evidence has been presented in the literature on how dermatitis affects each woman’s quality of life (QOL) (i.e., physical, emotional, social, work, and sexual aspects of life). Although research has been conducted with many topical interventions, these studies were generally not randomized, controlled trials (RCTs) and usually lacked a large enough sample to generate adequate evidence (Berardesca, 2004; Bostrom et al., 2001; Fisher et al., 2000; Maiche, Isokamagas, & Grohn, 1994; Mak, Molassiotis, Wan, Lee, & Chan, 2000; Miko et al., 2005; Potera, Lookinghill, & Stryker, 1982; Schmuth et al., 2002, Szumacher et al., 2001). For instance, many trials did not include a control group (Berardesca, 2004; Heggie et al., 2002), were not designed to compare one skin care agent to another (Berardesca, 2004; Maiche et al., 1994; Miko et al., 2005), or were limited by variables, like the heterogeneity of treatment site and dose of radiation received among the participants (Wells et al., 2004). A study that will overcome the existing limitations in the literature is warranted. The ideal way to generate evidence-based care is to conduct well-designed, adequately powered prospective RCTs, ideally in multiple centers. The current pilot study explored the feasibility of conducting a RCT of three commonly used topical agents for RID. The occurrence and severity of radiation dermatitis and any treatment interruption (dose delay) were measured among the women who enrolled in the trial. These women also were assessed with the Dermatology Life Quality Index (DLQI) after enrollment, prior to radiation therapy, and then again at select time points during and after their radiation treatments. Information learned from the pilot study will inform the design of larger, multicenter RCTs.

Methods

A literature review allowed for selection of the skin care products that had evidence of efficacy for use in patients undergoing radiation therapy. The study was approved by New York University’s (NYU’s) institutional review board before initiation of the trial at the NYU Clinical Cancer Center. A convenience sample of 30 women diagnosed with breast cancer who were to receive WBI using Whelan fractionation (42.56 Gy to the whole breast during 16 fractions/treatments) and met the specified inclusion criteria were recruited.

Inclusion criteria were women with stage I–II node-negative breast cancer, post-lumpectomy or partial mastectomy with negative margins, who were at least two weeks from last breast surgery with no visible signs of postoperative infection, and who were receiving a regimen of 42.5 cGy of 16 fractions whole breast external beam irradiation (Whelan fractionation).

Exclusion criteria included concurrent chemotherapy or less than two weeks from last chemotherapy; preexisting connective tissue disorder, including scleroderma, systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA); a previous history of allergic reaction to topical agents; NCCN contraindication for breast conservation therapy; and partial-breast radiotherapy or other fractionation regimens different from 42.5 cGy in 16 fractions.

The decision to restrict the eligibility to women undergoing the Whelan fractionation regimen (Whelan et al., 2002) was based on the following rationale: (a) the need for a relatively homogeneous group of participants in terms of stage and type of radiation treatment; (b) the proven, consistent approach of the Whelan regimen; and (c) the relevance of this information to a larger group of women, because this approach is the standard approach in Canada for most patients with early-stage breast cancer who have undergone breast conservation and is offered at many centers in the United States, including NYU.

This study accrued 30 women and randomly assigned them to one of three intervention groups (10 women in each group).
from September 2010 to July 2012. Arm 1 received a homeopathic cream of calendula applied to the treated breast twice daily. Arm 2 received treatment twice daily with a hydrogel cream (RadiaPlex®). Arm 3 received treatment with a medium-potency steroid regimen (0.1% mometasone furoate twice per week in weeks 1 and 2, then once daily in week 3; an emollient, Aquaphor®, was used daily throughout treatment).

At the time of consultation, the patient was approached to determine if she was interested in participating in the study. After hearing about the study, if the woman was interested in participating, informed consent was obtained. After signing consent, the woman was randomly assigned to one of the three topical skin care intervention groups. The participant’s information sheet included demographic information. When the patient returned for her simulation appointment (e.g., treatment planning), she was given the skin care teaching sheet for the skin care arm she was assigned to. The patient then received a sealed envelope in the presence of the nurse, containing the topical treatment (based on the arm assignment) and a printed teaching sheet. The skin care regimen was reviewed with the patient by the nurse, including how to perform a patch test prior to beginning radiation, to ensure that the patient was not allergic to the product. On the day of simulation, a baseline skin assessment was performed by the clinician on the breast team (Common Toxicity Criteria [CTC] grading of radiation dermatitis), and the DLQI (Loo, Diba, Chawla, & Finlay, 2003) was completed by the patient. The DLQI is a visual analog survey that assesses how patients are affected by their skin changes. It has a maximum score of 30 if the QOL is perfect. The tool provides a cumulative score and decreases if the patient is experiencing more negative affects to her activities of daily living because of her skin condition.

