Original Article

Role of Topical *Aloe vera* Gel in the Recovery of High-grade, Radiation-induced Dermatitis

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Abstract

Introduction: Radiation-induced dermatitis (RID) is a common adverse effect of radiation therapy, in spite of skin-sparing effect of megavoltage. Approximately 90% of the patients who received radiation therapy may develop skin reaction of any grade during therapy, leading to therapy delays, diminution of patients' health state, and quality of life. It has been noticed by many authors that there are several topical agents available which may be used for the prevention of RID. In this study, we used topical *Aloe vera* gel for the treatment of high-grade radiation dermatitis. **Materials and Methods:** This prospective study was conducted on 85 patients of head and neck, breast, and cervical cancer during 2015–2016. All the patients have received external beam radiotherapy by cobalt-60, at least 46 Gy (dose completed with high-dose rate brachytherapy in cancer cervix). According to the Radiation Therapy Oncology Group skin reaction grading, patients with Grade III and Grade IV skin reaction were advised to use *A. vera* gel on irradiated area thrice daily with routine skin and nursing care. **Results:** In this study, head and neck cancer patients were 42%, breast 23%, and cervical 35%. Sixty-seven percent were female and 33% were male patients. The median age of the patients was 43.3 years (range, 25–70 years). The prescribed radiation doses were 46–70 Gy, 2 Gy per fraction, for treatment duration of 32–52 days, using a field size of 80–380 cm^2 according to the treatment site. Of 85 patients, 65 were treated with concurrent weekly chemotherapy. Grade III (65.8%) and Grade IV (34.1%) dermatitis occurred in the 5^{th} week of radiotherapy, which causes treatment delay, ranging 2–10 days, according to the severity and patient-related factors. It has been noticed that after application of *A. vera* gel, dermatitis completely recovered within 3–7 days. The recovery time was prolonged in operated versus nonoperated patients of head and neck cancer. **Conclusion:** Rapid cell division in the skin leads to RID. 35%–40% of dose is received by the skin despite skin-sparing effect of megavoltage, and it increases in parallel opposing field. Till date, no treatment is available which can prevent RID. In our observational study, it was noticed that *A. vera* gel was effective in fast recovery of high-grade RID without any adverse reaction. This single-institution study is not large enough to justify its standardized use; further studies are required to establish *A. vera* gel as a treatment measure for RID.

Keywords: *Aloe vera, external beam radiotherapy, radiation-induced dermatitis, skin care*

Introduction

Radiation-induced dermatitis (RID) is a common adverse effect of radiation therapy despite skin-sparing effect of megavoltage. Approximately 90% of the patients who received radiation treatment may develop skin reaction of any grade during therapy, leading to therapy delays, diminution of the patients' health state, and quality of life.[1,2] The severity of radiotherapy-associated toxicities varies according to multiple treatment and patient-related factors, e.g., total radiation dose, dose fractionation schedule, volume of organ or tissue irradiated, use of concurrent versus sequential chemotherapy, comorbid conditions, functioning performance status, obesity, and high body mass index.[3] Modulation of acute radiation reactions must be considered a potent strategy to improve the therapeutic ratio in an effective cancer treatment. It has been noticed by many authors that there are several topical agents available which may be used for the prevention of RID. These agents include hydrocolloid dressings, gentian violet, topical steroids, hydrogen peroxide, salt water bathing, sucralfate, biafine, aqueous cream, and *Aloe vera* gel.[3] Although several studies have shown efficacy of different measures in treating or preventing RID, no single study has been large enough to justify its standardized use. *A. vera* is known for its anti-inflammatory property since ancient time. It has been reported to have a

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protective effect against radiation damage to the skin. *A. vera* contains 75 potentially active constituents, including vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids.[4] *A. vera* is inexpensive, easily accessible, and widely used for the patients as a preventive and treatment measure. In this study, we used topical *A. vera* gel for the treatment of high-grade RID.

