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Review

Prophylaxis and Management of Radiation-Induced Dermatitis

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Abstract

Radiation dermatitis is an acute skin reaction that occurs as a result of radiotherapy used to treat a range of different cancers. The severity of symptoms ranges from erythema to dry desquamation (dry, flaky skin with itching) to moist desquamation (serious exudate, edema, and blistering). While a variety of topical agents and dressings are used to ameliorate side effects, there is minimal evidence to support their use. This study aimed to review the evidence on radiation-induced dermatitis, its prophylaxis, and its management. Only a few studies have found that specific topical agents have a significant benefit. Film dressings are the most efficient means of preventing acute radiation dermatitis, whereas foam dressings were found to be beneficial in treating it. In a preventive situation, barrier films and silicone-based gel treatments may lower the severity of skin reactions and symptoms and entirely halt the onset of moist desquamation. Radiation dermatitis has been prevented and treated with a variety of topical and systemic medications, but there is not enough data to recommend one gel, cream, or ointment over another. However, no single therapeutic option is consistently effective.

Keywords: *radiation dermatitis, treatment, prevention, topical*

Introduction

Radiation therapy is a medical procedure that uses radioactive particles or high-energy waves to harm tumor cells and slow their growth. Radiation dermatitis or radiation burns are common adverse effects of radiation therapy (RT) to treat cancer. Most notably, in patients with head and neck cancer (HNC) or breast cancer, over 90% of patients undergoing RT will eventually develop dermatitis during or after the period of treatment. The severity of symptoms ranges from erythema to dry desquamation (dry, flaky skin with itching) to moist desquamation (serious exudate, edema, and blistering). The theories for the pathogenesis behind RT-induced dermatitis are that the effects of radiation on stem cells, cellular DNA damage from oxidative stress, and unusual medication hypersensitivity reactions all play a role (1). Normally, natural tissues have a high capacity for self-repair, but an imbalance between tissue damage and repair occurs when cells are exposed to repeated radiation. Therefore, care for this severe side effect is essential due to its high incidence and significantly detrimental influence on the quality of life.

Currently, no standard recommendation is available for the treatment of radiation dermatitis. However, the treatment methods for controlling this dermal toxicity can only be derived from clinical experience and a physician's propensity to use topical remedies. For clinicians to manage radiation oncology patients effectively, it is crucial to have a complete awareness of the current management options available. This current review study discusses various medications, types of dressings, and novel technologies that have been researched for the prophylaxis and management of radiation dermatitis, along with their mechanisms of action, and offers promising and effective treatment options for medical professionals.

Discussion

Prophylaxis of radiation-induced dermatitis

Topical steroids and non-steroid agents

Steroid topical agents are one of the prophylaxis options for radiation dermatitis, and they are emerging as a suitable alternative to non-steroid agents. Corticosteroids work to reduce inflammation by regulating leukocyte adherence to endothelial cells, reducing capillary permeability, inducing vasoconstriction, and inhibiting leukocyte proliferation and migration (2). Their clinical benefit has not yet been sufficiently established by clinical data. A pooled analysis of clinical studies could produce a more logical and conclusive finding, which in turn could guide practice (3). The topical corticosteroids in this review vary from mild to potent. Mometasone significantly reduced the occurrence of acute radiation dermatitis when compared to emollient in a randomized control trial (RCT) of individuals receiving preventive mometasone versus emollient (4). Schmuth et al. observed that patients receiving 0.1% methyprednisone had delayed and decreased both the peak severity of radiation-induced dermatitis and transepidermal water loss. They found that corticosteroid use had several advantages over dexpanthenol (5). However, Potera et al. discovered no discernible difference between topical steroid prophylaxis and control in terms of skin toxicity (6). The use of topical corticosteroids is advised by the Multinational Association of Supportive Care in Cancer (MASCC) guidelines (7) for radiation dermatitis based on the strong evidence from studies where prophylactic mometasone showed a substantial reduction in discomfort and irritation in breast cancer cases (8). Mometasone furoate (MMF) was found to reduce dermatitis symptoms in breast cancer patients in several RCTs. However, for breast cancer patients, the radiation dose prescribed is usually 50 to 60 Gy. The standard radiation dose of CRT for HNC is 70 Gy in 35 fractions (fr) for the definitive setting and 60 to 66 Gy in 30 to 33 fr for the postoperative setting. In a recent phase III clinical trial, Yokota et al. (9) provide evidence that topical steroids have the potential to lessen the serious nature of radiation dermatitis and thereby become an important therapeutic tool in managing radiation dermatitis induced by high-dose irradiation with chemotherapy in the care of head and neck cancer (HNC).

