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Original Article

The Effect of *Avena sativa* L. Cream on Acute Radiation Dermatitis in Breast Cancer Patients

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Abstract

Based on estimates, the skin reactions caused by radiation therapy in women with breast cancer range from 87 to 96%. Since the purpose of complementary and alternative medicine in nursing care is to alleviate suffering and increase patient comfort, the researchers decided to evaluate the medicinal properties of *Avena sativa* L. and the effectiveness of *Avena sativa* L. cream on skin problems caused by radiation therapy in women with breast cancer. In this clinical trial, 66 patients with breast cancer were divided into two groups: the intervention and the control group. From the beginning to the end of the radiation therapy, the Intervention group was treated with creams containing extracts of *Avena sativa* L. applied locally and three times a day, and the control group used cream lacking *Avena sativa* L. extract. The degree of skin problems, erythema, and dry and moist desquamation in the special intervals in both groups were evaluated. The study results revealed no significant difference in the degree of radio dermatitis in both groups. However, clinically, the incidence of dry desquamation in the intervention group is lower than in the control group but statistically insignificant. There was no significant difference between the two groups with moist desquamation and mild and bright erythema incidence. Conclusion: The results showed that local products made with *Avena sativa* L. extract can be used in radiation-induced skin reactions such as dry desquamation, and it is very effective. Therefore, further studies with larger sample sizes are recommended to prove this.

Keywords: *Avena sativa L.*; Breast cancer; Desquamation; Erythema; Radiation therapy; Skin problems.

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1. Introduction

Radiation therapy is often referred to as an adjunctive therapy to surgery, chemotherapy, or both in patients with breast cancer. Radiation-induced skin adverse events that occur in many

patients with breast cancer are an inevitable reaction. Radiotherapy can affect healthy cells, including skin cells to affected. Also, concurrently using chemotherapy and radiation therapy shows that skin reactions are still a serious problem for patients. Therefore, the skin in the area of radiotherapy should be monitored during treatment [1]. According to studies, more than 95% of patients suffer moderate to severe skin reactions caused by radiation therapy [2]. Acute radiation dermatitis(ARD) typically begins within 1–4 weeks following the initiation of breast RT and persists throughout treatment [3].

Several strategies have been proposed to treat or prevent acute dermatitis during radiotherapy. General strategies for all patients include public hygiene and gently washing with soap and water in the burn position. The treatments that can be used are herbal medicines such as Aloe vera, corticosteroids, medications containing Dexpanthenol, drugs containing Trolamine (Biafine), powders containing hyaluronic acid, dressing containing growth factors, sucralfate and ointments containing honey. So far, no standard method for it has been defined, and there is no consensus among doctors in most medical centers; radiation oncologists choose therapeutically based on their experience. There are also no controlled clinical trials in this case [4].

Increased longevity in chronic diseases results from efforts to improve the quality of life, leading to increased use of CAM therapies, particularly in the United States. Studies on using complementary and alternative medicine in different populations have shown that this treatment (CAM) in chronic diseases, including cancer patients, is more effective than in other diseases [5].

The most active part of complementary and alternative medicine is using medicinal plants as herbal medicine [6]. One of these medicinal herbs, *Avena sativa* L. plant with the scientific name *Avena sativa* L., has many therapeutic properties. It is effective in wound healing, antiseptic, and healing skin problems such as eczema and relieving pain. Oat extracts generally contain protein, fat, minerals, and soluble fiber beta-glucan [7].

Although research into the effect of oat extracts on wound healing and skin problems such as psoriasis has been performed, few studies on the impact of the plant on skin problems caused by radiation therapy have been conducted. According to the numerous problems caused by the side effects of radiation therapy to cancer patients and given the role of oncology nurses in reducing pain, preventing health problems and side effects of disease, and ultimately improving patient health since an aspect of the integrated nature of the nursing profession is known, this study aimed to determine the effectiveness of a cream containing *Avena sativa* L. extracts on the incidence of erythema as well as dry and moist desquamation, due to radiotherapy in breast cancer patients.

