Support Care Cancer (2017) 25:2857–2862
DOI 10.1007/s00520-017-3701-0

ORIGINAL ARTICLE

Practice patterns for the prophylaxis and treatment of acute radiation dermatitis in the United States

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Received: 20 December 2016 / Accepted: 31 March 2017 / Published online: 14 April 2017

Abstract
Purpose Due to the inconclusive evidence for available treatment options, management of radiation dermatitis (RD) varies among practitioners. This study defines and reviews the current treatment patterns for RD in the USA, providing guidance for practicing physicians as well as directions for future research.
Methods An online survey of 21 questions was emailed to all 5626 members of the 2013 American Society for Radiation Oncology (ASTRO) directory, which included radiation oncologists, residents, fellows, physician assistants, nurse practitioners, registered nurses and other care providers. The questions were designed to evaluate demographics of responders, their training and comfort in the management RD, and their patterns of care regarding prophylaxis and treatment of RD. Data was analyzed using simple summary and descriptive statistics.
Results Out of the 5626 emails sent, we were left with 709 physician respondents for our analysis, or a response rate of 12.9%. Although 84.7% of physicians felt that RD had a moderate or large impact on patients' quality of life during cancer treatment, only 30.1% received special training or specific instructional courses in treating RD during their medical training in residency or fellowship. Eighty-nine percent of surveyed physicians rely on observational and/or anecdotal findings to guide treatment decisions, and 51.4% reported using evidence-based treatments.
Conclusion The results of our study show that there is great variability in the topical agents and dressings used in practice by radiation oncologists to prevent and treat RD. This information may be useful to other practitioners to develop their own personal recommendations and can guide further research into strategies to prevent and treat radiation dermatitis.

Keywords Radiation · Radiotherapy · Radiation dermatitis · Prophylaxis · Treatment

Introduction

In 2015, there were expected to be 1,658,370 new cancer cases diagnosed in the United States, two thirds of which were expected to undergo radiotherapy as part of their treatment [1–3]. Radiotherapy is used to cure or provide palliative effects in cancer patients [2]. As radiotherapy works by targeting rapidly dividing cells, acute toxicity often occurs in the skin or mucosal surfaces and manifests as dermatitis, xerostomia, mucositis, dysphagia, weight loss, taste alterations, and nausea and vomiting [2]. Approximately 90% of patients receiving radiotherapy will experience an adverse skin reaction [4].

Acute radiation dermatitis (RD) occurs in a dose-dependent fashion and typically manifests within a few days to weeks after commencing external beam radiation therapy. Its presentation varies in severity and can include erythema, dry or

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moist desquamation, and ulceration when severe [5]. Chronic changes can occur within several months to years and include dyspigmentation, hair loss, atrophy, fibrosis, telangiectasias, ulceration, and necrosis of underlying structures [5]. The reaction severity varies based on the entire radiation dose, dose per fraction, treatment time, depth of dose, beam and energy types and the amount of radiated skin [5]. RD can significantly impair quality of life and patient compliance, possibly leading to treatment interruption. Therefore, prevention and treatment of RD is crucial [6].

Accurate grading of RD is essential and several different grading scales have been developed. The most widely used grading system is The National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03 (Table 1); however, the CTCAE only provides grading for acute, and not chronic, skin toxicities. Other grading systems include the Radiation Therapy Oncology Group (RTOG)/the European Organization for Research and Treatment of Cancer (EORTC) which does have both acute and late grading scales and the Late Effect on Normal Tissue (LENT) the Symptom Objectives Measures, Management, Assessment (SOMA) which only grades late-effect skin toxicities [1]. While there are many different grading systems for acute radiation dermatitis, most are on a scale of 0 to 5, with increasing clinical severity.

While a growing variety of topical agents and dressings are used in practice to prevent and treat RD, there is minimal evidence to support their use. Several systematic reviews of radiation dermatitis treatments have been published, most concluding that there was insufficient evidence to support the use of any particular intervention or agent for the treatment of acute radiation-induced skin reactions [7, 8]. Similarly, the most recent and up-to-date treatment guidelines established by The Multinational Association for Supportive Care in Cancer (MASCC) also concluded that there was a lack of sufficient evidence in the literature to support the superiority for any specific intervention in the treatment of acute radiation dermatitis [9]. However, the MASCC did find evidence to support the use of gentle washing with water and mild soap, topical steroids, and silver sulfadiazine cream for prophylaxis acute radiation dermatitis, and also found evidence to support against the use of *Aloe vera*, Biafine, and silver dressings for prophylaxis of acute radiation dermatitis [9].

