

This material is protected by U.S. copyright law. Unauthorized reproduction is prohibited. To purchase reprints or request permission to reproduce, e-mail reprints@ons.org.

Prevention and Treatment of Acute Radiation Dermatitis: A Literature Review

Mihkaila Maurine Wickline, RN, MN, AOCN®, CNS

Purpose/Objectives: To review historical and current research data on prevention and treatment of acute radiation dermatitis.

Data Sources: 18 research trials and 1 case report published from 1967–2001 and 1 unpublished research trial from 1972.

Data Synthesis: Washing the skin with mild soap and water and the hair with mild shampoo is safe during radiation therapy. Biafine® (Medix Pharmaceuticals, Inc., Largo, FL), chamomile cream, almond ointment, topical vitamin C, and gentian violet have not been proven effective and should not be used. Transparent, hydrocolloid, and hydrogel dressings have been beneficial, as have sucralfate cream and corticosteroid cream. Aloe vera may be beneficial and is not harmful.

Conclusions: The existing scientific data are lacking in quantity and quality. The current body of evidence is unable to provide clinicians with comprehensive guidelines for prevention and management of acute radiation dermatitis.

Implications for Nursing: Nurse clinicians and nurse scientists must partner to conduct further research to add to the limited resources about the prevention and management of acute radiation dermatitis and develop comprehensive evidence-based clinical practice guidelines.

Acute radiation dermatitis is a common side effect of radiotherapy. The majority of patients receiving radiation therapy will develop this skin toxicity, which is caused by the effect of radiation on the rapidly dividing cells of the basal layer of the epidermis as well as the dermis (Williams et al., 1996). Fisher et al. (2000) estimated that 87% of all women undergoing radiation therapy for breast cancer will develop some degree of radiation dermatitis. The intensity of the reaction depends on the radiation fraction schedule, total dose, anatomic treatment area, radiation type, and individual differences among patients (Bostrom, Lindman, Swartling, Berne, & Bergh, 2001; Sitton, 1992). Severe radiation dermatitis can be painful, may lead to localized and systemic infections, and can cause permanent scarring. Occasionally, severe reactions can necessitate temporary or permanent cessation of treatment, which could decrease the odds for cancer control or cure (Williams et al.).

Pathophysiology

The epidermis of the skin contains a self-renewing system where cell production at the basal layer equals cellular loss

Key Points . . .

- ▶ Acute radiation dermatitis is a significant problem for patients undergoing radiotherapy.
- ▶ No comprehensive, evidence-based consensus guidelines exist, and scientific data are limited about the management of radiation dermatitis.
- ▶ Additional research must be conducted to test currently used therapies and novel therapies with blinded, randomized clinical trials and large sample sizes to determine the best practice for managing radiation dermatitis.
- ▶ Therapies shown to have no effect on preventing or treating radiation dermatitis no longer should be used.

Goal for CE Enrollees:

To enhance nurses' knowledge related to the prevention and treatment of acute radiation dermatitis.

Objectives for CE Enrollees:

On completion of this CE, the participant will be able to

1. Describe the pathophysiology of acute radiation dermatitis.
2. Describe two interventions for prevention or treatment of acute radiation dermatitis that are supported by currently available evidence.
3. Identify one intervention that has not been proven effective for the prevention or treatment of acute radiation dermatitis.

Mihkaila Maurine Wickline, RN, MN, AOCN®, CNS, is a hematopoietic stem cell transplant clinical nurse specialist at the Seattle Cancer Care Alliance in Washington. (Submitted March 2003. Accepted for publication June 6, 2003.) (Mention of specific products and opinions related to those products do not imply endorsement by the Oncology Nursing Forum or the Oncology Nursing Society.)

Digital Object Identifier: 10.1188/04.ONF.237-247

(shedding) at the outermost cornified layer. The basal cell layer separates the epidermis from the dermis, where ground substance, fibers, nerves, and blood vessels are located (Sitton, 1992). Ionizing radiation generates free radicals and reactive oxygen intermediates that damage these cells (Goldberg & McGynn-Byer, 2000).

Erythema of the treatment area is very common in patients undergoing radiation therapy. Transient erythema that occurs within 24 hours of the first dose likely is caused by dilatation of the capillaries and increased vascular permeability. Erythema that extends past this period is caused by erythrocyte and leukocyte extravasation within the dermis (Sitton, 1992). Increased pigmentation, another common skin reaction, is caused by increased production of melanocytes, the body's attempt to protect the basal layer from further damage (Blackmar, 1997). Low doses of radiation cause a decrease in the mitotic rate of the basal cell layer, which causes temporary thinning of the epidermis. With intermediate doses of radiation, some of the basal cells are destroyed completely, which results in dry desquamation when the cells are replaced. With high doses of radiation, severe dermal changes, such as moist desquamation, ulcers, or necrosis, can be seen (Sitton).

Assessment and Staging

Assessment of irradiated skin will reveal many changes. Skin is usually dry because of sweat and sebaceous gland destruction. Loss of elasticity occurs because of skin atrophy and fibrosis (Goldberg & McGynn-Byer, 2000). Transient erythema can be observed within 24 hours of starting therapy and commonly is localized to the treatment field after two to three weeks of radiotherapy. Hyperpigmentation is common, as is flaky and pruritic skin. These changes are seen after two to four weeks of treatment. If the basal layer of cells is not able to proliferate rapidly enough to supply cells for the epidermis, the dermis will be exposed and moist desquamation will result. This usually occurs after four weeks of treatment and is characterized by bright erythema, clear serous exudates, and pain. Temporary hair loss can occur after three weeks of therapy (Blackmar, 1997).