2. Materials and Methods

2.1. Study Setting and Participants

This study is a randomized controlled clinical trial conducted in the Yazd radiation center, Shahid Ramezanzadeh. In this study, sixty-six

patients with breast cancer undergoing radiation therapy were divided into the control and intervention groups (*Avena sativa* L. cream treatment groups) after obtaining their consent.

Patients randomly and through closed envelopes (envelopes were sealed) were divided into Groups A (intervention group) and B (control group). The inclusion criteria were the definitive diagnosis of breast cancer, women over 18 years, treated with the same dose of radiotherapy (50-60 Gy, 1.8 to 2 Gy per day, from Saturday to Wednesday for one and a half months). Patients with hypersensitivity to botanicals and those with problems of uncontrolled diabetes and connective tissue were excluded from the study. Patients with dermatitis during radiotherapy of patients with grades 3 or 4 were also excluded from the study.

2.2. Preparation of Avena sativa L. Extract

The directions for preparing *Avena sativa* L. cream are as follows: First, get *Avena sativa* L. from the medical plant market in Tehran. Then, to prepare the oat extract, 100 grams of oat should be powdered, and 1000 ml of distilled water should be added. After that, the intended container was located on the fire in the laboratory. The material should boil for 10 minutes and be filtered. Next, the extract should get on ben-mary to be condensed. Finally, according to the pilot study, the cream that contained 4% oat extract was considered the benchmark (criteria).

2.3. Intervention

After preparing the cream, from the beginning of radiotherapy, the patients in the intervention group were required to rub it softly on the intended place three times a day_ at 8-hour intervals. One figure unit (FTU) of the cream needed to be rubbed on the place under radiotherapy treatment (of course, it is worth mentioning that the amount of cream to be used depends on the patient's Body Mass Index (BMI) and extent of the lesion), and the patients were advised to avoid washing the cream place for about three hours. Moreover, the control group was given the cream lacking *Avena sativa* L. extract.

In cases where symptoms of radiodermatitis in both groups (grade 3 or 4), the physician ordered routine treatment (use of corticosteroids) was started for patients. Also, it was emphasized that avoid using other ointments and wearing tight clothing during treatment. Patients were permitted to wash with soap and water gently.

2.4. Data Gathering

Demographic information related to the patient's general characteristics, pre- or post-menopausal status, patient's age, left and right breast, tumor location, involvement of lymph nodes, type of surgery, number of chemotherapy courses before starting radiotherapy, chemotherapy regimen, total dose of radiotherapy It was collected through a researcher-made questionnaire. Also, the condition of the patient's skin, such as erythema, dry desquamation, and the degree of radiodermatitis, at intervals of 10 days after the start of treatment (start of major erythema reaction), 18 days after the start of treatment (average period between the first ten days and the first 28 days), 28 The day after the start of treatment (beginning of dry scaling) and on the

last day of radiotherapy was collected through a questionnaire. The grade of acute radiodermatitis (ARD) was determined using the standard RTOG (**Table 1**) [8, 3]. Finally, itching, burning, and changes in daily activities were also studied by a skin self-assessment questionnaire in the mentioned time intervals. It should be noted that the patients were followed up for two weeks after the completion of radiotherapy.

Table 1: Radiation therapy oncology group acute radiation scoring criteria – skin.

0	No change over baseline
1	Dry desquamations, decreased sweating, mild erythema
2	Tender or bright erythema, patchy moist desquamation, moderate edema
3	moist desquamation other than skin folds, pitting edema
4	Ulceration, hemorrhage, necrosis

2.5. Data Analysis

The quantitative and qualitative variables were reported as each mean (SD)/median (IQR) and frequency (%), respectively. The distributed quantitative variables were compared between groups by using the Mann–Whitney U test. Moreover, repeated measurement was used to compare changes of variables in groups over time. Data were analyzed using a statistical package for social science (SPSS) software version 23.0, and P-values < 0.05 were considered statistically significant.