Non-steroid topical creams

In Europe, radiotherapy-induced dermatitis is prevented by using trolamine emulsion (biafine). This substance lessens dermal edema and vasodilation. Additionally, biafine enhances epithelial proliferation. However, numerous studies have been unable to demonstrate a definitive advantage in reducing radiotherapy-induced dermatitis. Trolamine has been taken into consideration due to its favorable tolerability, capability to moisturize skin, and ability to lessen local discomfort. Trolamine's effectiveness as a topical skin radioprotective agent has not been established, though (10). It was successfully used in the prophylaxis of radiation dermatitis in Abbas et al (11) 's investigation, however, the benefits were only seen in grade 3 radiation dermatitis. When compared to trolamine, certain controls demonstrated higher or comparable efficacy (12-14). In terms of

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preventing radiation dermatitis, a meta-analysis found no significant difference among trolamine and controls (15).

According to Wang et al. (16), biafine cream can successfully minimize acute skin damage caused by chemotherapy or irradiation. Though, in a recent study, mepitel film administered prophylactically dramatically reduced the rates of moist desquamation in HNC patients by 37% and the severity of acute radiation-induced skin responses by 29% when compared to biafine cream (17).

One of the more popular natural skin-soothing remedies is aloe vera. Aloe vera is said to provide pharmacological advantages such as being an anti-inflammatory, reducing swelling, moisturizing the patient's skin, penetrating tissue, having antifungal characteristics, relieving itching, being antibacterial, anesthetizing, cleansing, detoxifying, and stimulating cell growth. The efficacy of aloe vera to prevent radiation dermatitis has been investigated in clinical trials. Olsen *et al. (18)* explained that, adding aloe vera to mild soap had a beneficial effect at cumulative doses of > 2700 cGy. Haddad et al. (19) reported supporting evidence for aloe vera. From week 4 until the end of the evaluation period (4 weeks after radiotherapy), the reduction in dermatitis grade on the aloe side was statistically very significant. The biggest difference could be seen in weeks 5 and 6 of radiotherapy when the patients had received a high radiation dose. Studies have also reported a worse outcome with the use of aloe vera. In the Heggie et al. study, the aloe vera arm demonstrated a significantly greater probability of grade 2 or greater pain (P = 0.03) (20).

Hyaluronic acid

Hyaluronic acid (HA) has been used in oncology to reduce radiation dermatitis due to its accepted safety profile and effectiveness in decreasing inflammation. In a recent systematic review by Lee et al. (21), HA showed a better effect than other topical drugs and a lower incidence of desquamation events in breast cancer patients. In support of that, Cosention et al. discovered that the topical application of HA in patients with inflammatory diseases at the level of the vaginal and anal mucosa, following RT, resulted in an inventive method to help patients control the side effects (22). The new findings support the use of HA due to its effectiveness in reducing inflammation and improving tissue health and the symptoms associated with it. We can easily advocate for the clinical application of HA to inflamed tissues for all of the aforementioned reasons.

Sucralfate

Sucralfate, a non-absorbable substance, is the basic aluminum salt of sucrose octasulfate that acts directly on prostaglandin synthesis; it promotes angiogenesis and binds the epidermal growth factor to tissues. Hence, it has been widely used for several wound-healing conditions. Also, it has an anti-inflammatory effect by inhibiting gamma interferon and interleukin-2. However, there is conflicting evidence to support or refute the use of sucralfate. In a double-blind, RCT of 44 patients, Maiche et al. (23) discovered a significant benefit in erythema scores (P = 0.05) for sucralfate when compared to an equivalent base. Wells et al.'s investigation failed to prove the preventive use of sucralfate or aqueous cream to reduce acute skin toxicity compared with a no-cream group (24).