Many staging systems are found in the literature for reporting severity of radiation dermatitis and have three to seven stages. Most systems include erythema, dry desquamation, and moist desquamation, but other stages described in the literature are various degrees of erythema (just perceptible, mild, moderate, severe, and severe with edema) (Bostrom et al., 2001), epilation and suppression of sweat glands (Goldberg & McGynn-Byer, 2000), necrosis (Boot-Vickers & Eaton, 1999), and hyperpigmentation (Halperin, Gaspar, George, Darr, & Pinnell, 1993).

Intervention

An alarmingly small number of scientific studies has evaluated interventions for radiation skin reactions. Researchers have known of the effect of radiation on the skin for more than 100 years. Until the 1960s, clinicians actually estimated the dose of radiation given by assessing patients' level of erythema because doses could not be measured accurately (Sitton, 1992). Recommendations regarding the prevention and management of radiation dermatitis are diverse and rarely evidence-based (Boot-Vickers & Eaton, 1999). Bruner, Bucholtz, Iwamoto, and Strohl (1998) developed clinical guidelines for the care of skin reac-

tions that provide few specific suggestions for skin care. This article will review studies conducted on various therapies for radiation dermatitis since the 1960s (see Table 1).

Literature Review

Skin Cleansing During Radiotherapy

Two randomized studies evaluated whether washing the skin, hair, and scalp had any impact on the intensity of radiation dermatitis. In their study, Roy, Fortin, and Laroche (2001) evaluated skin care practices among radiation oncology centers in the United Kingdom and found that 4% of the centers did not permit patients to wash their skin in the treatment field during radiotherapy and 39% allowed water but not soap to the irradiated skin. In the study, 99 patients were randomized to either no washing during the entire course of radiotherapy (which was the standard of care prior to the 1980s) or washing with soap and water. The study concluded that washing the irradiated skin with soap and water during radiotherapy for breast cancer was not associated with any increased toxicity.

Westbury, Hines, Hawkes, Ashley, and Brada (2000) examined hair and scalp care during cranial irradiation; 109 patients were randomized to either not wash their hair during treatment or maintain their normal pattern of hair washing. The study also examined the subjective distress caused by changing hair-washing practices. They found that some patients who were randomized to avoid washing their hair did so anyway and reported distress, which the authors felt was caused by the request to alter their hygiene practices. When they compared the two groups, no statistically significant difference was found in skin reactions between the patients who did not wash their hair during radiotherapy and those who did.

Biafine

Biafine[®] (Medix Pharmaceuticals, Inc., Largo, FL) is a hypotonic, oil-in-water emulsion advertised for use in the prevention and treatment of dry and wet desquamation in patients receiving radiation therapy (Goldberg & McGynn-Byer, 2000). Biafine is 75% purified water, 6.8% liquid paraffin, 5.4% ethylene glycol stearate, and 3.6% stearic acid, with the remaining 10 ingredients comprising less than 10% of the formula (Spitalier & Amalric, 1973).

Biafine has been used widely in France since 1976 (Szumacher et al., 2001) after two physicians in Marseille in 1972 compared it alone and in combination with a corticosteroid cream at the end of radiotherapy to a vitamin and codfish oil ointment (the standard of care at their institution) and a corticosteroid cream at the end of radiotherapy (Spitalier & Amalric, 1973). This original trial, which was never published, demonstrated that Biafine, in addition to the steroid cream, produced the most favorable results, with only 33% of the patients experiencing a stage 3 immediate skin reaction (characterized in this study by frank exudative epidermitis of a limited area and confined to the entry sites of the breast or nodes) as compared to 63% of the patients receiving standard therapy. The Biafine-only arm produced better results than the standard therapy but was not as effective as when it was combined with a steroid cream at the end of treatment. From their study of 90 patients, the physicians concluded that Biafine is twice as effective as the previous best ointment and should be applied liberally and without interruption from the first session of radiation (Spitalier & Amalric).