2.6. Ethics Considerations

The Tehran University of Medical Sciences Ethics Committee approved and recorded the study protocol with the IRCT201311015987 NB code. Informed consent was obtained from participants in the study.

3. Results and Discussion

In this study, Sixty-six (66) cases of breast cancer who were referred to a radiotherapy center were screened and received each topical cream containing extracts of *Avena sativa* L. (N=33) or placebo (N=33). Overall, 69.7% of patients were treated with 40-50 GY total doses; from this aspect, there was no significant difference between the two groups. The average duration of therapy was 40 days in both groups. Forty-six (46) patients had lymph node involvement, and 36 had mastectomy. Demographic and baseline clinical characteristics of enrolled Patients are given in **Table 2**.

3.1. Outcomes

The findings of the Chi-square statistical test showed that in the first ten days of treatment, there was no bright erythema in all the patients in the intervention and control groups. Mild erythema was observed in only two patients in the intervention group and one in the control group. These findings did not show any significant differences ($p>0.05$).

Brightness erythema was not observed in any of the patients in both groups 18 days after the treatment, but there was mild erythema in both groups in equal amounts [9]. This difference also was not significant ($p>0.5$). Brightness erythema started in the fourth week of treatment (28 days after treatment) in the two groups, and the rates were 18/2% (n=6) and 12/1% (four patients).

Table 2: Patient demographic profile and baseline disease characteristics.

Groups / variables		intervention Number (percentage)	control Number (percentage)	p-value	Type of test
menopausal status	Before menopause	17(5/51)	12(4/36)	4/0	Fisher's Exact Test
	Post menopause	13(4/39)	16(5/48)		
	hysterectomy	3(1/9)	5(2/15)		
Total		33(100)	33(100)		
Lymph node involvement	Yes	24(2/72)	22(9/36)	7/0	Fisher's Exact Test
	No	9(3/27)	11(3/33)		
Total		33(100)	33(100)		
Breast	Left	20(6/60)	17(5/51)	6/0	Fisher's Exact Test
	Right	13(4/39)	16(5/48)		
Total		33(100)	33(100)		
Number of chemotherapy sessions	6session	4(1/12)	13(4/39)	02/0*	Fisher's Exact Test
	8"	26(8/78)	19(6/57)		
	12"	0	1(0/3)		
	16"	2(1/6)	0		
Total		32(9/96)	33(100)		
Age	Age >30	6(2/18)	5(2/15)	6/0	Chi-Square
	30-40	10(3/30)	7(2/21)		
	40-50	11(3/33)	11(3/33)		
	Age <50	6(2/18)	10(3/30)		
Total		33(100)	33(100)		

*Significant

The mild erythema in both groups was almost double; statistically, there was no significant difference (p=0.7).

On the last day of radiotherapy, all patients in both groups had suffered erythema, which is 15/2% (n=5). Patients in both groups were observed to have mild erythema. Brightness erythema was seen in 84/8% (n=28) of patients who were treated with creams containing extracts of *Avena sativa* L. and patients who used cream base without extracts of *Avena sativa* L., that there was no statistically significant difference between the two groups (p>0.05) (**Table 3**).

Findings also show that there was no moist and dry desquamation in any of the two groups in the first ten days of treatment. Dry desquamation started in the third week of treatment (18 days' post-treatment) in both intervention and control groups with rates of 9/1% (n=3) and 3% (one person), and there was no significant difference between the two groups (p=0.06).

Table 3: The comparison results between the intervention and control groups regarding erythema severity.