Pathogenesis

The pathogenesis of acute radiation effects in normal tissues from the view of cellular radiobiology can be described by a number of well-defined steps – induction, progression, and manifestation of tissue damage, followed by restoration.[5] Radiation-induced erythema begins to appear in the radiation therapy field within a few hours after irradiation due to capillary dilatation and increased capillary permeability.[6] Radiation therapy continues in fractions, swelling and proliferation of capillary endothelial cells appeared. The tunica intima and tunica media in arterioles are disrupted after 2–3 weeks of radiation therapy. Clonogenic keratinocytes, the target cells, show swelling, pyknosis of the nuclei, and cytoplasmic vacuolization. The moist desquamation phase of acute radiodermatitis begins 3–4 weeks after treatment begins and manifests as vascular dilatation and hyperemia, edema, and extravasation of erythrocytes and leukocytes. Approximately 4 weeks after treatment, small superficial blisters may form coalesce and rupture.[7,8]

Materials and Methods

This prospective study was conducted on 85 patients of head and neck, breast, and cervical cancer during 2015–2016. All the patients have received external beam radiotherapy by cobalt-60, at least 46 Gy (dose completed with high-dose rate [HDR] brachytherapy in cancer cervix). All the patients developed high-grade dermatitis in the 5th and 6th weeks of treatment. *A. vera* gel was applied on the irradiated area in all patients with Grade III and Grade IV dermatitis. Routine skin care, nursing care, and application of *A. vera* gel four times daily were taken into account. All the patients were examined, and the treatment response was evaluated biweekly by a radiation oncologist. The Radiation Therapy Oncology Group (RTOG) acute skin reaction grading system was followed to grade RID.

- Grade I: Follicular faint or dull erythema/epilation/dry desquamation, decreased sweating
- Grade II: Tender or bright erythema, patchy moist desquamation/moderate edema
- Grade III: Confluent moist desquamation other than skin folds, pitting edema
- Grade IV: Ulceration, hemorrhage, and necrosis.[9]

Results

In this study, head and neck cancer patients were 42%, breast 23%, and cervical 35%. Of 85 patients, 67% were female and 33% were male patients. The median age of the patients was 43.3 years (range, 25–70 years). All the patients were 80%–90% on the Karnofsky Performance Status Scale.

The prescribed external beam radiation doses were 46–70 Gy, 2 Gy per fraction. Head and neck cancer patients received 60–70 Gy, breast 50 Gy, and cervical 46–50 Gy plus HDR brachytherapy. The total treatment duration was 32–52 days, using a field size of 80–380 cm^2 according to the treatment site. Of 85 patients, 65 were treated with concurrent weekly chemotherapy with cisplatin, paclitaxel, or nab-paclitaxel [Table 1].

Grade III dermatitis occurred in 65.8% and Grade IV in 34.1% of patients [Table 2].

The high-grade dermatitis occurred the in 5th and 6th weeks of radiation treatment in spite of taken primary measures. The treatment delay ranged 2–10 days, according to the severity and patient-related factors [Table 3]. None of the patients had a complaint of allergic reaction or adverse effect of topical *A. vera* gel. The recovery time was prolonged in operated patients in comparison to nonoperated patients of head and neck cancer. It has been noticed that the recovery time was more in the patients with high body mass index, diabetes mellitus, and those who received concurrent chemotherapy. After application of *A. vera* gel, dermatitis completely recovered within 3–7 days [Figure 1].

Discussion

The prophylactic treatment of acute RID varies between different radiation oncology centers. Although various types of agents have been used, a standard of treatment for RID has not been addressed yet.

Richardson *et al*. reviewed five published randomized trials and noted that there is no evidence which suggests effectiveness of topical *A. vera* for the prevention and treatment of radiation dermatitis. They concluded that further methodologically rigorous, sufficiently powered research should be conducted.[3]

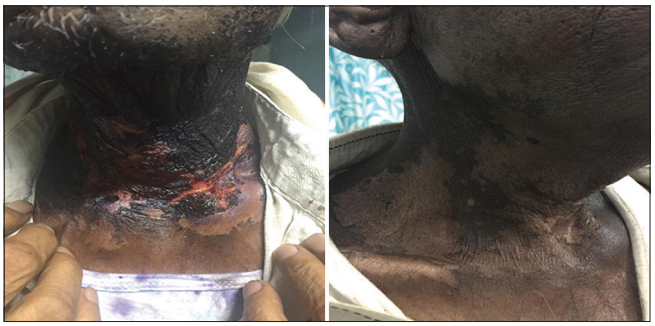

Figure 1: Patient of head and neck carcinoma before and after treatment with *Aloe vera* gel