Table 1. Research Studies on Prevention and Treatment of Radiation Dermatitis

Study	Study Design	Sample Size	Product(s) Tested	Outcome	Limitations
Bjornberg et al., 1967	Double-blinded comparative study with each subject serving as both treatment and control	104 wounds in 26 patients	Bethamethasone-17 valerate versus Vaseline versus Eucerin versus no treatment	Bethamethasone-17 valerate ointment had a significantly better effect than the other ointments and no treatment for the first five weeks of radiation; after five weeks, significant differences were not noted.	Experimental radiation was delivered to normal aspects of the thigh to provoke radiation dermatitis in four locations per patient. The study could not be replicated.
Spitalier & Amalric, 1973	RCT	90	Standard ointment and corticosteroid versus Biafine and corticosteroid versus Biafine alone	Biafine was twice as effective in attenuating and delaying acute radiation dermatitis.	Only patients with breast cancer were included; therefore, the results may not be generalizable. The nonblinded design could have introduced bias.
Glees et al., 1979	Double-blinded RCT	54	1% hydrocortisone cream versus 0.05% clobetasone butyrate cream	0.05% clobetasone butyrate cream caused more severe radiation skin reactions, but neither cream should be used as first-line therapy for radiation dermatitis.	Only patients with breast cancer were included; therefore, the results may not be generalizable.
Shell et al., 1986	Pilot RCT	16	Tegaderm versus hydrous lanolin and gauze	Radiation dermatitis healed in an average of 19 days with Tegaderm as opposed to 24 days with lanolin and gauze (not statistically significant).	The sample size was small, and the nonblinded design could have introduced bias.
Margolin et al., 1990	Noncomparative study	18	Duoderm	Duoderm can be effective in the healing process of moist desquamation as a result of radiotherapy.	The trial was not randomized, and the sample size was small.
Maiche et al., 1991	Blinded RCT	48	Chamomile cream versus almond ointment	No difference was found between the two topical therapies, and neither therapy could prevent radiation dermatitis.	Only patients with breast cancer were included; therefore, the results may not be generalizable.
Halperin et al., 1993	Double-blinded RCT	65	Topical vitamin C in vehicle versus vehicle alone	No discernible benefit was found when using topical vitamin C for preventing radiation dermatitis.	Only patients with primary or metastatic brain tumors were included; therefore, the results may not be generalizable.
Strunk & Maher, 1993	Case report	1	Vigilon	Vigilon was effective in treating the radiation dermatitis of a complicated patient.	This was a case report; the nonblinded design could have introduced bias.
Maiche et al., 1994	Double-blinded RCT	44	Sucralfate versus base cream	Acute radiation dermatitis was significantly prevented, but when present, it healed significantly faster in the sucralfate arm.	Only patients with breast cancer were included; therefore, the results may not be generalizable.
Williams et al., 1996	Double-blinded RCT	302	Aloe vera versus placebo gel	The dose of aloe vera gel did not protect against radiation dermatitis.	Only patients with breast cancer were included; therefore, the results may not be generalizable.
Delaney et al., 1997	Double-blinded RCT	39	Sucralfate in sorbolene versus sorbolene alone	No difference existed for the two arms in healing time or pain relief.	The sample size was small.
Fisher et al., 2000	RCT	172	Biafine versus best supportive care (Aquaphor® [Beiersdorf AG, Wilton, CT], aloe vera, other ointment, or no treatment)	No overall difference was found between Biafine and best care in the prevention of, time to, or duration of radiation-induced dermatitis.	Best care consisted of four therapies, making it difficult to generalize this arm; the nonblinded design could have introduced bias. Patient compliance was unclear among arms. Only patients with breast cancer were included; therefore, the results may not be generalizable.

(Continued on next page)

RCT—randomized clinical trial

Table 1. Research Studies on Prevention and Treatment of Radiation Dermatitis (Continued)

Study	Study Design	Sample Size	Product(s) Tested	Outcome	Limitations
Mak et al., 2000	RCT	65 wounds in 39 patients	Topical gentian violet versus hydrocolloid dressing	No significant difference was noted between the two groups, and neither group reduced wound-healing time from previous data.	Only patients with nasopharyngeal cancer were included; therefore, the results may not be generalizable. The nonblinded design could have introduced bias.
Westbury et al., 2000	RCT	109	Normal pattern of hair washing versus no hair washing	Normal hair washing during radiotherapy was not associated with increased toxicity and should not be discouraged.	Patients randomized to avoid washing hair completely did not comply; therefore, whether avoiding hair washing altogether decreases radiotherapy damage is unknown.
Banati et al., 2001	RCT (phase I) and double-blinded RCT (phase II)	85	Sucralfate cream versus topical antimicrobials and sucralfate versus vehicle alone	Skin treated with sucralfate healed significantly faster than topical antimicrobials or vehicle ointment.	Patients had second- and third-degree burns (not radiation dermatitis).
Bostrom et al., 2001	Double-blinded RCT	49	Mometasone furoate versus emollient cream	Mometasone furoate significantly decreased acute radiation dermatitis when compared to emollient cream.	Only patients with breast cancer were included; therefore, the results may not be generalizable.
Fenig et al., 2001	RCT	74	Biafine versus lipiderm versus no treatment	No advantage existed for Biafine or lipiderm over no treatment.	Only patients with breast cancer were included; therefore, the results may not be generalizable.
Olsen et al., 2001	Blinded RCT	73	Aloe vera versus no treatment	At low cumulative doses of radiation, no benefit was seen with aloe; with higher cumulative doses of radiation, the median time to skin changes was significantly longer.	Patient compliance was unclear among arms; patient assessments were not included in the data.
Roy et al., 2001	Blinded RCT	99	Mild soap (e.g., Ivory [®] [Procter & Gamble, Cincinnati, OH]), Dove [®] [Unilever, Inc., New York, NY]) and water versus no washing	Washing irradiated skin with mild soap was not associated with increased toxicity and should not be discouraged.	Only patients with breast cancer were included; therefore, the results may not be generalizable.
Szumacher et al., 2001	Noncomparative study	60	Biafine	Biafine does not prevent dry or moist desquamation in patients undergoing concomitant radiotherapy and chemotherapy.	The trial was not randomized. Only patients with breast cancer were included; therefore, the results may not be generalizable.

