Comparative Evaluation of Topical Corticosteroid and Moisturizer in the Prevention of Radiodermatitis in Breast Cancer Radiotherapy

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Abstract

Background: Radiodermatitis is a frequent side effect of breast cancer radiotherapy (RT). Treating radiation oncologist should know the prevention and treatment of every grade of radiodermatitis. Aims: The aim of this study was to compare the topical corticosteroid and moisturizer usage in breast cancer RT. Materials and Methods: Fifty patients with early-stage breast cancer undergoing breast-conserving surgery referred to our department for adjuvant RT between October 2009 and October 2016 were compared with regard to topical steroid or moisturizer usage. Patients were followed up weekly after the start of treatment. Results: Mean age was 46 years. Twenty-four patients had stage 1 breast cancer and 26 patients had stage 2 disease. KPS (Karnofsky performance score) was 100 for all patients. Five patients (20.8%) had grade 2 and seven (29.1%) patients had grade 1 acute radiodermatitis in the first group. Eleven (42.3%) patients had grade 2 and 12 (46.1%) patients had grade 1 acute radiodermatitis in the second group. Thirteen (54.1%) patients in the first group had no acute radiodermatitis and three (11.5%) patients in the second group had no acute radiodermatitis. No patient in either group experienced grade 3 radiodermatitis. Conclusions: Daily use of topical betamethasone for breast cancer RT improves dermal sparing, reduces acute radiodermatitis, and may be recommended for patients receiving RT to the breast.

Key Words: Breast cancer, moisturizer, radiotherapy, topical steroid

Introduction

Breast cancer is the most common type of cancer in females. Radiation therapy (RT) is an important part of breast cancer management used after surgery. Adverse effects of RT for breast cancer are skin irritation, changes in skin color, tenderness in treated area, fatigue, arm edema, swelling, radiation pneumonitis, cardiotoxicity and second malignancies.[1]

Radiation dermatitis often occurs after a period of 6–12 days. It may occur in different degrees in the forms of rash, edema, blisters, and/or skin necrosis. Lesions reach a top intensity at about 2–3 weeks. There is no standardized and specific therapy for radiodermatitis, and although incidence has diminished with novel RT techniques, it can influence the therapeutic schedule and change the patients’ quality of life. Treatment generally includes the use of topical moisturizers and/or corticoids.[1]

Radiation therapy can lead to acute or chronic skin changes. These changes can occur at both entrance and exit site of the irradiated area. Severity is influenced by the dose, fractionation, beam energy, irradiated volume, and vulnerability of skin surface. Poor nutrition status, preexisting vascular conditions or connective tissue disease, excessive skin folds, or genetics also play a role for adverse effects. The pathophysiology includes direct radiation injury plus a subsequent inflammatory response. Free radicals from ionizing radiation alter DNA, proteins, lipids, and carbohydrates. Epithelial basal cells, vascular endothelial cells, and Langerhans cells are affected. Proinflammatory cytokines, thrombotic factors, growth factors, and other molecules are activated.[2]

Acute skin changes may be seen after 10–14 h. Grade 1 changes are mild generalized erythema, dry desquamation, pruritus, scaling, dyspigmentation, and hair loss and grade 2 dermatitis includes tender or edematous erythema, moist desquamation in skin folds, and considerable pain following 4 or 5 weeks of RT with doses to the skin of 40 Gy or greater. These changes start...
to peak 1–2 week after the end of treatment and start healing 3–5 weeks after radiation. Total healing may take 1–3 months. Sometimes, dermatitis may progress to grade 3, which include confluent moist desquamation or even grade 4 that presents with ulcers, hemorrhage, and necrosis. [2]

Mild acute dermatitis should be managed symptomatically. Supportive care consists of washing with water, gentle cleansing with a mild agent, wearing loose, nonbinding clothing, and avoidance of irritants, antiperspirants, and ultraviolet exposure. Even though erythema and dry desquamation occur, creams or ointments can be used. Topical sucralfate or hyaluronic acid may be used to ameliorate symptoms of the patients. An extract from the calendula plant significantly reduced the occurrence of moderate-to-severe acute dermatitis from 63% to 41% when compared to trolamine, a nonsteroidal agent. [3,4]

Different topical agents containing Aloe vera, d-panthenol, almond, or chamomile have also been used with variable treatment response in studies. [5–10] The evaluation of topical antioxidants has not been established, and topical steroids are also controversial with conflicting results. Infection and skin atrophy are known side effects of topical steroids. As a result, steroids may ameliorate the symptoms, but they do not prevent dermatitis. Topical ascorbic acid did not show benefit for the prevention of radiation dermatitis. [11] Topical granulocyte-macrophage-colony-stimulating factor, tacrolimus, pimecrolimus, and platelet-derived growth factor are more specific agents investigated recently. [12]

The aim of this study was to compare the topical corticosteroid and moisturizer usage in breast cancer RT. Topical corticosteroid betamethasone was applied to the first group of patients and only moisturizer was used for the second group. The prevention and the treatment effect of topical corticosteroid were analyzed in the management of acute radiodermatitis caused by breast cancer RT.