Table 1: Patients and treatment characteristics

Characteristic	Head and neck (*n*=35) (male: 28, female: 7)	Breast (*n*=20)	Cervix (*n*=30)
Age (years)			
Median	39	45	46
Range	25-70	28-65	35-70
Rural	14	12	17
Urban	21	8	13
TNM stage	III-IV	II-III	Ib2-IIIb
Irradiated field size (cm^2)	80-224	342-380	196-255
Treatment dose (Gy)	60-70	50	46-60
Treatment duration (days)	45-52	35-40	32-45
Concurrent chemotherapy (weekly)	Cisplatin, paclitaxel	None	Cisplatin, paclitaxel, or nab-paclitaxel

Table 2: Radiation-induced dermatitis

Patients	Grade III	Grade IV
Head and neck (*n*=35)	23	12
Breast (*n*=20)	14	6
Cervix (*n*=30)	19	11

A study by Maddocks-Jennings *et al.* suggested that using a hydrophilic substance such as *A. vera* gel or vegetable oil that is high in essential fatty acids is as effective as mild steroid cream such as 1% hydrocortisone in reducing the severity of reactions; in addition, with plant-based treatments, there is no side effects that may occur with steroids.[1] This study supported our data that there was no side effect with topical *A. vera* gel.

In a randomized controlled trial by Olsen *et al*., 73 radiotherapy patients were compared for the use of *A. vera*. Patients were instructed to apply *A. vera* gel to the irradiated area at various interval throughout the day. The results did not demonstrate a major difference at low dosages, i.e., <2700 cGy; however, at higher cumulative dose, the RID was less at *A. vera* side.[10]

Heggie *et al*. studied 225 patients with breast cancer undergoing radiotherapy and randomized to either topical *A. vera* gel or topical aqueous cream group to be applied 3 times per day throughout the treatment. In this study, they found that *A. vera* gel did not significantly reduce radiation-induced skin side effects in comparison to aqueous cream.[11]

A Phase III trial comparing an anionic phospholipid (APP)-based cream and *A. vera*-based gel in the prevention of radiation dermatitis in 45 pediatric patients treated with fractionated external beam radiotherapy. They used both the agents side by side in the same patient with daily skin care. The investigator concluded that APP-based cream is more effective than *A. vera*-based gel for the prevention and treatment of radiation dermatitis due to unique mechanism of action of APP cream, i.e., repair of lamellar system of skin.[12]

In a two-arm Phase III randomized double-blind study by Williams *et al*., 194 patients of breast or chest wall used placebo gel in the first arm and 108 patients used *A. vera* gel on half versus no treatment on other half of the irradiated area in the second arm. They noticed that the scores of skin dermatitis were virtually identical in both treatment arms during both of the trials. The only toxicity from *A. vera* gel was rare contact dermatitis in some patients. They concluded that *A. vera* gel does not protect against RID.[13]

In a self-controlled clinical trial by Haddad *et al*., they found that there was no major difference between the aloe treated and untreated halves of the radiotherapy fields in weeks 1–3 of radiation; however, from week 4 until 1 month after treatment, the reduction in dermatitis grade on the aloe side was statistically very significant. They concluded that the effect was more evident in patients undergoing radiotherapy with larger treatment fields and higher doses of radiation. This study recommended that prophylactic use of *A. vera* reduces the intensity of RID.[14]

Conclusion

Rapid cell division in the skin leads to RID. 35%–40% of dose is received by the skin despite skin-sparing effect of megavoltage, and it increases in parallel opposing field. The prevention and treatment of RID is needed by all the patients; however, till date, no treatment is available which can prevent RID. In our observational study, it was noticed that *A. vera* gel was effective in fast recovery of high-grade RID without any adverse reaction. To better understand the effect of *A. vera*, the study might be designed with patients of the same disease, radiotherapy treatment site, dose, and concurrent chemotherapy regimen. This single-institution study is not large enough to justify its standardized use, and further studies are required to establish *A. vera* gel as a treatment measure for RID.

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Table 3: Time of dermatitis occurrence, treatment delay, and recovery

	Grade	Occurrence (day of T/t)	Treatment delay (days)	Days in recovery with *Aloe vera*
Head and neck	III, IV	28-40	3-10	3-5
Breast	III, IV	30-35	2-5	5-7
Cervix	III, IV	25-40	5-10	4-7

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Conflicts of interest

There are no conflicts of interest.

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