RCT—randomized clinical trial

Three trials have been conducted with Biafine with less favorable results. In 2000, a phase II trial studied Biafine cream applied prophylactically in 60 Canadian women undergoing radiotherapy for breast cancer (Szumacher et al., 2001). This study was unable to demonstrate that Biafine could prevent grade II dermatitis in at least 20% of patients, which was its primary objective. An American phase III study was conducted comparing best supportive care to Biafine as a prophylactic agent for women undergoing breast irradiation (Fisher et al., 2000). The researchers found no overall difference between best supportive care, which was determined by each institution's product of choice, and Biafine in the prevention of, time to, or duration of radiation-induced dermatitis in the 172 women they analyzed. The third study was a randomized trial conducted in Israel by Fenig et al. (2001). The investigators studied 74 patients with breast cancer and compared no treatment with Biafine and a lipid-based moisturizing agent contain-

ing antipruritic properties. The researchers concluded that although 86% of the women in both the Biafine and lipid-based cream arms expressed satisfaction with their respective creams, neither product seemed to have a radioprotective effect.

Transparent, Hydrocolloid, and Hydrogel Dressings

In the early 1960s, scientists determined that the rate of re-epithelialization was twice as fast for wounds covered with occlusive moist dressings than for wounds that were allowed to dry, thus beginning the trend toward moist wound healing (Hom, Adams, Koreis, & Maisel, 1999). A vascular, moist environment aids new epithelial cells that must migrate across a wound for healing to occur. The dry crust that forms when a wound is left open to air can be interpreted as a foreign body. Epidermal cells have to move under the crusted eschar to find the moist vascular bed needed for wound coverage, which lengthens healing time (Strunk & Maher, 1993).

Several dressing types are used in radiation dermatitis that can provide moist healing: transparent, hydrocolloid, and hydrogel dressings. Prior to their use, the standard dressing was dry gauze over a topical cream (Shell, Stanutz, & Grimm, 1986). In 1986, Tegaderm® (3M, St. Paul, MN) transparent dressing was the first dressing to be studied. In a study comparing Tegaderm to dry, sterile gauze over hydrous lanolin cream, researchers revealed that an occlusive dressing was superior to a conventional dressing, although the difference failed to reach statistical significance. Eight patients with dry and moist desquamation in the Tegaderm group healed in an average of 19 days, whereas eight patients with dry and moist desquamation in the conventional-dressing group healed in an average of 24 days. An additional benefit of the Tegaderm dressing was that it could remain in place for several days and did not need to be removed for radiation therapy. The conventional dressing had to be removed daily for radiation, which could have a deleterious effect on healing epithelium (Shell et al.).

The second dressing studied was Duoderm® (Convatec, Princeton, NJ) hydrocolloid dressing. A noncomparative study assessed moist wound healing with the Duoderm dressing in 18 patients with moist desquamation during radiotherapy. The dressing was evaluated on the basis of healing time, safety, wound temperature, bacterial growth, and patient comfort. Healing time was 12 days, which is shorter than reported with Tegaderm transparent dressings, and the majority of the patients (15 of 18) rated the comfort of the dressing as excellent or good. Duoderm kept the wound warm, which has been shown to assist in wound healing, and bacterial presence in the wound did not lead to any clinical infections. The major problem with this dressing was that it contains melted gel. This was the most frequent cause of dressing changes and was worse during hot weather (Margolin et al., 1990).

The third dressing reported in the literature is Vigilon® (C.R. Bard, Inc., Murray Hill, NJ), a hydrogel sheet dressing. No clinical trials have been conducted with this hydrogel product, which is 96% water, but its use in radiation dermatitis has been published in case reports. In 1991, Roof reported using Vigilon to treat radiation dermatitis because it provided pain relief, absorbed wound exudates, maintained moisture in the wound bed, and was nonadherent, resulting in atraumatic removal for daily radiation therapy. Strunk and Maher (1993) reported a challenging case of a man with coexisting cicatricial pemphigoid (i.e., a rare skin disorder necessitating high-dose systemic corticosteroid therapy) and esophageal carcinoma requiring radiation therapy. The patient had moist desquamation and necrosis and was treated successfully with Vigilon. The patient reported marked increased comfort with the hydrogel.

Almond, Chamomile, Gentian Violet, and Vitamin C Topical Preparations

Almond ointment and chamomile cream were compared in a physician evaluator-blinded study in Sweden (Maiche, Grohn, & Maki-Hokkonen, 1991), where chamomile cream had been the standard therapy for skin protection during radiotherapy for the previous 10 years. Objective data (skin reaction severity) and subjective data (pain and itching) were collected for 48 patients undergoing radiotherapy for breast cancer. Each woman used both creams: one above the scar and one below the scar on the treated breast. This study failed to detect any statistically significant difference in the performance of either preparation, although patients who used the

chamomile cream developed dark erythema later than the patients who used the almond ointment. The patients preferred the chamomile cream because it absorbed quickly and did not stain their clothes. Neither group reported pain or itching. The radiation dermatitis generally cleared within two weeks of the final radiation dose, but in some cases, this took up to three months, leading the investigators to report that neither preparation was able to prevent erythema.

Gentian violet has been used to treat moist desquamation because of its antifungal and antiseptic effects. In one study, gentian violet was compared to hydrocolloid dressings in 39 patients who had completed radiotherapy and had a moist desquamation skin reaction in a Hong Kong hospital (Mak, Molassiotis, Wan, Lee, & Chan, 2000). The standard of care in that institution was gentian violet with open healing at the time the research was conducted. Healing time, pain, and patient satisfaction with dressing type were measured. Healing time was equivocal between the two groups, with the hydrocolloid dressing (extrathin Duoderm) group healing after 11.42 days and the gentian violet group healing after 11.7 days. Patients in both groups experienced pain: the hydrocolloid group when the dressing was removed, exposing the dermis, and the gentian violet group when the product dried the skin, causing cracks to the dermis. The satisfaction scores were higher with the hydrocolloid even though the melted gel of the dressing was a problem for some patients. Gentian violet was very drying to the skin and caused tightness that restricted movement in some patients. It also stained their skin and clothes, which was not aesthetically acceptable.