Silicone gel

The preventive effects of silicone-based products on radiation dermatitis have recently shown some encouraging results. It has been demonstrated that these compounds reduce fibrosis and inflammation. Mechanisms of action might reduce transepidermal water loss and mechanical friction. StrataXRT is a silicone-based gel that is easily applied and has no bolus effect on the skin during radiotherapy (25-27). Grade 2 and 3 skin toxicity is prevented and delayed by StrataXRT, according to Chan et al.'s (25) research. Applying StrataXRT topically results in the formation of a thin, flexible, protective coating that is waterproof and gas permeable. This setting promotes quicker skin repair and faster wound healing (26).

Barrier film and dressing products

A relatively new strategy for the treatment of radiation-induced skin responses is based on the use of skin protection products in the form of dressings, films, or solutions that build polymeric barriers on the skin's surface. The fundamental idea is that skin reactions can be avoided by maintaining the keratinized surface and shielding the basal stem-cell layer that has been impacted by radiation from friction and superficial abrasion. Early research on radiation-induced dermatitis yielded encouraging findings. However, according to recent data, this strategy has received little consideration in radiotherapy (28). Studies indicated that mepitel film can stop moist desquamation from developing, which lessens the intensity and frequency of skin reactions (29-31).

A different barrier-forming skin covering known as hydrofilm polyurethane has also shown promise in

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preventing radiation-induced skin irritation (32). Compared to the control lotion (10%), Schmeel et al. discovered that hydrofilm prevented moist desquamation. In addition, the hydrofilm group's RTOG skin reaction ratings were lower (32). These findings imply that the prophylactic application of barrier films may lessen the severity of skin responses and symptoms as well as fully halt the onset of moist desquamation. In addition to that, soft polysiloxane dressings were shown to stop acute radiation dermatitis (33).

The most effective means of preventing acute radiation dermatitis is film dressings, while foam dressings were shown to be beneficial in treating it, according to a recent systematic analysis that examined the effectiveness of various film dressing products (34).

Management of radiation-induced dermatitis

Skincare advice

To prevent rubbing or friction in the treatment region, patients are encouraged to wear loose-fitting clothing, avoid using cosmetics, be in excessive heat or cold, and get too much sun. Additionally, an electric razor or clipper should be used if shaving the treated skin is necessary. Individual patients are advised to follow these skin care measures since they are safe and might help stop additional injury.

Topical steroid agents

A wide variety of products are used for the topical treatment of radiation dermatitis once it appears, though few have been tested in clinical trials. It includes mometasone furoate cream (4, 35), methylprednisolone aceponate cream, and beclomethasone, which can significantly improve radiation dermatitis. However, there is limited evidence to support the use of one cream, gel, or ointment over another. Moreover, the use of steroidal agents is limited because they can cause thinning of the skin and introduce bacterial infections.

Systemic therapies

Amifostine (36), a thiol derivative, has shown radiation-protective effects in animal experiments. The efficacy of amifostine was examined as a cytoprotective drug against acute radiation-induced skin responses by Kouvaris et al. (37) and Dunst et al. (38). Patients who took amifostine had considerably less severe dermatitis, a lower mean gross dermatitis score, and a shorter mean treatment interruption duration, according to Kouvaris et al. (37). According to Dunst et al., (38) patients who did not receive amifostine had higher maximum grades of erythema. The requirement for permanent venous access for daily injections with that drug is a drawback.

Gujral et al (39) investigated the efficacy of oral enzymes and detected a significant benefit in favor of enzyme therapy. However, it should be taken into account that the side effects described in those trials were more severe than those reported in trials evaluating topical treatments. The side effects associated with oral enzymes also deserve further consideration in clinical practice and future research (14).

Pentoxifylline is believed to enhance microcirculation by making red blood cells more flexible. In Aygenc et al. (40) investigation, there was no discernible difference in the skin reaction score between the patient who administered pentoxifylline and the comparison group; nevertheless, a discernible difference in the skin reaction score for late skin modifications was seen in eight weeks after RT.

Supplements in an earlier animal study by Ertekin et al. (41) demonstrated that zinc supplements have the most protection for radiation dermatitis (RT+10 Zn group). Later, Lin et al. (42) proved that zinc supplementation used in association with radiotherapy could postpone the development of severe dermatitis in patients with HNC. In addition to that, they explained that zinc supplementation can also alleviate the degree of mucositis and dermatitis. Results were supported by small numbers of trials, and further research is required.