	Type of erythema	**intervention group**	**control group**	**p-value**
The severity of erythema ten days after the prescription (Week 2ed)	No erythema/Number/percentage	31 9/93	32 97%	**p>0/05**
	Mild erythema / Number/percentage	2 1/6	1 3%	
	Brightness erythema/Number/percentage	0	0	
	Number/percentage	33 100	33 100	
The severity of erythema 18 days after the prescription (week 3rd)	No erythema/Number/percentage	25 5/78	25 5/78	**p>0/05**
	Mild erythema / Number/percentage	8 2/24	8 2/24	
	Brightness erythema/Number/percentage	0	0	
	Number/percentage	33 100	33 100	
The severity of erythema 28 days after the prescription (week 4th)	No erythema/Number/percentage	11 3/33	10 3/30	**P=0/7 Chi-Square**
	Mild erythema / Number/percentage	16 5/48	19 6/57	
	Brightness erythema/Number/percentage	6 2/18	4 1/12	
	Number/percentage	33 100	33 100	
The severity of erythema 32 days after the prescription (week 5th)	No erythema/Number/percentage	3 1/9	3 1/9	**P=0.5 Chi-Square**
	Mild erythema / Number/percentage	17 5/51	13 4/39	
	Brightness erythema/Number/percentage	13 4/39	17 5/51	
	Number/percentage	33 100	33 100	
The severity of erythema on the last day of the treatment (last week)	No erythema/Number/percentage	0	0	**p>0.05**
	Mild erythema / Number/percentage	5 2/15	5 2/15	
	Brightness erythema/ Number / %	28 8/84	28 8/84	
	Number / %	33 100	33 100	

Incidence of moist desquamation started in the fourth week of treatment (28 days after treatment) in both groups, which is 6.1% (two patients) of patients in the intervention group and 3% (n=1) of patients in the control group. There was no statistically significant difference between the two groups (p>0.05). However, the rate of desquamation in the fifth week of treatment demonstrated a significant difference between the two groups (p= 0.02).

Accordingly, the dry desquamation in the control group and the moist desquamation in the intervention group were more. In other words, the rate of dry desquamation in the intervention group was 3% (one person). However, in the control group, it was 2.21% (n= 7), and the moist desquamation in the intervention group was 21/2% (7 patients), and in the control group, it was 6/1% (two people) (**Table 4**).

Data analysis using the Mann-Whitney statistical test showed a significant difference in the reduction of itching and burning in the intervention group ($p<0.05$) (**Figures 1** and **2**).

The t-test results showed that contextual variables such as age, breast surgery, and the number of chemotherapy have no effect on the dermatitis grade in both groups of patients, and this difference was not statistically significant ($p<0.05$).

In addition, it was shown that the total dose of radiotherapy during treatment and contextual variables have no effect on the type and severity of radiation-induced dermatitis in both groups of patients, and this difference is not statistically significant ($p<0.05$).

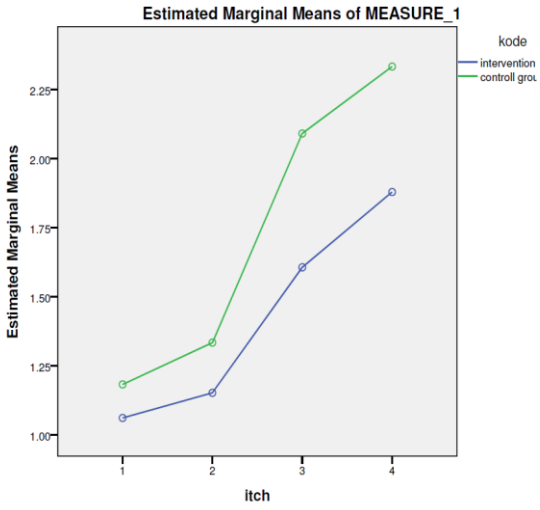

Figure 1. Comparison of the intervention and control groups in terms of itching variable.