Vitamin C cream also has been examined for its role in preventing radiation dermatitis. Halperin et al. (1993) compared topical vitamin C with placebo in 65 patients who received cranial irradiation. All patients used the treatment and the control solution—the vehicle alone—one on each side of the head during radiotherapy in this double-blind, randomized study. Because ascorbic acid has radioprotective effects on normal tissue from its antioxidant properties, researchers developed an aqueous solution of L-ascorbic acid to determine whether local application provided skin-sparing effects. They were unable to demonstrate that the vitamin C topical solution held any radioprotective effects in patients receiving radiotherapy to the head, and more patients preferred the placebo or no treatment to the vitamin C topical solution.

Sucralfate Cream

Sucralfate cream has received attention as an agent for radiation dermatitis since the 1990s. Oral sucralfate is used widely in the treatment of gastric ulcers and to protect mucous membranes during radiotherapy and chemotherapy. It stimulates cell growth by increasing the amounts of prostaglandin E and epidermal growth factor. Sucralfate has an anti-inflammatory effect and increases epithelial circulation (Maiche, Isokangas, & Grohn, 1994). Some studies have shown an antibacterial effect of sucralfate, although this mechanism is not understood (Banati, Chowdhury, & Mazumder, 2001).

The first randomized clinical trial with sucralfate cream for radiation dermatitis was published by Maiche et al. (1994). These Finnish investigators had seen the effects of oral sucralfate on preventing intestinal mucositis during pelvis irradiation, as well as the beneficial effects of sucralfate cream on aging skin, and postulated that topical sucralfate would have a beneficial effect on patients undergoing electron beam radiotherapy.

They studied 44 patients undergoing radiotherapy for breast cancer; every patient used both creams, one on either side of the scar, so that each patient served as her own control. The authors found that the skin treated with sucralfate cream fared significantly better than the skin treated with placebo. Areas treated with the sucralfate cream were slower to develop grade 1 and 2 reactions. The recovery time of the skin lesions also was faster on the areas treated with sucralfate cream, and at the end of radiotherapy, the grade of the skin reaction in the sucralfate-treated areas was lower than the grade in the placebo-treated areas. No allergic reactions were seen, and patients considered the cosmetic appearance of both creams to be excellent.

Delaney, Fisher, Hook, and Barton (1997) looked at sucralfate cream in sorbolene compared to sorbolene alone in the management of moist desquamation during radiotherapy. This Australian study enrolled patients receiving radiation for breast or head and neck cancer and other malignancies who had developed a measurable area of moist desquamation during therapy. This study differed from the study by Maiche et al. (1994) in that it looked at sucralfate cream as a treatment rather than prophylaxis for radiation dermatitis. The trial included 39 patients and measured time to healing and pain from the randomization date. No statistical difference was seen in either measure between groups. The authors reported, however, that the data were consistent with a 50% reduction in time to heal as compared with the placebo, but the reduction was not fully seen because the planned sample size of 120 was not achieved as a result of poor accrual.

Banati et al. (2001) studied the use of sucralfate cream in second- and third-degree burns. Although the mechanism of injury is much different in burns and radiation dermatitis, the resulting partial-thickness wound (in second-degree burns) is comparable, so the data are included in this review. Two phases of the study were reported. The first phase compared patients treated with sucralfate cream with patients receiving other topical antimicrobials (N = 60). The second phase compared patients treated with sucralfate cream to patients receiving a placebo cream made with the same ingredients as the sucralfate cream but without the sucralfate (N = 25). In the subset of patients with second-degree burns, which more accurately can be compared with radiation dermatitis, the rate of epithelialization was 18.8 days in the sucralfate group compared to 24.6 days in the topical antimicrobial group. This difference was statistically significant. In the second phase of the trial, the patients receiving treatment with sucralfate cream again were found to heal much more quickly than those receiving treatment with the placebo. Patients described the cream as soothing and painless on administration. No allergic reactions were appreciated, nor were any systemic side effects noted.

Aloe Vera Gel

Aloe vera has long been promoted in a large variety of skin conditions. It has been used for at least 1,000 years in Greece, Egypt, India, Mexico, Japan, and China. Aloe is a plant with more than 150 species and is native to South Africa. Regardless of its widespread use, few controlled, randomized clinical trials exist. In a review, Vogler and Ernst (1999) found only 10 studies that were controlled and used aloe vera monopreparations, despite a search through four databases from their inception to 1998. The use of aloe in the treatment of radiation dermatitis has been reported in the literature as

early as 1935 (Williams et al., 1996). Two studies have looked at the effectiveness of aloe vera in radiation skin care.

Williams et al. (1996) evaluated aloe vera's role in preventing radiation dermatitis. Two phase III trials were conducted, with the first double-blind study examining the effect of aloe vera gel versus a placebo gel on 194 women undergoing radiotherapy for breast cancer. The second trial compared aloe vera gel with no treatment in 108 patients. Both the patients and healthcare providers rated skin reactions. Skin dermatitis scores were almost identical in both treatment arms during both trials. The only toxicity was a rare contact dermatitis.