During the course of treatment with WBI, each patient was seen by a clinician (MD or NP and an RN) once weekly and in follow-up at one week, one month, and three months after radiation therapy. At each of these visits, a routine skin assessment with CTC grading for radiation dermatitis was performed and recorded. The patient also completed the DLQI form at each of these time points. Any need for treatment interruption either of the cream or radiation was recorded. If a patient developed moist desquamation, the assigned topical agent was discontinued, and the patient was started on an in-house regimen of occlusive Xeroform® until resolution.

Results

The 30 patients were equally distributed among the three skin care arms. All 30 patients developed at least grade 1 radiation dermatitis, as was expected with WBI at a dose of 42.56 Gy. The maximum grade of radiation dermatitis experienced by women in the study was grade 2, experienced in all three arms at the time point of one week after completion of radiation therapy. No statistical difference was noted in the three treatment arms in the time to development of RID or in the maximum grade of the observed radiation dermatitis reactions. No patient developed an allergy to any of the three products. No treatment interruptions in radiation therapy or in the use of the topical skin care products were reported.

In general, only a small decrease was noted in patients’ DLQI scores throughout treatment. No statistical difference was noted among the three intervention arms when compared for changes in DLQI scores at matched time points. Week 3 DLQI scores, for example, were as follows: Arm 1 = 27.4, Arm 2 = 28.6,

### Implications for Practice

- Choose a topical skin care agent for patients based on superiority in limiting the side effect of radiation-induced dermatitis and avoiding treatment interruptions and dose delays.
- Raise awareness of the cost differential per skin care topical agent compared to product superiority.
- Implement optimal follow-up time points of one week after radiation to accurately measure the skin toxicities and to provide symptom relief and support.
Arm 3 = 27.7 (p > 0.05). Figures 1–3 provide images of minimal radiation dermatitis to the maximal radiation dermatitis for each of the three trial arms.

Discussion

The current standard of care for follow-up after WBI is to see patients one month after completion of radiation treatment. In this study, maximum RID was observed at one week post-radiation, making this the most appropriate time to assess the skin after radiation, to accurately measure the maximum grade of skin dermatitis, and to provide symptom relief and support. No statistical differences were noted on self-evaluated QOL (p > 0.05), regardless of arm, across all time points of evaluation. The time interval to maximal reaction was equal among the three skin care arms, as was the time to resolution. No participants needed to interrupt their treatment during radiation. This pilot and feasibility study was not powered to draw generalizable conclusions. However, the findings inform the need for a larger multicenter trial to compare the three products in a larger sample of patients with breast cancer.

Conclusion and Implications for Practice

A larger-scale RCT using the same three skin care products is needed to confirm the preliminary findings of this study (e.g., equivalence of the products). Findings from a larger RCT also would inform evidence-based practice guidelines and aid in selection of the most convenient, cost-effective skin care product. Since the cost difference between the three skin care topical arms is considerable (see Table 1), it may result in significant saving to the healthcare system. Nurses are poised to develop and conduct research that can question current practice methods that ensure optimal patient outcomes while resulting in significant cost savings.

References


<table>
<thead>
<tr>
<th>Arm</th>
<th>Regimen</th>
<th>Approximate Cost ($)</th>
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<tbody>
<tr>
<td>1</td>
<td>Calendula cream</td>
<td>10.99 for 6.7 oz tube</td>
</tr>
<tr>
<td>2</td>
<td>RadiaPlex®</td>
<td>59.32 for 6 oz tube</td>
</tr>
<tr>
<td>3</td>
<td>Mometasone furoate (plus Aquaphor®)</td>
<td>47.91 (plus Aquaphor)</td>
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</tbody>
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TABLE 1. Average Cost of Skin Care Products