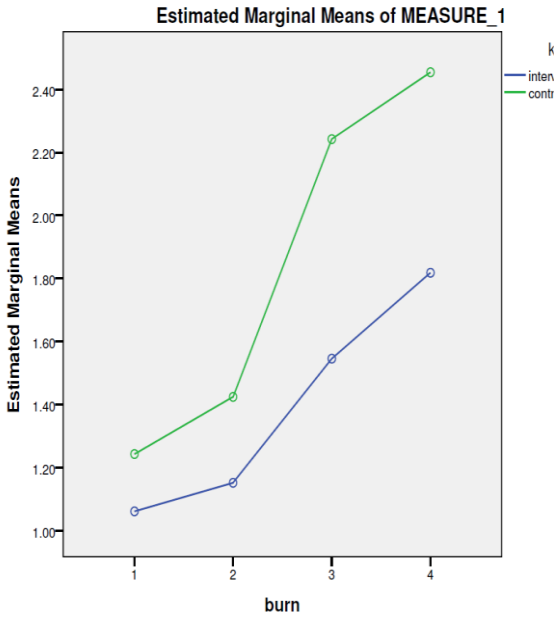

Figure 2. Comparison of the intervention and control groups in terms of burning variable.

Radiation dermatitis is one of the most bothersome side effects of adjuvant radiation therapy for breast cancer [10]. Here, we show the efficacy and safety of *Avena sativa* L. topical Cream after receiving RT to prevent radiotherapy induced dermatitis (RID).

The results of the present study demonstrated that *Avena sativa* L. Cream can significantly delay and decrease the incidence of ARD and its severity in breast cancer patients receiving RT compared with those receiving the placebo. Moreover, the maximum grade of RID over time was significantly diminished in *Avena sativa* L. groups. RID is the most common adverse effect of breast cancer RT. Around 95% of patients during RT develop local inflammatory symptoms, such as erythema, dry or moist desquamation, edema, and ulcers.

Table 4: Comparison results between the intervention and control groups regarding dry and moist desquamation.

	The incidence of desquamation 10 days after the prescription (Week 2ed)			The incidence of desquamation 18 days after the prescription (Week3rd)			The incidence of desquamation 28 days after the prescription (Week4th)			The incidence of desquamation 32 days after the prescription (Week 5th)			The incidence of desquamation in the last week		
Type of desquamation	Dry (number/%)	Moist (number/%)	Number (%)	Dry (number/%)	Moist (number/%)	Number (%)	Dry (number/%)	Moist (number/%)	Number (%)	Dry (number/%)	Moist (number/%)	Number (%)	Dry (number/%)	Moist (number/%)	Number (%)
intervention group	0	0	0	3 (9/1)	0	9 (1)	4 (12/1)	2 (6/1)	18 (9)	1 (3/0)	7 (21/2)	24 (2)	1	11 (33/3)	36 (3)
control group	0	0	0	1 (3/0)	0	3 (0)	0	1 (3/0)	3 (0)	7 (21/2)	2 (6/1)	27 (3)	0	11 (33/3)	33 (3)
p-value	Fisher's Exact Test			P=0.6			P=0.09 Chi-Square			P=0.02* Chi-Square			P=0.6 Chi-Square		

The severe presentations of radiodermatitis, e.g., moist desquamation, ulcers, and skin fibrosis, may necessitate discontinuation of the RT [11].

Topical steroids such as mometasone 0.1% and hydrocortisone have been evaluated for their anti- inflammatory properties. The results of the previous studies suggested that low doses of corticosteroids may be beneficial in reducing itching and irritation in patients with radiodermatitis. Moreover, steroids are contraindicated in the presence of infection as they could mask the signs and symptoms of infection and worsen it. This subsequently impairs patients' QOL and negatively influences the outcomes of the patients [12, 13].

The pathogenesis of radiodermatitis is somewhat complex and comprises radiation tissue injury followed by an inflammatory reaction. An erythematous skin reaction develops through increased vascular permeability and vasodilation. This is followed by inflammatory responses [14]. Inflammation occurs within the first 24 hours after the start of radiotherapy with a generation of free radicals and reactive oxygen in the rapidly dividing cells of the basal layer and dermis. This condition decreases the stem cells, induces a change in endothelial cells, and promotes inflammation [9].

