European Journal of Oncology Nursing 18 (2014) 499–504

Contents lists available at ScienceDirect

European Journal of Oncology Nursing

journal homepage: www.elsevier.com/locate/ejon

Retrospective study of radiotherapy-induced skin reactions in breast cancer patients: Reduced incidence of moist desquamation with a hydroactive colloid gel versus dexpanthenol

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Keywords:
Radiotherapy-induced skin reactions
Radiation dermatitis
Radiodermatitis
Breast cancer
Moist desquamation
Dexpanthenol
Hydroactive colloid gel
Hydrocolloid
Hydrogel

A B S T R A C T

Purpose: Dermatitis is a very frequent and distressing side effect of radiation therapy that may necessitate a treatment interruption when evolving towards more severe forms such as moist desquamation (MD). The aim of this study was to compare the efficacy of two topical agents, a dexpanthenol cream vs a hydroactive colloid gel combining absorbing and moisturising properties, in preventing MD in breast cancer patients.
Methods: This retrospective study compared two successive groups of breast cancer patients undergoing radiotherapy after breast-sparing surgery between 2008 and 2012. A group of 267 patients applied a 5% dexpanthenol cream on the irradiated zone throughout the course of their radiotherapy. Another group of 216 patients applied first the dexpanthenol cream then replaced it by the hydroactive colloid gel after 11–14 days of radiotherapy. Radiation treatment (total dose, technique, and equipment) was the same for the two groups. The clinical outcomes were the occurrence and time to onset of moist desquamation.
Key results: The overall incidence of MD was significantly lower in patients who applied the hydroactive colloid gel (16%) than in those who applied the dexpanthenol cream (32%, odds-ratio = 0.35). Also, MD occurred significantly later with the hydroactive colloid gel than with the dexpanthenol cream (hazard ratio = 0.39).
Conclusions: Compared with the dexpanthenol cream, the hydroactive colloid gel significantly reduced the risk of developing MD in patients undergoing radiotherapy for breast cancer. These promising results warrant further research on the efficacy of hydroactive colloid gels in managing radiation dermatitis.

Introduction

Skin reaction or dermatitis is a frequent side effect of radiation therapy, affecting up to 95% of cancer patients treated with radiotherapy (McQuestion, 2011). They can occur as acute or late side effect of radiotherapy (i.e., within or beyond 90 days of treatment) with various degree of severity, depending on multiple factors that can be intrinsic (i.e., patient-related) or extrinsic (i.e., treatment-related). For instance, intrinsic factors include breast size or the sensitivity of the exposed region (e.g., large breasts and body regions containing skin folds, such as the groin, are more susceptible to skin reactions). Extrinsic factors include the total radiation dose and the dose delivered per fraction (the onset and severity of skin reactions being dose-related) or the concurrent use of other cancer therapies (see for example Porock, 2002). Typically, acute radiotherapy-induced skin reactions manifest within 2–3 weeks of radiotherapy, peak towards the end, and heal within a month after completion of therapy (Wells and MacBride, 2003). They are graded by severity on a continuum ranging from dryness or red rashes (irritation or mild erythema) and dry desquamation (itchy, peeling skin) to more severe moist desquamation (painful, sloughing skin blisters with serous exudate) and ulceration.

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http://dx.doi.org/10.1016/j.ejon.2014.04.009
1462-3889/

Managing radiotherapy-induced skin reactions, also known as radiation dermatitis or radiodermatitis, represents a major clinical challenge to radiotherapy departments. First, skin reactions are particularly distressing to patients and can seriously affect their quality of life (Munro et al., 1989). Second, as skin reactions evolve towards more severe dermatitis such as moist desquamation, they might lead to a reduction of the delivered doses or even an interruption of radiation treatment that can negatively influence treatment outcome (Feight et al., 2011). Therefore, skin care is an essential function of the radiation team. However, to date, there is no consensus among radiotherapy departments on how radiodermatitis should be prevented or treated (Salvo et al., 2010). Although several guidelines and recommendations have been published (e.g., Bolderston et al., 2006; Feight et al., 2011; Glean et al., 2001; McQuestion, 2011; Wong et al., 2013), little evidence-based protocols have been developed and many departments still apply a treatment policy based on clinical experience and anecdotal evidence, leading to a great variability in clinical practice (e.g., D'Haese et al., 2005; Harris et al., 2012).