Materials and Methods
Fifty patients with early-stage breast cancer receiving adjuvant RT between October 2009 and October 2016 at our department were included in this study. Eligibility criteria included ≤65 year of age, Eastern Cooperative Oncology Group performance status of 0–1, and no previous history of breast RT. Informed consents of all patients were obtained.

Computed tomography (CT)-simulation images were acquired for each patient as per our institutional protocol. [13–16] Breast target volumes and relevant critical structures were delineated on CT-simulation images. RT planning was performed by using the PrecisePLAN (Elekta, UK) Treatment Planning System. Prescribed whole breast dose was 50 Gy in 25 fractions followed by a tumor bed boost of additional 10 Gy in 5 fractions. The linear accelerator (Synergy, Elekta, UK) available at our department was used for treatment delivery. Two groups were compared with regard to topical steroid or moisturizer usage during breast cancer RT. The first group consisted of 24 patients who were prescribed topical steroid betamethasone starting with the initial delivery of RT till the end of treatment. The second group included 26 patients who used only daily moisturizer with RT. Age, stage, KPS, and National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 scores were noted and analyzed between these two groups. Patients were followed up weekly after the start of the treatment. Grade 1 toxicity was defined as asymptomatic or mild symptoms, grade 2 toxicity was defined as moderate, and grade 3 toxicity was defined as severe or medically significant symptoms. Treatment and follow-up characteristics are summarized in Table 1.

Statistical analysis
In descriptive statistics, mean and standard deviation were used for normally distributed variables, which were analyzed using the paired t-test, and median (minimum–maximum) was used for nonnormally distributed variables, which were analyzed using the Wilcoxon signed rank test. Statistical Package for the Social Sciences, version 15.0 (SPSS, Inc. Chicago, IL) software was used for analysis and the level of significance was set at P < 0.05.

Results
Between October 2009 and October 2016, 50 consecutive patients with early-stage breast cancer referred to our department for adjuvant radiotherapy (RT) after breast-conserving surgery were included in this study. Mean age was 46 years. Twenty-four patients (48%) had stage I and 26 patients (52%) had stage II breast cancer. Patient characteristics, mean age, stage, and grade scoring of all groups are shown in Table 2. KPS was 100 for all patients. Five patients (20.8%) had grade 2 and seven (29.2%) patients had grade 1 acute radiodermatitis in the first group. Eleven (42.3%) patients had grade 2 and 12 (46.1%) patients had grade 1 acute radiodermatitis in the second group. Twelve (50%) patients in the first group and three (11.5%) patients in the second group had no acute radiodermatitis. No patient in either group experienced grade 3 radiodermatitis. Topical treatment with betamethasone cream resulted in clinically and statistically significantly less skin reactions compared to moisturizer (P < 0.05).

Discussion
Acute radiodermatitis typically occurs during the course of breast RT with varying degrees of severity. Preventive topical steroid usage may improve radiation dermatitis in conventional RT. Potent topical steroid results in
significantly less radiation dermatitis compared to emollients regardless of RT fractionation.[17] Prophylactic steroids are recommended for the high-risk groups.[18]

About 1% hydrocortisone cream was used for prophylactic treatment with RT of breast cancer patients in one study. Only 5 of 21 patients experienced moist desquamation and topical steroid also delayed these reactions in this patient group.[19] Skin-directed topical antioxidants have been suggested as viable agents in a critical review by Kodiyan et al.[20]

Mometasone furoate was applied during and after RT in breast cancer patients in a randomized trial. It significantly reduced radiation dermatitis with its positive effects on quality of life. This topical preparation has been strongly recommended by authors as a viable treatment.[21] Potent steroids and placebo were randomized in one controlled study in a group of patients receiving RT. Betamethasone usage resulted in better results compared to emollient or moisturizers.[22]

