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SHORT COMMUNICATION

Aloe vera for prevention of radiation-induced dermatitis: a self-controlled clinical trial

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ABSTRACT

To evaluate an *Aloe vera* lotion for prevention of radiation-induced dermatitis, all patients with a prescription of radiotherapy to a minimum dose of 40 Gy were eligible provided that their treatment area could be divided into two symmetrical halves. Patients were given a lotion of *Aloe vera* to use on one half of the irradiated area, with no medication to be used on the other half. The grade of dermatitis in each half was recorded weekly until 4 weeks after the end of radiotherapy.

The trial enrolled 60 patients (mean age: 52 years; 67% women). Most patients had breast cancer (38%), followed by pelvic (32%), head-and-neck (22%), and other cancers (8%). Field size was 80–320 cm^2 (mean: 177 cm^2), and the dose of radiotherapy was 40–70 Gy (mean: 54 Gy). Concurrent chemotherapy was administered in 20 patients. From week 4 to week 6 of radiotherapy and then at weeks 2 and 4 after radiotherapy, the mean grade of dermatitis with and without *Aloe vera* was 0.81 and 1.10 ($p < 0.001$), 0.96 and 1.28 ($p < 0.001$), 1.00 and 1.57 ($p = 0.006$), 0.59 and 0.79 ($p = 0.003$), and 0.05 and 0.21 ($p = 0.002$) respectively. Age and radiation field size had a significant effect on the grade of dermatitis. Based on these results, we conclude that the prophylactic use of *Aloe vera* reduces the intensity of radiation-induced dermatitis.

KEY WORDS

Aloe vera, radiation-induced dermatitis, radiotherapy, prevention

1. INTRODUCTION

Radiation is a powerful tool for controlling cancer; about two thirds of patients diagnosed with cancer are treated with radiotherapy. But despite new improvements in irradiation techniques, most patients still experience side effects from treatment. Acute dermatitis is a common side effect of radiation therapy, occurring in about 95% of patients treated with this modality[1]. Radiation skin reactions are easily noticeable and vary from slight erythema to ulcer and necrosis[2]. The severity of the reaction depends on the radiation dose and field size, the quality and distribution of radiation, the use of concurrent chemotherapy, and specific individual factors[3].

The radiation oncology literature contains no consensus or universal standard of care for the prevention or treatment of radiotherapy skin toxicities, and physicians intervene basically using their own clinical experiences. A review by the Supportive Care Guidelines Group of Cancer Care Ontario concluded that the evidence is insufficient to support or refute specific topical agents such as corticosteroids, sucralfate cream, ascorbic acid, and *Aloe vera,* among others, for the prevention or management of radiotherapy acute skin reactions[4]. The most used medication in this setting would perhaps be topical corticosteroids, but other agents, too, have been claimed to be better for the purpose, including in a report from our own department, which concluded that *Calendula* 0.1% ointment is as effective as betamethasone in reducing acute radiation dermatitis, with fewer side effects[5]. Therefore, at this time, there is no general understanding about this issue among radiation oncologists.

Aloe vera is an anti-inflammatory herbal remedy with a longstanding history. It has been reported to have a protective effect against radiation damage to the skin. *Aloe vera* contains 75 potentially active constituents, including vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids[6]. *Aloe vera* has been widely used for the treatment of radiation dermatitis; a 1995 study in Radiation Therapy Oncology Group institutes indicated that half routinely used aloe gel as a prophylactic treatment[7]. But despite this long record in the management of radiation dermatitis, *Aloe vera* is not a common feature of current standard practice guidelines[3,4].

Evaluation of *Aloe vera* in a randomized trial against the best current practice or a placebo would have inherent ambiguities, because the best current practice is not known or generally agreed on, and because even a placebo might have a significant effect on radiation skin reactions through its moisturizing or other properties. Considering those factors and the uncertainties about the use of aloe for the prevention of radiation dermatitis, we decided to examine the issue in a self-controlled clinical trial.

2. METHODS

All adult patients diagnosed with head-and-neck, breast, and pelvic cancers referred to our radiation oncology department were eligible for the study provided that they were prescribed a dose of at least 40 Gy and that their anatomic radiation treatment area could be easily divided into two symmetrical halves with no difference in the radiation dose prescribed to each half. Exclusion criteria were a previous history of radiation, the presence of skin diseases in the radiation area, and underlying diseases such as diabetes leading to increased susceptibility of patients to skin problems.

For the intervention, a commercially-available lotion containing aloe for radiation treatment was provided to patients, who were asked to use the lotion on only one half of the body in the radiation therapy field twice daily from the beginning of treatment until 2 weeks after the end of radiotherapy, with no medication to be used on the other half. The lotion provided to the patients included *Aloe vera* in addition to lanolin oil, glyceryl stearate, diluted collagen, tocopherol, allantoin, and paraben. In the case of symptomatic dermatitis, treatments routine in our department (topical corticosteroids) were prescribed to the patients to use on the entire treatment area.

