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The Investigation of Prophylactic Effect of StrataXRT Gel on Radiation-Induced Dermatitis in Breast Cancer Patients: A Randomized Clinical Trial

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Abstract

Background: Breast cancer is among the most prevalent cancers in women. Radiotherapy is an important part in treatment of breast cancer, associated with some side-effects, including skin dermatitis. Dermatitis may be severe and impair quality of life. Multiple agents have been studied, but no standard treatment is yet available. Silicone based gel (StrataXRT) was promising in some studies in reducing skin inflammation and also radiotherapy-induced dermatitis.

Method: This was a randomized trial on 100 women with breast cancer who had undergone quadrantectomy for breast cancer. They received StrataXRT gel or best supportive care during radiotherapy. Dermatitis area and grade of dermatitis were measured.

Results: Regarding the mean size of radiation-induced dermatitis area, there was a significant difference between the intervention (36.88 cm^2 ± 69.93) and control (83.83 cm^2 ± 79.34) groups (P = 0.002). During radiotherapy, except in the fourth week, dermatitis was significantly more severe in the control group.

Conclusion: It seems that StrataXRT is helpful in decreasing radiotherapy-induced dermatitis.

Keywords: Breast neoplasms, Radiotherapy, Dermatitis

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Introduction

Breast cancer is the most prevalent cancer among women in the world. Treatments consist of surgery, systemic chemotherapy, hormone therapy, and radiotherapy. The standard surgery is usually breast conserving and most patients require breast radiation during the course of breast cancer treatment. One of the

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most common complications of radiotherapy is acute skin reaction, which may vary from mild redness to severe desquamation. About 85% of patients undergoing radiotherapy develop moderate to severe skin reactions that result in itching and pain and decrease quality of life. Severe dermatitis may even lead to treatment interruption and this can reduce the chances of cure.[1-4]

Different local and even oral agents have been used for prevention and treatment of dermatitis, such as corticoesteroids, aloe vera, Biafine, hyaluronidase-based creams, sucralfate, and amifostine (oral agent), but none has been proven safe and effective. Therefore, there is currently no standard and generally accepted prevention method for radiation dermatitis.[2-4]

Recently, silicone-based products have demonstrated some promising effects. These agents have been shown to decrease inflammation and fibrosis. Mechanism of action may decrease mechanical friction and transepidermal water loss. StrataXRT is a silicone-based gel and is applied easily and has no bolus effect on skin during radiotherapy.[5, 6] Hence, this study aimed to investigate the effect of StrataXRT silicone gel on the prevention of radiation-induced dermatitis in breast cancer patients.

Methods and Materials

This work was a single-center randomized controlled clinical trial conducted at Radio-Oncology department of Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz, Iran (IRCT code: IRCT20181030041507N1). Shiraz University of Medical Sciences ethics committee approved the study (IR.SUMS.MED.REC.1397.240). All the patients had breast cancer along with partial mastectomy (quadrantectomy) and were candidates for radiation therapy.

Primarily, 100 of the patients referred to our clinic, with no exclusion criteria, were randomized into two groups. Exclusion criteria were previous radiotherapy in the chest wall or breast area, history of systemic or cutaneous diseases, such as diabetes mellitus, collagen vascular disease, or taking medications affecting wound healing, such as systemic steroids. Regarding the possible effect of chemotherapy on dermatitis, carcinoma in situ was also an exclusion criterion. The patients were randomly allocated into two groups, intervention group or control group, and informed consent form for the study was signed by them. Randomization was assigned from the www.random.org website. All the patients had received chemotherapy and radiotherapy was the started three weeks after the completion of chemotherapy. Chemotherapy regimens in all the patients were doxorubicin- and taxane-based. Randomization was carried out by a radio-oncologist and blinding was not possible.

Radiotherapy field included the whole breast in all the patients and supraclavicular, posterior axilla, and internal mammary areas in some of them who had lymph node involvement. Whole breast was treated in all the patients by use of a 6mV photon with a standard dose of 1.8-2 Gy / day and five consecutive days per week for 5-5.5 weeks. The radiation dose was 50 Gy. Boost dose was not administered for any patients.

The patients were advised to wash radiotherapy site twice daily with water and soap and then, apply StrataXRT gel on the chest wall with a thickness of 1-2 mm. Prior to receiving radiation, the gel had to be removed (washed) from the skin to prevent further burns. The interval between twice daily uses of StrataXRT gel was six hours. The other group was considered as a control and daily irradiation as in the previous group was also recommended. Both groups were examined weekly and the grade of dermatitis was recorded. The patients received routine treatment in both groups, if one had grade 2 dermatitis or more. Dermatitis was scored according to RTOG scoring criteria. Dermatitis size was also measured using transparent paper per square centimeter.