During the past two decades of research, the efficacy of various biological and chemical

compounds such as antioxidants, cytoprotective factors, and vitamins have been investigated. Yet, no proven modality is available to prevent RID [11].

Topical steroids such as hydrocortisone have been evaluated for their anti-inflammatory properties, which suggests that low doses of corticosteroids may be beneficial in reducing itching and irritation in patients with radiodermatitis [13, 14].

Moreover, long- term application of high-potency topical steroids may cause skin thinning and atrophy, which may be problematic [15]. Also, steroids are contraindicated in the presence of infection as they could mask the signs and symptoms of infection and worsen it [11, 16].

Reviews of recent studies have shown that *Avena sativa* L. has anti-inflammatory and antioxidant properties. So far, no product containing *Avena sativa* L. relieves itching and inflammation in the pharmaceutical market is available.

In the current study, the peak incidence of erythema was found in the fifth week of treatment in both groups, and there was no significant difference. In the study of Frhan et al.,2004 who investigated topical betamethasone ointment in skin reactions caused by radiotherapy, it was shown that the maximum intensity of dermatitis occurred in the fifth week of treatment, and there was no significant difference between the two groups [17].

Ebrahimi et al., 2013 examined the impact of Elaeagnus angustifolia extract on skin reactions caused by radiation therapy in patients with breast cancer, which showed that 87.5% of the patients suffered from dryness and itching; after applying the cream, dryness and itching completely disappeared in 78.5% of these patients. The present study also showed that in the fifth week of the dry desquamation, 3% was seen in the *Avena sativa* L. group vs. 21.2% of the control group, which could make *Avena sativa* L. cream reduce dry desquamation as seen [18].

A study was conducted in 2022 to analyze the effect of topical administration of ozonated Aloe vera oil on the expression of TGF-β and collagen density in treating radiation dermatitis. This study proved that the administration of Aloe vera oil with or without ozonation resulted in better healing than the group without therapy and was equivalent to or better than the hydrocortisone group [19].

The results of the current study have shown that topical administration of *Avena sativa* L. cream was superior to the placebo cream in preventing ARD incidence and related symptoms. At the end of the treatment, according to the RTOG scale, grade 2 dermatitis in the patient of the intervention group was less than in the control group, which was not significantly different.

For instance, herbal products' anti-inflammatory and antioxidant activity has been demonstrated in different experimental and clinical evidence [11]. Rafati et al., 2019 demonstrated that the topical administration of Nigella sativa 5% gel with anti-inflammatory and antioxidant properties delayed and decreased the severity of ARD and its related symptoms compared to the placebo [20]. In this study, we observed that the topical application of *Avena sativa* L. cream to the radiation-exposed breast area can effectively prevent the occurrence of ARD.

Karbasforooshan et al., 2018 performed a study to investigate the efficacy of silymarin gel in preventing radiodermatitis in patients with breast cancer. The acute skin reactions were assessed according to RTOG/EORTC. However, after five weeks of RT, only 9.8% of patients in the silymarin group experienced Grade 2 radiodermatitis compared to 52% in the placebo group [15]. The current study found that 18 patients in the intervention group with grades 1 and 15 had grade 2 radiodermatitis. In contrast, the control group was the exact opposite of the intervention group, and there was no statistically significant difference between the two groups.

This study suffered from some limitations. First, the sample size of our study was small because of the strict inclusion and exclusion criteria. The study was not adjusted for other possible confounding factors, including nutritional status, genetics, and body mass index (BMI), which could have affected dermatitis's occurrence and intensity.

4. Conclusion

This randomized controlled clinical trial showed that the preventive use of the *Avena sativa* L. cream significantly delays and diminishes the maximum grade of ARD in breast cancer patients undergoing RT. So it is suggested that it is institutional to prepare creams containing extracts of *Avena sativa* L., and little but effective step has to be taken to improve the comfort and recovery of patients.

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Conflict of interest

The authors declare to have no conflict of interest.

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