Due to the inconclusive evidence for available treatment options, management of RD varies among practitioners. Prior surveys in other countries such as Australia have demonstrated variation in skin care practices and that a considerable number of these practices were based only on anecdotal evidence [10]. Furthermore, it is unknown what the practice patterns for RD are currently in the USA. This study defines and reviews the current treatment patterns for RD in the USA, providing guidance for practicing physicians as well as directions for future research.

Table 1 CTCAE grading scale for radiation dermatitis, grade

1	Faint erythema or dry desquamation
2	Moderate to brisk erythema; particularly moist desquamation; mostly confined to skin folds and creases; moderate edema
3	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion
4	Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated
5	Death

Methods

Using the online survey software and questionnaire tools of surveymonkey.com, we conducted a pattern of care survey of the current management of RD from August 2014 to January 2015 across the United States. An institutional review board approved the study. The questions were designed to evaluate demographics of responders, their training and comfort in the management RD, and their patterns of care regarding prophylaxis and treatment of RD. We included in designing the survey all topical preparations that have been reported in the literature and whether or not they had supporting evidence. We also allowed for a free text response in case the responder's choice was not included in our list. This online survey of 21 questions was emailed to all 5626 members of the 2013 American Society for Radiation Oncology (ASTRO) directory, which included radiation oncologists, residents, fellows, physician assistants, nurse practitioners, registered nurses, and other care providers. In order to maximize the response rate for the survey, reminders to all non-responders were sent every 2 weeks for 4 months. Data was analyzed using simple summary and descriptive statistics.

Results

Response rate

Out of the 5626 email addresses for the 2013 ASTRO members, 121 emails were bounced back, leaving 5505 emails delivered. Seven-hundred eighty-one providers responded to our survey, which resulted in an overall response rate of 14.19%. As the ASTRO directory was comprised mainly of physicians, with a rarity of other care providers, we decided to only include practicing physicians (attendings, fellows, residents), and to not include the other tertiary care providers who may have responded. Thus, we were left with 709 physician respondents for our analysis, which resulted in a corrected response rate of 12.9%. The response rate was likely higher however we were unable to

eliminate all non-physicians from the total number of surveys sent out, as this data was not available to us.

Physician responder background

Physician respondents were well represented in various geographic locations, demographics, and practice settings. Although 84.7% of physicians felt that RD had a moderate or large impact on patients' quality of life during cancer treatment, only 30.1% received special training or specific instructional courses in treating RD during their medical training in residency or fellowship. Given the paucity of evidence regarding effective strategies for prevention and treatment of RD, it was not surprising that 89% of surveyed physicians rely on observational and/or anecdotal findings to guide treatment decisions, and 51.4% reported using evidence-based treatments. While the majority of physicians felt either very comfortable (68.8%) or moderately comfortable (29.4%) in managing patients with RD, a little over half (52.6%) of responders have had to shorten radiation therapy due to the development of RD in their patients. Table 2 summarizes the demographics, beliefs, practice patterns and management outcomes of our physician responders.

Table 2 Physician responder answers

Title	%
Attending physician	96%
Fellow	0.3%
Resident	3.7%
Time in practice	
1–5 years	19.5%
6–10 years	18.2%
11–15 years	10.8%
16–20 years	12.5%
>20 years	39%
Practice setting	
Private practice	34.1%
Academic setting	34.8%
Oncology center	23.7%
Multidisciplinary center	4.1%
Community hospital	0.1%
Locum tenens	0.1%
Veterans Affairs hospital	0.9%
Other	4.9%
Special training for RD management	
Yes	30.1%
No	69.9%
Recommendation choices	
Observational/anecdotal evidence	89%
Evidence-based research	51.4%
Comfort level in managing RD	
Very comfortable	68.8%
Moderately comfortable	29.4%
Unsure	0.7%
Moderately uncomfortable	0.1%
Very uncomfortable	1%
Belief of patient significance of RD	
Large impact	20.2%
Moderate impact	64.5%
Small impact	15.3%
No impact	0%
Had to shorten radiation because of RD	
Yes	52.6%
No	47.4%

Prophylaxis of RD

Regarding RD prophylaxis, there was a wide variety of recommendations given by the providers (Table 3). The most commonly recommended topical agent was *Aloe vera* (53.8%), followed by washing with gentle soap (50.7%), topical corticosteroids (29.5%), Biafine (27.6%), calendula (21.1%), petroleum-based ointments (17.7%), nothing (15.4%), hyaluronic acid cream (9.4%), silver sulfadiazine cream (4.2%), sucrafate derivatives (3.1%), Miaderm (2.4%), and silver leaf dressing (2.3%).