Olsen et al. (2001) compared aloe vera gel with mild soap cleansing to mild soap cleansing alone during radiotherapy. This U.S. study examined the time to first observed skin change with prophylactic use of aloe vera in 73 patients. The investigators found that at low cumulative radiation doses ($\leq 2,700$ cGY), no difference existed between the two study groups, but at higher cumulative doses ($\geq 2,700$ cGY), the median time to detectable skin change was five weeks in the aloe vera and soap arm compared with three weeks in the soap-only arm. They concluded that with increased cumulative doses, a protective effect seems to result from adding aloe vera to the skin care regimen.

Corticosteroid Cream

Topical steroid creams have received mixed reviews in the treatment of radiation dermatitis. The idea of applying a drug to radiation-damaged skin when the mechanism of the drug can delay healing is somewhat counterintuitive. Bruner et al.'s (1998) guidelines for radiation-induced skin reactions stated, "Hydrocortisone cream can be applied to irritated, inflamed skin but should not be used on moist skin reactions because it may enhance infection" (p. 19). Several studies have been conducted since the 1960s that have assessed the efficacy of these topical preparations.

In 1967, Swedish investigators Bjornberg, Hellgren, Magnusson, Mattsson, and Rosengren compared bethamethasone-17 valerate, Vaseline® (Unilever, Inc., New York, NY), Eucerin® (Beiersdorf AG, Wilton, CT), and no treatment with 26 patients receiving experimental radiation administered in four equal areas on the inner thighs. The creams were applied three times a day beginning with the first radiation dose in this double-blind study. During the first five weeks of treatment, the steroid cream performed better than the other creams and no treatment. After six weeks, statistical significance for the superiority of the steroid cream was not demonstrated over Vaseline, although it still had a significantly better effect than Eucerin or no treatment.

Glees, Mameghan-Zadeh, and Sparkes (1979) compared two different steroid creams in patients in the United Kingdom once they reached a dose of 2,000 rad whether a skin reaction was present or not. The aim of this trial was to determine the general effectiveness of topical steroid therapy in controlling radiation dermatitis and whether one cream was superior to the other. In the study, 28 patients used 1% hydrocortisone cream and 26 patients used 0.05% clobetasone butyrate. Significantly more patients in the clobetasone butyrate arm developed severe reactions, and five of the patients in this arm (compared with two in the hydrocortisone arm) withdrew from the study to be treated with other agents when their skin reaction was deemed too severe by the radiotherapist to continue in the study. Although the hydrocortisone cream

performed better than the clobetasone cream, the authors concluded that neither cream should be used in the prevention or treatment of radiation dermatitis because 96.4% of the hydrocortisone patients and 88.5% of the clobetasone butyrate patients experienced moderate to maximum radiation dermatitis.

More recently, another steroid cream has been studied in the prevention of acute radiation dermatitis. A Swedish double-blind randomized trial was conducted on 49 women undergoing breast irradiation and compared mometasone furoate, a potent corticosteroid cream, with a placebo emollient cream (Bostrom et al., 2001). Both groups also used daily emollient cream. The results were favorable for the steroid cream. Data collected included a visual skin inspection and objective erythema and pigmentation measurement with a reflectance spectrophotometer. The creams were applied from the beginning of therapy and continued throughout the study period, even if patients developed moist desquamation. The patients in the steroid arm had lower erythema and pigmentation scores measured with the reflectance spectrophotometer, as well as lower visual skin-assessment scores, with only 25% of patients in the steroid group compared to 60% in the emollient-only group scoring a grade 4, 5, or 6 on the authors' six-point scale for measuring radiation reactions. The study revealed that the steroid cream in combination with an emollient cream was statistically and significantly superior to emollient cream only in reducing acute radiation dermatitis.

Recommendations for Practice

Few recommendations can be made from the current literature for preventing and treating acute radiation dermatitis. The scientific studies available primarily have been conducted with small sample sizes, which can render the results insignificant. Much of the literature has been written about women undergoing irradiation to the breast; therefore, results may not be generalizable to all treatment fields. In addition, reports about the therapies are conflicting, which may result, in part, from the many different scales used to measure the severity of radiation dermatitis.

The available evidence does provide some data that can be used in clinical practice. Patients can wash their hair and skin safely with mild soap and shampoo during radiation therapy. Biafine, chamomile cream, almond ointment, topical vitamin C, and gentian violet have not been proven effective and should not be used. Transparent, hydrocolloid, and hydrogel dressings can be beneficial, although the sample sizes used in studying these dressings were limited. Of these, the hydrogel sheet dressing is most pleasing to patients because it is nonadherent, allows for atraumatic removal, and is soothing when applied. Aloe vera gel has not been shown to provide any major benefit, although one small study reported that it prolongs the time to skin damage at higher doses of radiation. Because it is a fairly benign product, aloe vera likely does no harm to patients undergoing radiotherapy, although the benefit may be small. Sucralfate and corticosteroid creams have been the most promising topical agents in the prevention and treatment of radiation dermatitis.

