Topical Micronutrient Products Significantly Reduced Radiation Dermatitis and Improved Patient Quality of Life Scores in a Year-Over-Year Study of Eighty Two Patients

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Abstract

The objective of the study was to determine if new micronutrient skin care technologies could outperform the Standard-of-Care (SOC) by reducing the incidence of radiodermatitis while improving the patient's perceived Quality-of-Life during radiotherapy. Breast cancer patients have benefited from skin sparing technologies, but remain at high risk of skin breakdown associated with radiation dermatitis. Ninety two to ninety six percent of breast cancer patients will experience skin reaction and lost Quality-of-Life. The study utilized validated scoring documents developed by the Oncology Nursing Society and Dermatology Life Quality Index (DLQI). Eighty two patients receiving radiotherapy were evaluated in the year-over-year study. Forty one patients received the SOC, Natural Care® Gel from Bard Medical and Aquaphor® Healing Ointment from Beiersdorf AG. The following 41 patients received Remedy micronutrient skin care products from Medline Industries, Inc. The results of the study demonstrated that Remedy micronutrient skin care products significantely reduced radiodermatitis. The incidence of dry desquamation and small to moderate wet desquamation was reduced by 50% over the SOC. Additionally, over 10% of the patients receiving the SOC sustained infections during the course of their radiotherapy and one patient had to discontinue care. No infections or discontinuation of care were reported in the Remedy group. Further, 46% of the Remedy patients reported no reduction in their quality of life due to skin related problems including product application values, resulting in higher rates of skin care compliance. Remedy patients averaged a Quality-of Life (QL) score of 0.53 with the best possible score being 0 and the worst possible score being 30, indicating the highest possible impairment of QL.

ONS SCORE	NCG/AQ	REMEDY	PERCENT IMPROVEMENT
0	0	1	100
1	25	27	8
2	7	7	0
3	6	4	50
4	3	2	50
5	0	0	NA
6	0	0	NA

Table I. Number of patients in each respective group along with the specified ONS toxicity scoring criteria. The Remedy™ line outperformed the Declared Institutional Preference significantly. The incidence of dry desquamation and small to moderate wet desquamation was 50% less in the Remedy™ treatment group.

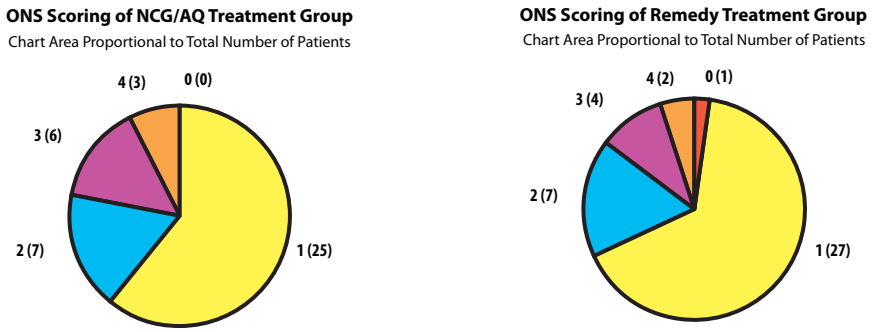

Figure I. Number of patients that received ONS skin breakdown scores between 0 – 4 in NCG/AQ treatment group and Remedy treatment group, respectively.

Introduction

Skin is the largest organ of the human body and provides protection against the external environment. In addition, skin restores itself every 28 days and is the body's largest producer of enzymes and hormones. Skin consists of three layers; the dermis, epidermis and the protective, semi-permeable stratum corneum that permits terrestrial life[1]. The stratum corneum is metabolically active and protects against excessive transepidermal water loss (e-TEWL), mechanical trauma, microbial infection, temperature variation and percutaneous toxin absorption[2]. However, ionizing radiation commonly disturbs or damages several of the skin's protective functions. Studies have shown that 36-100% of patients receiving radiotherapy experience some degree of skin reaction 7-14 days into treatment[3,4]. During treatment, patients may experience pruritus, erythema, edema, desquamation, necrosis, ulceration and/or hemorrhage[5]. The whole of possible skin reactions associated with radiotherapy are collectively known as radiation dermatitis.

In the past 20 years radiotherapy has experienced tremendous advances, allowing for increased tissue sparing techniques. Nevertheless, radiotherapy routinely causes severe acute and chronic damage of the skin[6]. In fact, skin injury may be the dose-limiting factor for radiotherapy[7]. Once a threshold dose has been exceeded, the severity of the radiation effect at any point on the skin increases with increasing dose. The most currently available fluoroscopic measuring systems do not provide the operator with sufficient information to perfectly minimize skin dose[8].