Treatment of acute RD

The majority of providers (97.3%) determine their treatment choices for acute RD based on the severity of RD present (grade 1/dry desquamation vs. grade 2–3/moist desquamation), and there were several differences between their favored treatment recommendations. For grade 1/dry RD, physicians most commonly recommended bland emollients (77.5%), followed by *Aloe vera* (46.9%), continued prophylactic therapy (36.9%), Biafine (21.6%), calendula (15.8%), Vitamin E (11.9%), silver sulfadiazine cream (5.6%), barrier cream (3.7%), topical antibiotics (3.4%), hyaluronic acid cream 2.7%), no treatment (1.8%), dressings (1.5%), honey impregnated gauze(1.1%) and soaks (1.1%) (Table 3). For grades 2–3/moist RD, physicians most commonly recommended silver sulfadiazine cream (77.2%), followed by bland emollients (34.2%), dressings (27.2%), barrier cream(17.9%), topical antibiotics (16.6%), topical corticosteroids (12.5%), Biafine (12.1%), soaks (11.8%), drying gels (8.2%), antiseptics (4.5%), Calendula (3.4%), honey impregnated gauze (3.3%), and others (Table 4).

Of note, in our survey petroleum-based ointments included products such as Vaseline and Aquaphor, while bland emollients were defined in the survey as petroleum-based ointments as well as over the counter moisturizing creams

Table 3 RD Prophylaxis used by physicians

Topical Agent	%	Recommended by the MASCC
Aloe vera	53.8%	No
Washing with gentle soap	50.7%	Yes
Topical corticosteroids	29.5%	Yes
Biafine	27.6%	No
Calendula	21.1%	Insufficient evidence
Petroleum-based ointments	17.7%	Insufficient evidence
No treatment	15.4%	
Hyaluronic acid cream	9.4%	Insufficient evidence
Silver sulfadiazine cream	4.2%	Yes
Sulcrafate derivatives	3.1%	Insufficient evidence
Miaderm	2.4%	
Silver leaf dressing	2.3%	No

and lotions. Dressings were defined as various hydrophilic and hydrocolloid dressings, and the most commonly recommended one was Mepilex foam dressing. Soaks were entered by providers into the "free text" category and included various options such as saline, salt, hydrogen peroxide and white vinegar, but Domeboro compresses (aluminum acetate astringent) was the most commonly recommended soak.

Discussion

The results of our study show that there is great variability in the topical agents and dressings used in practice by radiation oncologists to prevent and treat RD. Our study found that 89% of physicians rely on observational and/or anecdotal findings to steer their treatment options, while only 51.4% use evidence based research, highlighting the need for large well-controlled studies to guide treatment strategies. For the most recent evidence-based recommendations, we referenced the MASCC clinical practice guidelines from the Skin Toxicity Study Group. The MASCC is an international, multidisciplinary organization dedicated to cancer research and the Skin Toxicity Study Group is just one of the MASCC's many study groups assembled with the task of developing evidence-based guidelines for the prevention and treatment of acute and late radiation induced skin toxicity [9]. These established guidelines are based on the highest level of evidence and were published in 2013. When comparing the results of what the providers in our study recommended to the recommendations of the MASCC panel, several interesting findings were seen.

First, the MASCC panel strongly recommends the prophylactic use of gentle washing with water (with or without a mild cleanser), which only about half (50.7%) of our participants encouraged. The MASCC also strongly recommends the use of prophylactic steroids to reduce discomfort of burning and

Table 4 Grade 1 RD Therapies used by physicians

Topical Agent	%
Bland emollients*	77.5%
Aloe vera	46.9%
Continue prophylaxis	36.9%
Topical corticosteroids	30.1%
Biafine	21.6%
Calendula	15.8%
Vitamin E	11.9%
Silver sulfadiazine cream	5.6%
Barrier cream	3.7%
Topical antibiotics	3.4%
Hyaluronic acid cream	2.7%
No treatment	1.8%
Dressings (hydrophilic/hydrocolloid)*	1.5%
Honey impregnated gauze	1.1%
Soaks*	1.1%
Miaderm	1.0%
Lidocaine	0.6%
Sucralfate	0.1%

Table 5 Grade 2-3 RD Therapies used by physicians

Topical Agent	%
Silver sulfadiazine cream	77.2%
Bland emollients*	34.2%
Dressings (hydrophilic/hydrocolloid)*	27.2%
Barrier cream	17.9%
Topical antibiotics	16.6%
Topical corticosteroids	12.5%
Biafine	12.1%
Soaks*	11.8%
Aloe vera	11.6%
Drying gels	8.2%
Antiseptics	4.5%
Calendula	3.4%
Honey impregnated gauze	3.3%
Gentian Violet	3.3%
Silver leaf dressing	3.0%
Vitamin E	2.7%
Hyaluronic acid cream	1.6%
Lidocaine	1.1%
Chamomile	1.0%
No treatment	0.6%
Sucralfate	0.4%