In our institution, the standard skin care protocol for breast cancer patients undergoing radiotherapy includes the application of a topical agent on the irradiated zone throughout the course of the radiation treatment. For many years our institutional preference was an oil-in-water emulsion containing 5% dexpanthenol (Bepanthol® Cream, Bayer AG, Leverkusen, Germany). Dexpanthenol is an alcohol analogue of pantothenic acid (a provitamin known to accelerate and improve wound healing by promoting epithelial formation and regeneration) that acts like a moisturizer when used topically and reduces itching and irritation (Biro et al., 2003). Later on, another product was introduced in our institutional skin care protocol to prevent the development of moist desquamation: after 12 days of radiotherapy, at fraction 13, the dexpanthenol cream was replaced by a hydroactive colloid gel (Flamigel®, Flen Pharma NV, Kontich, Belgium). (Since this gel is delivered by the nurses, a fixed starting point was chosen to facilitate the implementation of the new practice routine; day 13 corresponding to the middle point of the period during which skin reactions generally develop.) This gel combines the moisturising and absorbing properties of hydrocolloids and hydrogels (hydrocolloids maintain optimal tissue hydration by absorbing exudates, while hydrogels restore optimal tissue hydration by donating moisture to the wound). Combining these properties enables the interaction with the wound bed to maintain an optimal moist environment, which accelerates wound healing, reduces pain, and prevents desiccation, scars, and infection (e.g., Field and Kerstein, 1994). As they can regulate the moisture of the wound bed, hydroactive colloid gels can be recommended for both dry and exuding skin wounds (Korting et al., 2011), what makes them particularly suitable for the management of radiodermatitis. Moreover, they present the additional advantage of being easy to use and to remove and do not necessarily require secondary dressing or additional taping, which reduces the discomfort, irritation, or tissue damage commonly associated with dressing changes. Finally, their cooling effect on the skin attenuates sensations of pain and burning (Ferreira Alves et al., 2009). Such advantages are not negligible because they alleviate patients' discomfort, pain and irritation – aspects that also ought to be taken into account in skin care practice (McQuestion, 2011).

Dexpanthenol has shown beneficial effects on a wide range of skin disorders (Ebner et al., 2002) but evidence regarding its efficacy in preventing or managing radiation dermatitis is lacking (e.g., Feight et al., 2011). For instance, Løkkevik et al. (1996) found no clinically important benefits of applying dexpanthenol (vs no treatment) for managing skin reactions in laryngeal and breast cancer patients. In fact, in its latest guidelines, the Skin Toxicity Study Group of the Multinational Association of Supportive Care in Cancer (MASCC) found insufficient evidence to support the efficacy of dexpanthenol and therefore recommended against its prophylactic use (Wong et al., 2013).

In the wound care literature, hydrocolloid or hydrogel dressings are commonly recommended for the management of minor acute cutaneous wounds, superficial to partial thickness burns, or chronic wounds (such as diabetic foot lesions or pressure ulcers), with beneficial effects on healing rates, infection, and pain (e.g., Chaby et al., 2007; Singh et al., 2004; Wasiak et al., 2013). The past decade, hydrocolloid and hydrogel dressings have also increasingly emerged in the radiodermatitis literature and in clinical practice (e.g., Harris et al., 2012), though their effectiveness is far from being established (for reviews see for example Kedge, 2009 or Wong et al., 2013). Yet formulations that combine moisturising and absorbing properties (as gels, not as dressings) are virtually absent in studies to date, in both the radiodermatitis and the wider wound care literature. A few case reports documented the use of a hydroactive colloid gel on recalcitrant wounds (among which a burn wound of the perineum following radiotherapy) and reported beneficial effects in terms of healing, pain relief, comfort, and ease of application (Panasiti et al., 2006; Van den Plas et al., 2009). Also, a randomized controlled trial evaluating the efficacy of a hydroactive colloid gel on burn wounds found significant benefits in terms of healing rates and pain relief (Yang et al., 2013; available in abstract form only). But to our knowledge, only one study investigated the effect of such a hydroactive colloid gel on acute radiodermatitis (Huang et al., 2005; available in abstract form only). In this randomized controlled trial, 60 patients receiving radiotherapy for head and neck cancer were assigned to either the hydroactive colloid gel or the routine clinical practice from the onset of skin reactions. The authors compared healing rates and the incidence of grade $\geq$3 skin reactions (scored according to the Radiation Therapy Oncology Group – RTOG – grading tool, grade 3 corresponding to confluent moist desquamation and grade 4, to ulceration and necrosis). They found significant differences in favour of the hydroactive colloid gel, with higher healing rates (83% vs 47% for routine clinical practice) and a lower incidence of severe skin reactions (10% vs 33% for routine clinical practice). Thus hydroactive colloid gels seem to be potentially promising for the management of acute radiation dermatitis but to date the available data is insufficient to draw firm conclusions regarding their efficacy.

The objective of this study was to compare these two topical agents in managing acute radiation dermatitis. More specifically, we retrospectively compared the effect of the dexpanthenol-containing emulsion and the hydroactive colloid gel on the incidence and time to onset of radiotherapy-induced moist desquamation in two successive cohorts of breast cancer patients.

Materials and methods

Participants

This retrospective study was approved by the local Medical Ethics Committee, as required by our institutional policies, and was thus conducted in compliance with ethical regulations.

The study population consisted of women treated in our radiotherapy department for invasive or non-invasive breast adenocarcinoma during the past four years. In an attempt to control for extrinsic risk factors and maximize homogeneity between the patients, strict inclusion and exclusion criteria were applied: Patients were considered for inclusion if they had undergone breast-sparing surgery and completed conventional radiation therapy with an irradiation fractionation regime of 25 daily fractions of 2 Grays (Gy) to the whole breast (five times a week) followed by a 16-Gy boost (in 2-Gy fractions) to the tumour bed. Adjuvant hormone