During radiotherapy, vascular injury occurs, followed by leukocyte infiltration and barrier breakdown. Leukocyte infiltration is frequently observed in irradiated skin and plays a significant role in tissue damage. Cell adhesion molecules (CAMs) expressed on leukocytes and endothelial cells control the transmigration of leukocytes out of the blood vessel lumen. CAMs including platelet, leukocyte, and endothelial-selectins, vascular cell adhesion molecule-1, as well as β1 and β2 integrins are involved in the trafficking of leukocytes through the inflamed endothelium[9]. Leukocyte transmigration is also accompanied by monocyte and macrophage infiltration, causing inflammation, pruritus and other symptoms associated with radiation dermatitis[10]. Furthermore, radiation deposition results in DNA damage manifested by single and double-strand breaks in the sugar phosphate backbone of epidermal and dermal skin cells[11]. Most cell types do not show morphologic evidence of radiation damage until they attempt to divide[12]. Since skin cells have extraordinarily high rates of division, symptoms associated with sub-lethal and potentially lethal damage may appear almost immediately.

Patients and Methods

Objectives

- Determine if a skin care regimen using Remedy skin care products mitigates radiation-induced tissue damage in breast cancer patients receiving radiotherapy.
- Compare efficacy of Remedy skin care products to other products used to prevent skin injury.

Drug Information

The Remedy products are endermic, providing for the administration of medicine by absorption through the skin. Micronutrients with a molecular weight of less that 500 Daltons can enter or exit the skin (500 Dalton Rule). These micronutrients include amino acids, vitamins, antioxidants and polyunsaturated fatty acids (PUFAs) comprised as a balance of n-3/n-6.

- Amino acids – glycine, L- cysteine and L-proline.
- Vitamins B3, B6, A, C and D3
- Antioxidants –Hydroxytyrosol and L-taurine.
- PUFAs, n-3/n/6

Patient Inclusion Criteria

- Patients with newly diagnosed histologically documented breast cancer.
- Female patients greater than 18 years of age.
- Patients receiving only radiotherapy for their breast cancer.
- Four weeks post-surgical and recovered from surgical side effects.
- Not using skin care products other than those prescribed by physician.
- No skin tumor involvement.
- No rash, ulceration or open wound in the treatment field.
- Be available for follow-up.
- Have signed informed consent.

Patient Exclusion Criteria

- Patients with cancer other than breast cancer.
- Patients receiving concurrent immunotherapy.
- Patients using skin care products other than specified by protocol.
- Patients who previously used Remedy skin care products.
- Patients with medical conditions that prevent compliance with protocol.
- Patients unwilling or unable to give informed consent.

Treatment Regimen

Patients will follow a Remedy regimen with results being compared in a year-over-year evaluation against SOC. The Remedy regimen was as follows:

1. 4-IN-1 No-Rinse Cleansing Lotion: apply to damp cloth or directly to skin. Gently clean with moist cloth. Use twice daily, morning and bedtime.
2. Skin Repair Cream: apply to breast and back two times a day, as above.
3. Nutrashield Skin Protectant: apply to breast and back following application of Skin Care Repair Cream.
4. 4-IN-1 Antiseptic Cleanser: apply as a deodorant replacement if needed.
    - Begin regimen starting with simulation and continuing for one month following the completion of therapy.
    - Avoid application of tape or adhesives directly on treatment area.
    - Avoid powder, alcohol, cologne, creams, ointment or deodorant in treatment area.
    - Avoid exposure to sunlight, any source of heat (heating pads; sun lamps), or cold (ice packs; extremely cold weather).
    - Treated area should not be shaved.

Criteria for Evaluation

The validated Oncology Nursing Society (vONS) criterion for skin evaluation was used by physician prior to treatment to document observations weekly during radiotherapy and weekly for four weeks following completion of radiotherapy. The vONC criteria are as follows:

ONS SCORE: 0 **Normal skin within the radiation field.**
ONS SCORE: 1 **Faint/dull erythema, follicular reaction, epilation, dry desquamation, decreased sweating.**
ONS SCORE: 2 **Bright erythema.**
ONS SCORE: 3 **Dry desquamation.**
ONS SCORE: 4 **Small to moderate wet desquamation.**
ONS SCORE: 5 **Confluent moist desquamation.**
ONS SCORE: 6 **Ulcerations, hemorrhage, or necrosis.**