*Of note, in regards to responses in our survey, petroleum-based ointments included products such as Vaseline and Aquaphor, bland emollients were defined in the survey as petroleum-based ointments as well as over the counter moisturizing creams and lotions. Dressings were defined as various hydrophilic and hydrocolloid dressings

itching, which only 29.5% of providers recommended. The panel also makes a weak recommendation supporting the prophylactic use of silver sulfadiazine cream in patients with radiotherapy to the breast to reduce RD score, which in our study only 4.2% recommended; however body location was not specified in our study.

Next, the MASCC panel strongly recommends against the use of *Aloe vera* prophylactically based on three randomized trials, which showed no significant benefit when compared to aqueous cream, mild soap or no treatment [11–13]. Despite this, *Aloe vera* was the most commonly recommended topical agent, by over half (53.8%) of our providers. The MASCC panel also makes a strong recommendation against the use of Biafine for the prophylaxis of RD given no demonstrable benefit seen, however this was recommended by over a quarter (27.6%) of our providers. Furthermore, the panel makes a weak recommendation against silver leaf dressings prophylactically given reductions seen in only one small study which had many study design flaws. Our responders also seemed to not favor this, as silver leaf dressings were the least recommended agent by only 2.3% of providers.

Finally, the MASCC panel concluded that there was insufficient evidence to support or refute several of the following topical agents for the prophylaxis of RD, however many of these products were found to be recommended by our providers. Some of these topical agents for which there was insufficient evidence included calendula cream (recommended by 21.1%), petroleum-based ointments (recommended by 17.7%), hyaluronic acid-based creams (recommended by 9.4%) and topical sucralfate (recommended by 3.1%). Of note, Miaderm cream was recommended by 2.4% of our providers for prophylaxis of RD, but because this product is a combination of calendula, hyaluronic acid and *Aloe vera*, we listed this separately as the panel had different recommendations for each agent independently.

Lastly, regarding the treatment of acute RD, whether it was grade 1/dry or grade 2–3/moist, our providers had a huge variety in the armamentarium of the agents that they recommended (Tables 3, 4 and 5). For grade 1/dry desquamation, the majority (77.5%) of our providers recommended bland emollients, with the likely intent of helping dry skin stay moist while maintaining a protective moisture barrier. For grade 2/moist RD, the majority (77.2%) or our providers recommended silver sulfadiazine cream, with the likely intent that this cream is bacteriostatic and used primarily for the treatment of second and third degree burns, which may help the open erosions seen in moist RD. However in the MASCC panel review for the treatment of acute RD, neither of these most popular agents as chosen by our responders was recommended.

Despite the lack of guidance regarding treatment of RD, we believe physicians should be routinely recommending the three prophylactic modalities for which there is compelling evidence: washing, topical steroids, and silver sulfadiazine. However, our study found that while 52.6% of physicians have to sometimes stop or decrease the dose of radiation due to the development of RD, 15.4% of providers did not recommend anything at all to help prevent RD. Better and larger studies are clearly needed to guide physicians on how to best prevent and manage radiation dermatitis to prevent these interruptions in treatment.

On the other end of the spectrum, given the cost of medication, time and hassle in applications, and the risk of developing side effects such as allergic or irritant contact dermatitis, medications that have been shown to not provide any benefit or have insufficient evidence to support their use, should obviously be avoided when possible.

Conclusion

This study is unique in that it highlights the practice patterns for the prophylaxis and treatment of RD by many radiation oncologists across the USA. While the MASCC panel has several recommendations for prophylaxis of RD, overall they did not find evidence to support any specific intervention for acute RD once it developed [9]. Therefore, our study helps to provide the recommendations from hundreds of radiation oncologists across the USA, many of whom have been practicing for over 20 years and have an abundance of personal experience in managing RD. This information may be useful to other practitioners to develop their own personal recommendations. It should also be used to guide further research into strategies to prevent and treat radiation dermatitis.

Given the cost, morbidity and mortality associated with managing RD and the problems associated with having to shorten radiation therapy should severe RD develop, better adherence to evidence-based guidelines may improve patient compliance, quality of life and cancer outcomes.

Acknowledgements The authors acknowledge Justin C. Voss and Prashoban Bremjit for gathering all the physician contact information for the survey.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no competing interests.

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