Statistics

All the statistical analyses were performed using SPSS 24 statistical software. Central and scattering indices, such as frequency, percentage, mean and standard deviation, were employed to describe the data. Initially, Kolmogorov-Smirnov test was applied to examine the normality of the

Table 1. Patients and tumor characteristics in the two arms

	Control group	Strata group	*P*-Value
Age	45.08(±14.38)	43.04 (±10.61)	0.422
Stage			0.256
T1	21 (42.0%)	15 (30.0%)	
T2	22 (44.0%)	29 (58.0%)	
T3	5 (10%)	6 (12.0%)	
T4	2 (0.4%)	0 (0%)	
Node status			0.189
N0	18 (36.0%)	27 (54%)	
N1	23 (46.0%)	17 (34%)	
N2	7 (14.0%)	6 (12%)	
N3	2 (4.4%)	0(0%)	
ER			0.671
ER +VE	32 (64.0%)	35 (70.0%)	
ER -VE	18 (36.0%)	15 (30.0%)	
PR			0.808
PR +VE	28 (56%)	31 (62.0%)	
PR -VE	22 (44.0%)	19 (38.0%)	
HER 2			0.808
HER 2 +VE	22(44%)	15 (30%)	
HER2 -VE	28 (56%)	35 (70%)	
Field size (mm^2)	229.66 ± 73.20	237.79 ± 115.68	0.675

HER-2: Human epidermal growth factor receptor 2; ER: Estrogen receptor; PR: Progesterone receptor

data distribution. Afterwards, normal distributed data, the chi-square test, and the t-test were used to compare qualitative and quantitative variables, respectively. For non-normal distributed variables, the Mann-Whitney test was utilized. All the *P*-values were expressed two-sided and the statistical significance was evaluated to be 0.05.

Results

A total of 100 women with breast cancer were enrolled in the study and finished their treatment successfully. Baseline clinical and pathological characteristics of the patients are illustrated in table 1. There were no statistically significant differences between the intervention and control groups in the patients' age, tumor stage, node stage, hormone receptor and human epidermal growth factor receptor 2 (HER-2) status, and mean radiotherapy field size.

However, the mean size of maximum area of radiation-induced dermatitis was significantly different between the intervention (69.93 cm^2 ± 36.88) and control (83.83 cm^2 ± 79.34) groups (P = 0.002). During radiotherapy, as mentioned in table 2, except in the fourth week, dermatitis was significantly more severe in the control group. During the weeks 1-5 in StrataXRT arm, there were 0, 0, 0, 1, and 2 patients with grade 3 dermatitis. In the control group, there were 0, 0, 0, 2, and 23 patients with grade 3 dermatitis. In the fifth week, in the control group, one patient had grade 4 dermatitis. As mentioned in table 2, the differences in all the weeks, except the fourth one, were of statistical significance.

In addition, no side-effects of StrataXRT silicone gel were observed by the physician and the patients under study and the medication were safe in the intervention group.

Discussion

Radiotherapy is an important part of cancer treatment. About 75% of patients with malignant disease receive radiotherapy. Although skin is a normal tissue, it may get involved with dermatitis that could be a severe side-effect. It is estimated that 95% of patients develop dermatitis during radiotherapy. It has been revealed that while patients frequently tell about their feeling and discomfort of dermatitis to their physicians, their oncologists pay less attention to these problems.

Table 2. Grade of dermatitis during radiotherapy course in the two arms

	StrataXRT					Control					
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	*P*-value
Week 1	49 (98.0)	1 (2.0)	0	0	0	40 (80.0)	10 (20.0)	0	0	0	0.008
Week 2	7 (14.0)	42 (84.0)	1 (2.0)	0	0	0	49 (98.0)	1 (2.0)	0	0	0.023
Week 3	0	36 (72.0)	14 (28.0)	0	0	0	19 (38.0)	31 (62.0)	0	0	0.01
Week 4	0	5 (10.0)	44 (88.0)	1 (2.0)	0	0	0	48 (96.0)	2 (4.0)	0	0.064
Week 5	0	3 (6.0)	45 (90.0)	2 (4.0)	0	0	0	26 (52.0)	23 (46.0)	1 (2.0)	< 0.001

It may be due to the absence of an effective and standard treatment for radiotherapy-induced dermatitis.[1] The current work was a prospective study and was conducted to find the effects of a new drug in radiotherapy-induced dermatitis. StrataXRT was successful in decreasing dermatitis, but had some weak points in our research. In the present study which was small, the dose of radiotherapy was 50 Gy. Other sites of body may need higher doses or skin sensitivity may be different. Limitation of this study was the small number of participants.