Implications for Future Research

A great deal of research is needed to determine the best interventions for radiation dermatitis. New research must be

conducted using a standardized staging system for severity of radiation dermatitis before results can be interpreted and generalized. The National Cancer Institute along with representatives from the Radiation Therapy Oncology Group revised and expanded the common toxicity criteria (CTC) with a goal of integrating medical, surgical, and radiotherapy criteria into a standardized system. This system graded all cancer treatment-related toxicity on a 0–5 scale: 0 = no adverse event, 1 = mild adverse event, 2 = moderate adverse event, 3 = severe and undesirable adverse event, 4 = life-threatening or disabling adverse event, and 5 = death related to an adverse event. The result of their combined efforts can be found in the radiation dermatitis section of the CTC version 2.0. The new criteria are 0 = no skin reaction; 1 = faint erythema or dry desquamation; 2 = moderate to brisk erythema or a patchy moist desquamation mostly confined to skin folds and creases; 3 = moderate edema, confluent moist desquamation 1.5 cm in diameter, and not confined to skin folds; and 4 = pitting edema, skin necrosis, or ulceration of full thickness dermis that may include bleeding not induced by minor trauma or abrasion (Trotti et al., 2000). The National Cancer Institute of Canada uses a nearly identical CTC scale, after adopting a revised version in 1998 (Szumacher et al., 2001). The use of this standard scale in North America can lead the way in adopting a worldwide uniform scale for measuring and reporting radiation dermatitis severity. With the research that needs to be conducted on appropriate therapy for this common skin problem, a standard toxicity scale is necessary.

Of the agents previously studied, more research needs to be conducted on aloe vera, sucralfate cream, corticosteroid cream, and various dressings. These studies need to be conducted with patients undergoing therapy for various cancers, so the results can be more generalizable. The studies also need to have larger sample sizes for the results to be proven with greater statistical significance. To obtain larger sample sizes, multiple clinical sites should be used.

In addition to conducting more trials with previously studied agents, research should be done on new products. The current armamentarium is limited, and even if the most effective of the known products is found, room still will exist for improvement. Oral radioprotective agents should be developed and studied. One drug, azelastine, has been effective in reducing the severity of acute radiation dermatitis without affecting the antitumoral effect of radiation therapy in mice when administered orally (Murakami et al., 1997). Other potential preventive agents are polymer adhesive skin sealants, historically used to protect the skin of bedridden patients from skin breakdown. One study reported positive results in minimizing radiation-induced moist desquamation using these products (Hazuka, Goebel, McCutchan, Sousa, & Greff, 1997).

In conclusion, the scientific research in the area of radiation dermatitis is limited. Radiation therapy is a mainstay of cancer treatment, and skin reactions are a very common and life-altering side effect of patients undergoing this therapy. Future research must be conducted to provide better evidence for prevention and treatment of acute radiation dermatitis, and novel therapies must be investigated.

Author Contact: Mihkaila Maurine Wickline, RN, MN, AOCN®, CNS, can be reached at mihkai@u.washington.edu, with copy to editor at rose_mary@earthlink.net.