These results are consistent with the outcomes of our study. Use of steroids initially starting on the first day of treatment or after the occurrence of symptoms is controversial. It has been suggested that it may be better to use steroids with RT as a preventive measure rather than using after symptoms are manifested.[23] In a study by Omidvari et al., all patients treated with chest-wall RT experienced acute radiation dermatitis of different degrees during the course of their disease.[24] Prophylactic usage of betamethasone delayed radiation dermatitis but did not prevent it. Our results are consistent with the study by Omidvari et al. and also betamethasone prevented acute radiodermatitis in most of the patients in our study. Petrolatum, which was used as an alternative to steroid, had no effect on prevention and delay of acute radiation dermatitis in the study by Omidvari et al.[24]

Shukla et al. randomized beclometasone spray and control group in the management of acute radiation dermatitis after surgery of breast cancer.[25] Control group was not allowed to use any topical application including moisturizer or emollient. Skin adverse effects were noted if erythema, dry and wet desquamation occurred. Topical steroid significantly reduced wet desquamation compared to control group. Results of this study are consistent with our results. Cancer Care Ontario’s Supportive Care Guidelines Group recommend a plain, nonscented lanoline-free hydrophilic cream and a low-dose topical corticosteroid cream for prevention of itching and irritation of skin caused by RT.[24] In a study by

| Table 1: Treatment and follow-up characteristics |
|-----------------------------------------------|
| **Group 1** | **Group 2** |
| Total RT dose | 50 Gy - 5 patients | 50 Gy - 8 patients |
| | 50 + 10 Gy - 19 patients | 50 + 10 Gy - 18 patients |
| Dose per RT fraction | 2 Gy | 2 Gy |
| Medication | Topical betamethasone | Topical moisturizer |
| Eligibility criteria | ≤65 years of age, ECOG performance status of 0-1, and no previous history of breast RT | ≤65 years of age, ECOG performance status of 0-1, and no previous history of breast RT |
| Follow-up time | 18-36 months (mean 25) | 16-40 months (mean 24) |
| CTCAE version 5.0 | Grade 1 - Asymptomatic or mild symptoms, clinical or diagnostic observations only, intervention not indicated | Grade 1 - Asymptomatic or mild symptoms, clinical or diagnostic observations only, intervention not indicated |
| | Grade 2 - Moderate; minimal, local, or noninvasive intervention indicated; limiting age appropriate instrumental ADL | Grade 2 - Moderate; minimal, local, or noninvasive intervention indicated; limiting age appropriate instrumental ADL |
| | Grade 3 - Severe or medically significant but not immediately life-threatening, hospitalization or prolongation of existing hospitalization indicated, limiting self-care ADL | Grade 3 - Severe or medically significant but not immediately life-threatening, hospitalization or prolongation of existing hospitalization indicated, limiting self-care ADL |
| | Grade 4 - Life-threatening consequences, urgent intervention indicated | Grade 4 - Life-threatening consequences, urgent intervention indicated |
| | Grade 5 - Death | Grade 5 - Death |

ECOG=Eastern Cooperative Oncology Group, RT=Radiotherapy, ADL=Activities of daily living

| Table 2: Patient characteristics |
|----------------------------------|
| **Group 1** | **Group 2** |
| Number of patients | 24 | 26 |
| Age (mean) | 46 | 46 |
| Stage | 1 - 12 patients | 1 - 13 patients |
| | 2 - 12 patients | 2 - 13 patients |
| Grade 1 radiodermatitis | 7 (29.2%) | 12 (46.1%) |
| Grade 2 radiodermatitis | 5 (20.8%) | 11 (42.3%) |

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Maddocks-Jennings et al., usage of hydrophilic Aloe vera gel or vegetable oil is as effective as mild steroid creams for the patients undergoing RT. In a study by Schmudt et al., topical methylprednisolone and dexamethasone were compared for management of radiation dermatitis in patients receiving RT. Both creams usage ameliorated but not prevented radiation dermatitis as per result of this study.

Skin reactions were evaluated with reflectance spectrophotometer in a double-blind randomized study. Potent steroid mometasone furoate significantly reduced radiation dermatitis compared to emollient cream but there was no difference in pigmentation between the groups. Potera et al. evaluated 0.2% hydrocortisone valerate and placebo in 19 cancer patients and scored all each week according to symptoms such as soreness, burning, itching, erythema, desquamation, and ulceration. No differences were observed in two groups for acute or late reactions.

Our study showed that betamethasone was a potent steroid, which might be used for prevention of radiodermatitis. Results of the study appear to be consistent with the relevant literature. Acute radiodermatitis has a negative effect on the quality of life of breast cancer patients receiving RT. In conclusion, daily use of topical betamethasone for breast cancer RT improves dermal sparing, reduces acute radiodermatitis, and should be recommended for patients receiving RT to the breast.

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**Conflicts of interest**

There are no conflicts of interest.

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