Patient Quality of Life

Establishing a treatment protocol for radiation dermatitis is of importance and should take into account patient QL. The current international QL criterion for patients receiving skin care is based on the validated Dermatology Life Quality Index (vDLQI) developed by Andrew Y. Finlay, M.D. The vDLQI is the dermatology industry standard for measuring QL. The vDLQI has been sited in more than 130 published articles and abstracts, in 17 countries and 21 languages.[13]

Each question is answered either "Very much" (score 3), "A lot" (score 2), "A little" (score 1) or "Not at all" (score 0). Questions 3 – 10 also have the option "Not relevant" (score 0). The first part of question 7 has the choices "Yes" (score 3), "No", or "Not relevant". The second part of question 7 has the choices "A lot", "A little", or "Not at all". The minimum score is 0 and the maximum score is 30, indicating the highest possible impairment of quality of life[13].

Quality of Life Results

Twenty-six members of the Remedy treatment group completed vDLQI questionnaires during five weeks of radiotherapy. Patients using the Remedy products reported lower impairment scores and higher rates of compliance, resulting in greater vDLQI values. According to patient reviews, QL was maintained due to the products' effectiveness against pain and pruritus, and decreased "greasiness" and "stickiness". In particular, patients reported low impairment scores for vDLQI-Question #1 throughout the entire treatment period. Question #1 asked patients to determine the degree to which their skin had been "itchy, sore, painful and/or stinging" during the previous week.

Patients being treated with Remedy products maintained an average Question #1-impairment score of 0.53. Furthermore, at the end of Week 5 when radiotherapy damage had the most time to accumulate, the mean impairment score was below 1.0. A score of 0.0 signifying impairment that is "Not at all" recognized, and a score of 1.0 indicating impairment that is recognized "A little". In fact, over 46% of the patients reported either no change in impairment or a lesser degree of impairment from Week 1 to Week 5.

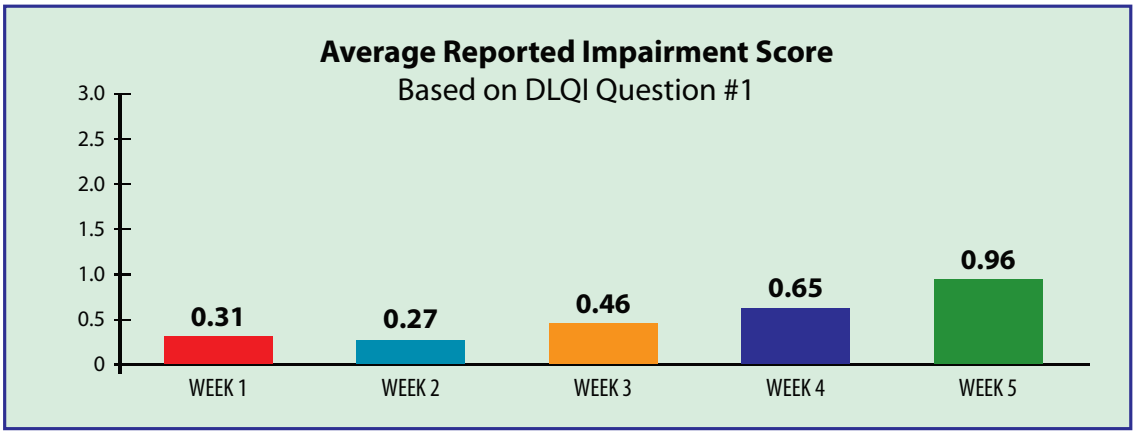

Figure II. During five weeks of radiotherapy, patients being treated with the Remedy™ skin care line averaged a Question #1-impairment score of only 0.53 (Over the last week, how itchy, sore, painful or stinging has your skin been?). Over 46% of the patients self-reported either no change in impairment or a lesser degree of impairment from Week 1 to Week 5.

Conclusion

The response of skin to radiotherapy is highly complex and is dependent on numerous radiation-related, treatment-related, and patient-related factors. Establishing an effective treatment protocol for radiation dermatitis is of great significance and should take into account patient QL. Remedy micronutrient skin care products significantly reduced radiodermatitis. The products reduced the incidence of dry desquamation and small to moderate wet desquamation by 50% over the SOC. Patients treated with the Remedy products self-reported lower symptomatic impairment scores and higher rates of compliance, resulting in greater vDLQI values. Breast cancer patients being treated with radiotherapy should benefit from topical adjunctive care that provides tissue protection from radiation dermatitis. Currently, the products preferred for skin care during radiotherapy provide no micronutrient benefits. The skin is a complex organ that requires specific balances of antioxidants, PUFAs, vitamins and amino acids in order to maintain homeostasis. Current stands-of-care regimens should be reevaluated based upon these findings.

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