Several agents have been studied widely to treat, decrease, or prevent radiation-induced dermatitis. Steroids have anti-inflammatory effects and are supposed to decrease radiotherapy side-effects that have inflammatory mechanisms. Ulff et al. in a study on 202 patients with breast cancer, randomized the patients into two groups. The patients received steroid (betamethasone) or moisturizer and had different types of surgery (mastectomy or quadrantectomy) and radiotherapy schedules. In the patients receiving standard radiotherapy or hypofractionated schedules, steroid reduced dermatitis. This decrement was seen to be statistically significant. In the conventional group, grade 2 and 3 RTOG was significantly less observed. Meanwhile, there are some worrisome side-effects with corticosteroids. By using it for a long time, skin atrophy and decreased collagen synthesis may occur. In addition, skin atrophy is a side-effect of radiotherapy.[7]

Hyaluronic acid is a protein in connective tissues and is supposed to have protective effects against radiation. Pinnix et al. compared hyaluronic acid and simple ointment in the treatment of radiation dermatitis in breast cancer patients. Subsequently, 92 patients received hyaluronic acid and simple ointment simultaneously in the same breast. Not only hyaluronic acid was not successful in decreasing dermatitis incidence and severity, but increased toxicity and as a result the study was closed after 72 patients were enrolled.[8]

Amifostine is an oral radioprotective agent and is shown to reduce radiotherapy-induced side-effects, but this agent is studied more in head and neck cancers. Amifostine may have interference with tumor response and there are some debates about it. Moreover, amifostine may produce nausea, vomiting, allergic reactions, and hypotension. This agent is not studied in conventional radiotherapy for breast cancer.[9]

Wells et al. compared sucralfate cream with aqueous cream and no treatment in 366 patients. In their study, the tumor sites were breast, head and neck, and anorectal area. Dermatitis was measured according to RTOG score. In addition, quality of life was also measured. Therein, no differences was observed in these three arms in preventing radiotherapy-induced dermatitis. Interestingly, other factors, such as body mass index, smoking, and using bolus, were more important than treatment.[10]

Trolamine emulsion or Biafine is applied in European countries to prevent radiotherapy-induced dermatitis. This agent reduces vasodilation and dermal edema. Biafine also improves epithelial proliferation. On the other hand, multiple studies have failed to show absolute benefit in preventing radiotherapy-induced dermatitis. In a prospective trial (RTOG 97-13), biafine was compared to best supportive care and no differences in dermatitis was found. Interestingly, only those patients with large breast had less toxicity six week after radiotherapy.[1, 11]

StrataXRT produces a film-coated layer on

the skin when applied. This layer is gas-permeable but not water-permeable. In this condition, wound healing may be improved.[6] Chan et al. examined the effects of StrataXRT silicone gel on the prevention and treatment of radiation-induced dermatitis in patients with head and neck cancer. That study revealed that skin toxicity at the end of radiotherapy in StrataXRT gel-treated group was significantly lower. At the end of treatment, StrataXRT gel group showed a lower percentage of grade 2 (80%) and grade 3 (28%) skin toxicity compared with the glycerine treatment group (91% and 45%, respectively). StrataXRT arm had a 12% lower risk of grade 2 dermatitis and a 36% lower risk of grade 3 skin toxicity. StrataXRT gel decreased the risk of grade 2-3 dermatitis by 41% and 49.4% compared with glycerin arm. There were no cases of discontinuation of treatment and side-effects of the drug in any of the groups. They concluded that StrataXRT gel is effective in preventing and delaying grade 2 and 3 skin toxicity.[5]

Ahn et al. in a prospective study on 49 patients compared StrataXRT with a moisturizing cream. They found no differences in dermatitis between the two arms. Interestingly, all of their patients in both arms had RTOG grade 1. This is not usual in our center as most of our patients develop grade 2 or more dermatitis during radiotherapy. When skin was examined with electronic devices, erythema index and melanin index were significantly lower in StrataXRT arm.[6] In the present study, StrataXRT silicone gel compared to the control group significantly prevented and reduced the rate of radiation-induced dermatitis in the patients with breast cancer that peaked at the fifth week of treatment.

Although our sample size was not large enough, the results were promising. Regarding no effective agent being available for radiotherapy-induced dermatitis, further studies are required.

Conclusion

Given that there are three studies on StrataXRT, including the present work, the results were promising and further research is needed to help patients.

Conflict of Interest

None declared.

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