For evaluation of dermatitis, weekly examinations from the start of radiotherapy until 2 weeks after its end were conducted by the trial investigators. In each assessment, the amount of lotion used was checked, and the lotion necessary for the following week was given to the patient. Grading of dermatitis was performed according to the Radiation Therapy Oncology Group acute radiation morbidity scoring criteria (available at http://www.rtog.org/ResearchAssociates/AdverseEventReporting/AcuteRadiationMorbidityScoringCriteria.aspx).

The study received approval from our university's research ethics committee, and written informed consent was obtained from all patients.

3. RESULTS

The trial enrolled 60 patients, of whom 67% were women. Mean age of the participants was 52 years (range: 21–78 years). Most patients had breast cancer (38%), followed by pelvic (32%), head-and-neck (22%), and other cancers (8%).

The prescribed radiation doses were in the range 40–70 Gy (mean: 54 Gy), given as 1.8 Gy or 2 Gy per fraction, for a treatment duration of 26–49 days (mean: 38 days), using a field size of 80–320 cm^2 (mean: 177 cm^2). Of the 60 patients, 20 were treated with concurrent chemotherapy, which included 5-fluorouracil, capecitabine, or cisplatin according to routine chemoradiation protocols appropriate for the disease.

The maximum grade of dermatitis on both halves of the radiotherapy area was 3. At the 5th week of radiotherapy in the 53 patients evaluated, dermatitis on the aloe side was evaluated as grade 1 in 42, grade 2 in 3, and grade 3 in 1, and on the opposite side, grade 1 in 32, grade 2 in 17, and grade 3 in 1.

During the weekly dermatitis evaluation, no significant difference between the halves of the irradiated area was observed in the trial patients until the end of the 3rd week of radiotherapy; however, from that point on, the mean grade of dermatitis was lower on the aloe-treated half, with a statistically significant difference for weeks 4 ($p < 0.000$), 5 ($p < 0.000$), and 6 ($p = 0.006$) of radiotherapy, and weeks 2 ($p = 0.003$) and 4 ($p = 0.002$) afterward. Only 1 patient was evaluated in week 7 of radiotherapy (grade 2 dermatitis was observed on both sides). Table I and Figure 1 provide full details.

In week 5 of radiotherapy, 92% and 82% of the 53 evaluable patients had at least grade 1 dermatitis on the untreated and aloe-treated side respectively.

TABLE I Grade of dermatitis during the weeks of radiotherapy and the month afterward on the untreated and aloe-treated sides of the radiation area

Time point	*Aloe applied*	*Mean grade*	*Patients (*n*)*	p *Value*
Dermatitis during radiotherapy				
Week 2	No	0.07	60	
	Yes	0.05	60	0.321
Week 3	No	0.53	59	
	Yes	0.46	59	0.103
Week 4	No	1.10	59	
	Yes	0.81	59	0.000
Week 5	No	1.28	53	
	Yes	0.96	53	0.000
Week6	No	1.57	14	
	Yes	1.00	14	0.006
Week 7	No	2.00	1	
	Yes	2.00	1	—
Dermatitis post-radiotherapy				
Week 2	No	0.79	39	
	Yes	0.59	39	0.003
Week 4	No	0.21	57	
	Yes	0.05	57	0.002

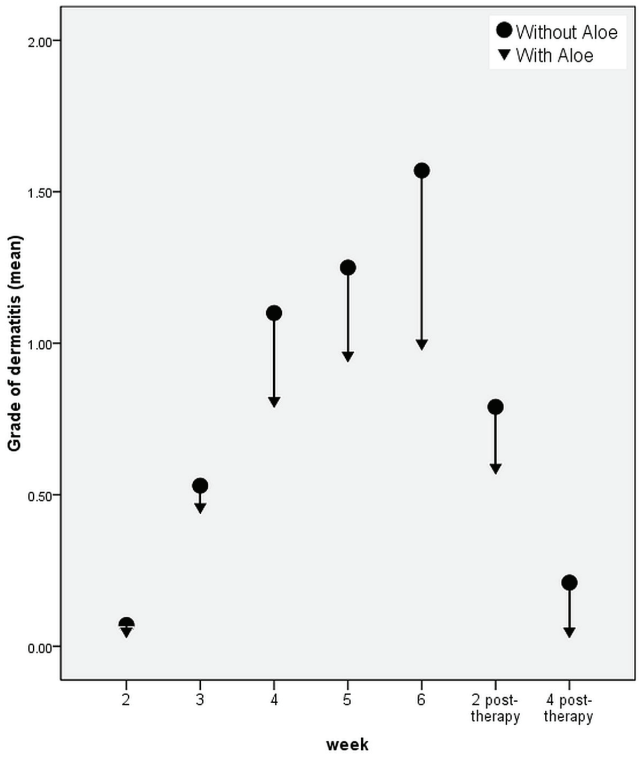

FIGURE 1 Mean grade of dermatitis, weeks 2–6 of radiotherapy and weeks 2 and 4 after radiotherapy, with and without Aloe vera.