Foam dressing

RCTs and, additionally, one pilot study (43) provide favorable evidence for the foam dressing concerning other outcome measures. Based on the RISRAS (radiation-induced skin reaction assessment scale) scores, Zhong et al. (44) and Paterson et al. (45) found that radiation dermatitis severity was statistically significantly lower in the foam dressing group, favoring the use of the foam dressing for managing moist desquamation in nasopharyngeal carcinoma patients and breast cancer patients, respectively. Evidence suggests there may be some benefit to using a foam dressing for managing some signs and symptoms of RD, but this evidence is insufficient and does not show any benefit for improving healing.

Gel dressings

Findings from the clinical trial studies evaluating the management of radiation dermatitis are conflicting. Gollins et al. investigation showed that the time to healing was statistically significantly faster when using

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the hydrogel dressing (HR = 7.95, 95% CI 2.20 to 28.68, p = 0.002). This study also noted that the hydrogel was associated with a difference in mean healing time of over two weeks, which is clinically significant (46). However, this study is underpowered and used a small sample. Another small trial by Mak et al. reported no difference in healing time (47). Another large-scale study by Macmillan et al. (48) did not support the routine use of hydrogels in the care of those with moist desquamation and suggested that the healing times were prolonged without any improvement in patient comfort. Given the study's limitations and the possibility of bias, this recommendation is difficult to make.

Silver-containing dressings

A small sample RCT by Vavassis et al. (49) was observed to lower the severity of the reaction within the same grade (grade 2) of the included patient, as well as accelerate healing and provide improved pain control over silver sulfadiazine. A case review of grade 3 radiation dermatitis in an HNC patient was effectively managed by a silver-containing antimicrobial dressing that yielded remarkable results (50); The Niazi et al. study, found that reducing radiation dermatitis in cases with lower gastrointestinal malignancy with a silver-clear nylon dressing is helpful (51), is another source of supporting evidence. Even though more studies are warranted to evaluate the clinical benefit of silver-leaf-containing dressing.

Biodressings

The main purpose of biodressings is to accelerate the recovery from severe or acute radiation dermatitis. Kouvaris et al. (52) found that women receiving radiotherapy for vulvar cancer could prevent and treat acute radiation dermatitis by using a gauze dressing impregnated with granulocyte-macrophage colony-stimulating factor. Lee et al. (53) showed that a foam bandage containing epidermal growth factor significantly accelerated the healing of severe acute radiation dermatitis in HNC patients. In a study conducted in India, LoboGajiwala et al. assessed the use of lyophilized and irradiated human amniotic membrane as a biological dressing for grades 2 and 3 radiation dermatitis (54). In their study, all of the patients who received treatment showed quick healing.

Laser therapy

Based on DERMIS trial findings, laser therapy (LT) might be effective to manage acute radiation dermatitis. Epidermal grafting, along with laser therapy, has also been proven to be a successful treatment strategy. In a case study of three children who developed persistent radiation dermatitis, they were treated with LT and skin grafting, which showed satisfactory clinical outcomes (55). Following the DERMIS study, 120 breast cancer patients were enrolled in the randomized phase III TRANSDERMIS trial to confirm the efficacy of photobiomodulation (PBM) using the same procedure and a more reliable approach. Their investigation was successful, demonstrating PBM's efficacy as a supportive treatment to avert acute radiodermatitis after adjuvant radiotherapy for breast cancer (56). Recent research points to low-level laser therapy as a potential treatment for dermatitis.

Mode of radiation delivery

According to Freedman et al. (57), intensity-modulated radiation therapy (IMRT) significantly reduced moist desquamation in radiation dermatitis patients as compared to normal radiation delivery methods. Patients receiving IMRT with light-emitting-diode photo modulation experienced much less dry and moist desquamation than those receiving IMRT alone (58)

Conclusion

Many topical agents and specialized wound dressings, as well as systemic therapies, are being used for the prophylaxis and treatment of radiation dermatitis. Only a few studies have found that specific topical agents have a significant benefit. In accordance with the study's findings, film dressings are the most efficient means of prophylaxis of radiation dermatitis, although foam dressings were observed to be beneficial in treating it. In a preventive situation, barrier films and silicone-based gel treatments may lower the severity of skin reactions and symptoms and entirely halt the onset of moist desquamation. However, no single therapeutic option has been found to be consistently effective.

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Conflict of interest

There is no conflict of interest

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Data availability

Data that support the findings of this study are embedded within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

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