References

- Banati, A., Chowdhury, S., & Mazumder, S. (2001). Topical use of sucralfate cream in second and third degree burns. *Burns*, 27, 465–469.
- Bjornberg, A., Hellgren, L., Magnusson, B., Mattsson, I., & Rosengren, B. (1967). Topical treatment of radiation dermatitis with bethamethasone-17-valerate, Vaseline and Eucerine—A double-blind comparison. *Clinical Radiology*, 18, 463–464.
- Blackmar, A. (1997). Radiation-induced skin alterations. *Medsurg Nursing*, 6, 172–175.
- Boot-Vickers, M., & Eaton, K. (1999). Skin care for patients receiving radiotherapy. *Professional Nurse*, 14, 706–708.
- Bostrom, A., Lindman, H., Swartling, C., Berne, B., & Bergh, J. (2001). Potent corticosteroid cream (mometasone furoate) significantly reduces acute radiation dermatitis: Results from a double-blind, randomized study. *Radiotherapy and Oncology*, 59, 257–265.
- Bruner, D.W., Bucholtz, J.D., Iwamoto, R., & Strohl, R. (Eds.). (1998). *Manual for radiation oncology nursing practice and education*. Pittsburgh, PA: Oncology Nursing Society.
- Delaney, G., Fisher, R., Hook, C., & Barton, M. (1997). Sucralfate cream in the management of moist desquamation during radiotherapy. *Australasian Radiology*, 41, 270–275.
- Fenig, E., Brenner, B., Katz, A., Sulkes, J., Lapidot, M., Schachter, J., et al. (2001). Topical Biafine and lipidem for the prevention of radiation dermatitis: A randomized prospective trial. *Oncology Reports*, 8, 305–309.
- Fisher, J., Scott, C., Stevens, R., Marconi, B., Champion, L., Freedman, G., et al. (2000). Randomized phase III study comparing best supportive care to Biafine as a prophylactic agent for radiation-induced skin toxicity for women undergoing breast irradiation: Radiation Therapy Oncology Group (RTOG) 97-13. *International Journal of Radiation Oncology, Biology, Physics*, 48, 1307–1310.
- Glees, J., Mameghan-Zadeh, H., & Sparkes, C. (1979). Effectiveness of topical steroids in the control of radiation dermatitis: A randomized trial using 1% hydrocortisone cream and 0.05% clobetasone butyrate (Eumovate). *Clinical Radiology*, 30, 397–403.
- Goldberg, M.T., & McGynn-Byer, P. (2000). Oncology-related skin damage. In R.A. Bryant (Ed.), *Acute and chronic wounds: Nursing management* (2nd ed., pp. 367–386). St. Louis, MO: Mosby.
- Halperin, E., Gaspar, L., George, S., Darr, D., & Pinnell, S. (1993). A double-blind, randomized, prospective trial to evaluate topical vitamin C solution for the prevention of radiation dermatitis. CNS Cancer Consortium. *International Journal of Radiation Oncology, Biology, Physics*, 26, 413–416.
- Hazuka, M.B., Goebel, R.H., McCutchan, S., Sousa, K., & Greff, R.F. (1997). A new approach to the prevention of radiation-induced skin desquamation using a polymer adhesive skin sealant (PASS): Final results of a prospective study [Abstract 239]. Retrieved January 20, 2004, from http://www.asco.org/ac/1,1003,12-002490-00_18-001997-00_19-0011064,00.asp
- Hom, D., Adams, G., Koreis, M., & Maisel, R. (1999). Choosing the optimal wound dressing for irradiated soft tissue wounds. *Otolaryngology and Head and Neck Surgery*, 121, 591–598.
- Maiche, A., Grohn, P., & Maki-Hokkonen, H. (1991). Effect of chamomile cream and almond ointment on acute radiation skin reaction. *Acta Oncologica*, 30, 395–396.
- Maiche, A., Isokangas, O., & Grohn, P. (1994). Skin protection by sucralfate cream during electron beam therapy. *Acta Oncologica*, 33, 201–203.
- Mak, S., Molassiotis, A., Wan, W., Lee, I., & Chan, E. (2000). The effects of hydrocolloid dressing and gentian violet on radiation-induced moist desquamation wound healing. *Cancer Nursing*, 23, 220–229.
- Margolin, S., Breneman, J., Denman, D., LaChapelle, P., Weckbach, L., & Aron, B. (1990). Management of radiation-induced moist skin desquamation using hydrocolloid dressing. *Cancer Nursing*, 13, 71–80.
- Murakami, R., Baba, Y., Nishimura, R., Furusawa, M., Yokoyama, T., Yamashita, Y., et al. (1997). The effect of azelastine on acute radiation dermatitis in mice models. *International Journal of Radiation Oncology, Biology, Physics*, 37, 907–911.
- Olsen, D., Raub, W., Jr., Bradley, C., Johnson, M., Macias, J., Love, V., et al. (2001). The effect of aloe vera gel/mild soap versus mild soap alone in preventing skin reactions in patients undergoing radiation therapy. *Oncology Nursing Forum*, 28, 543–547.
- Roof, L. (1991). The use of Vigilon primary wound dressing in the treatment of radiation dermatitis. *Oncology Nursing Forum*, 18, 133–134.
- Roy, I., Fortin, A., & Larochele, M. (2001). The impact of skin washing with water and soap during breast irradiation: A randomized study. *Radiotherapy and Oncology*, 58, 333–339.
- Shell, J., Stanutz, F., & Grimm, J. (1986). Comparison of moisture vapor permeable (MVP) dressings to conventional dressings for management of radiation skin reactions. *Oncology Nursing Forum*, 13(1), 11–16.
- Sitton, E. (1992). Early and late radiation-induced skin alterations. Part I: Mechanisms of skin changes. *Oncology Nursing Forum*, 19, 801–807.
- Spitalier, J.M., & Amalric, R. (1973). *Value of Biafine in the prevention and treatment of immediate skin reactions following radiotherapy: Comparative study*. Unpublished manuscript.
- Strunk, B., & Maher, K. (1993). Collaborative nurse management of multifactorial moist desquamation in a patient undergoing radiotherapy. *Journal of ET Nursing*, 20, 152–157.
- Szumacher, E., Wighton, A., Franssen, E., Chow, E., Tsao, M., Ackerman, I., et al. (2001). Phase II study assessing the effectiveness of Biafine cream as a prophylactic agent for radiation-induced acute skin toxicity to the breast in women undergoing radiotherapy with concomitant CMF chemotherapy. *International Journal of Radiation Oncology, Biology, Physics*, 51, 81–86.
- Trotti, A., Byhardt, R., Stetz, J., Gwede, C., Corn, B., Fu, K., et al. (2000). Common toxicity criteria: Version 2.0. An improved reference for grading the acute effects of cancer treatment: Impact on radiotherapy. *International Journal of Radiation Oncology, Biology, Physics*, 47, 13–47.
- Vogler, B., & Ernst, E. (1999). Aloe vera: A systematic review of its clinical effectiveness. *British Journal of General Practice*, 49, 823–828.
- Westbury, C., Hines, F., Hawkes, E., Ashley, S., & Brada, M. (2000). Advice on hair and scalp care during cranial radiotherapy: A prospective randomized trial. *Radiotherapy and Oncology*, 54, 109–116.
- Williams, M., Burk, M., Loprinzi, C., Hill, M., Schomberg, P., Nearhood, K., et al. (1996). Phase III double-blind evaluation of an aloe vera gel as a prophylactic agent for radiation-induced skin toxicity. *International Journal of Radiation Oncology, Biology, Physics*, 36, 345–349. 

For more information . . .

- ▶ Radiation Therapy Oncology Group
www.rtog.org
- ▶ Joint Center for Radiation Therapy
www.jrcr.harvard.edu/jrcr

Links can be found at www.ons.org.

The continuing education examination and test form for the preceding article appear on the following pages.