At the 5th week, age was significant for grade of dermatitis ($p = 0.01$ aloe side and $p = 0.02$ untreated side). The only other factor with a statistically significant effect on grade of dermatitis in week 5 of treatment was field size ($p = 0.001$ for the untreated side and $p = 0.04$ for the aloe side). Concurrent chemotherapy was also significant in the 5th week for the untreated side ($p < 0.000$), but not for the aloe side ($p = 0.135$). We did not observe a significant effect for other patient and treatment factors.

No complications were caused by *Aloe vera* in the trial.

4. DISCUSSION

A number of trials and studies have been conducted for the use of *Aloe vera* in prevention or treatment of radiation dermatitis, with conflicting results. In a trial by Olsen *et al.*[8], 73 radiotherapy patients were compared for the use of aloe. The results did not demonstrate a major difference at low dosages (<27 Gy). However, in the group using aloe, the appearance of radiation-induced dermatitis was less at higher radiation doses, indicating a protective effect of aloe. In contrast, Heggie *et al.*[9] studied 225 patients with breast cancer undergoing radiotherapy and randomized to either aloe gel or aqueous cream. Those authors concluded that aloe did not significantly reduce radiation side effects on skin. Williams *et al.*[10], too, found that aloe gel did not protect against radiation dermatitis with the radiotherapy dose and schedule used in their report of two randomized trials.

Our results accord with findings of Olsen *et al.* We found that there was no major difference between the aloe-treated and the untreated halves of the radiotherapy fields in weeks 1–3 of radiation; however, 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.

Richardson *et al.*[3] reviewed the use of aloe for the prevention of radiation dermatitis. They found five published randomized trials (including the ones already discussed). In their review of the trials, they noted many methodology problems, such as difficulties in ensuring adequate blinding. Considering those factors, they concluded that, based on current research, there is no evidence to suggest that aloe gel is effective for the prevention or treatment of radiation skin reactions. We agree that the methodologic difficulties might have affected the ability to interpret results. Also as mentioned earlier, the use of a placebo in this setting might have a moisturizing or other effect on radiation dermatitis. Thus, we think that our method of testing aloe in a self-controlled clinical trial may have helped to overcome some of the methodology problems. Of course, we cannot rule out the effect of investigator bias in judging the skin reaction, because we did not use any form of blinding.

5. CONCLUSIONS

The findings in our trial demonstrate a protective effect of *Aloe vera* lotion against radiation-induced dermatitis. The effect was more evident in patients undergoing radiotherapy with larger treatment fields and higher doses of radiation.

6. ACKNOWLEDGMENTS

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7. CONFLICT OF INTEREST DISCLOSURES

The authors have no financial conflicts of interest to disclose.

8. REFERENCES

1. Ryan JL. Ionizing radiation: the good, the bad, and the ugly. *J Invest Dermatol* 2012;132:985–93.
2. Hymes SR, Strom EA, Fife C. Radiation dermatitis: clinical presentation, pathophysiology, and treatment 2006. *J Am Acad Dermatol* 2006;54:28–46.
3. Richardson J, Smith JE, McIntyre M, Thomas R, Pilkington K. *Aloe vera* for preventing radiation-induced skin reactions: a systematic literature review. *Clin Oncol (R Coll Radiol)* 2005;17:478–84.
4. Bolderston A, Lloyd NS, Wong RK, Holden L, Robb–Blenderman L on behalf of the Supportive Care Guidelines Group of Cancer Care Ontario's Program in Evidence-Based Care. The prevention and management of acute skin reactions related to radiation therapy: a systematic review and practice guideline. *Support Care Cancer* 2006;14:802–17.
5. Fotouhi M, Samee F, Amoozegar Hashemi F, Haddad P, Meysami AP. Topical *Calendula* and betamethasone valerate in prevention of acute radiation dermatitis: a randomized prospective trial [Persian]. *Tehran Univ Med J* 2007;65:23–9.
6. Surjushe A, Vasani R, Saple DG. *Aloe vera*: a short review. *Indian J Dermatol* 2008;53:163–6.
7. Fisher J, Scott C, Stevens R, *et al.* Randomized phase III study comparing best supportive care to Biafine as a prophylactic agent for radiation-induced skin toxicity for women undergoing breast irradiation: Radiation Therapy Oncology Group (RTOG) 97-13. *Int J Radiat Oncol Biol Phys* 2000;48:1307–10.
8. Olsen DL, Raub W Jr, Bradley C, *et al.* The effect of *Aloe vera* gel/mild soap versus mild soap alone in preventing skin reactions in patients undergoing radiation therapy. *Oncol Nurs Forum* 2001;28:543–7.
9. Heggie S, Bryant GP, Tripcony L, *et al.* A phase III study on the efficacy of topical *Aloe vera* gel on irradiated breast tissue. *Cancer Nurs* 2002;25:442–51.
10. Williams MS, Burk M, Loprinzi CL, *et al.* Phase III double-blind evaluation of an *Aloe vera* gel as a prophylactic agent for radiation-induced skin toxicity. *Int J Radiat Oncol Biol Phys* 1996;36:345–9.

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