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Original article

Secondary effects resulting from hormone therapy on the quality of life and sexuality: analysis of the effectiveness of the use of specific dermatological products

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Abstract. *Background*: Breast Cancer (BC) treatments could determine urogenital symptoms which can negatively impact sexual functions and quality of life (QoL) and reduce compliance to therapy of the female cancer patient. *Aim:* The aim of the study is to investigate the impact of secondary effects on the urogenital system resulting from hormone therapy on the quality of life of cancer women; in particular, this study wants to evaluate if a specific dermatological treatment could reduce the secondary effects of hormone therapy on the urogenital system and consequently improve women's sexuality and quality of life (QoL). *Methods:* Forty-nine women with BC were recruited. The women were divided into two groups and randomized in an Experimental (EG) and a Control Group (CG). For 42 days, EG use a specific dermatological treatment, while CG use a non-specific treatment. Participants were asked to perform 3 self-reports (Analogue scales for detecting the following symptoms, K10, WHOQoL-Brief) at three points: at baseline (T0), after 21 days (T1) and after 21 days (T2) from enrolment. *Results:* The specific dermatological treatment in the EG was associated with statistically significant decreases in vaginal pain, vaginal burning, vaginal itching, vaginal dryness and with a statistically significant increase in QoL, after 42 days (T2). *Conclusions:* The use of specific dermatological products decreases urogenital symptoms caused by hormone therapy and increases, consequently, the quality in sexual function and quality of life of women with breast cancer (QoL).

Key words: Dermocosmetological treatments, Breast Cancer, urogenital symptoms, hormone therapy

Introduction

In women, breast cancer represents the most common malignancy, with 55000 new cases per year in Italy alone, diagnosed both in the age group ranging from 0-49 years (40%) and in the one between 50-69 years (35%)[1]. To treat breast cancer, medicine nowadays has several therapeutic principals at its disposal, including surgery, radiotherapy, and chemotherapy. For hormone-sensitive tumors, medicine has an important therapeutic weapon such as hormone therapy. Although hormone therapy has resulted in lowering the risk of recurrence and a lower mortality[12], it is not without side effects

These effects vary in intensity depending on the drug category (Tamoxifen and Aromatase)[11] and the woman's induced or spontaneous menopausal status. In general, the side effect common to both pharmacological categories concern the urogenital area. The urogenital system is very sensitive to estrogen deprivation since these hormones are present in the vulva, vagina, pelvic floor muscles, endopelvic fascia, and urethra. A decrease in estradiol concentration causes atrophy of the vulvovaginal epithelium and inflammation of the uroepithelium, consequently, symptoms of estrogen deprivation include vaginal dryness, itching, discharge, incontinence, and dyspareunia. The loss of elasticity in the vagina with a reduction in its distensibil-

ity results in a shortening and narrowing of the vagina[5]. About 63% of women with breast cancer report urogenital symptoms related to hormone treatments[4]. The most common symptom is insufficient vaginal lubrication, followed by dyspareunia, itching or irritation, vaginal discharge, and urinary inflammation[4]. Pelvic prolapse and incontinence may occur as an effect of estrogen deprivation in the periurethral tissue. In addition, a change in vaginal ph and normal flora may predispose women to urinary tract infections[14]. It should be considered, however, that these data may be underestimated, as only one-fifth of women tell health professionals about their menopause-related urogenital symptoms[5].

Urogenital symptoms that arise following hormonal treatment for breast cancer can negatively impact their sexual functions and quality of life. These changes can result in dyspareunia, which can lead to an avoidance of coitus to contraction and rigidity. The severity of sexual symptoms and vaginal dryness has shown a negative correlation with their perceived quality of life and more specifically the perceived quality of life as a couple[9]. It is worth noting that side effects and lowered quality of life may lead to decreased adherence to the therapy and a final cessation of hormone therapy. In conclusion, it is necessary to monitor the impact of hormone therapy whose long duration implies prolonged side effects, affecting the patient's quality of life and mood. The aim of the study is to investigate the impact of secondary effects on the urogenital system resulting from hormone therapy on the quality of life of cancer women. In particular, we hypothesized that specific dermatological treatments could significantly improve women's wellbeing, decreasing the negative impact of urogenital symptoms and improving their QoL.

Materials and Methods

A total of 49 women with a diagnosis of hormone-sensitive breast cancer (mean age: 52.10 ± 6.57 years) voluntarily took part to this study.

From a clinical point of view, the median age of diagnosis was 51 years. Further, most of the sample received chemotherapy (n = 39, 81.3%), and a concurrent radiological (n = 27, 55.1%) or surgical treatment (n = 42, 85.7%). The inclusion criteria consisted of a diagnosis of hormone-sensitive breast cancer, the patient's age ranging between 20 and 60 years, and being an Italian native speaker. The exclusion criteria consisted of a history (or a current diagnosis) of psychiatric and/or neurological diseases, and a history of sexual dysfunctions prior to the development of the breast cancer.

The study was approved by the local ethics committee. All participants provided a written informed consent before beginning the study.

This randomized single blinded experimental trial was performed at the U.O.C. of Oncology of ASST Bergamo Est. Those who volunteered were then assigned to one of the study groups (Experimental or the Control), and filled out a battery of measures at baseline (T0), after 21 days (T1) and after 42 days (T2) from enrolment. A total of 29 women with a diagnosis of hormone-sensitive breast cancer were assigned to the experimental group, while 20 were assigned to the control group. All the participants in the research were asked to use an amount of products equal to 5 ml, 2 times a day for a total period of 42 days. The difference between the two groups (EG; CG) is the type of products used by the women:

The EG used two specific products as a treatment, namely the intimate cleanser (containing anti-irritating and protective Allantoin; restructuring and moisturizing Betaine; long-lasting moisturizing trehalose; Zanthalene, anti-itch, soothing and calming) and the humectant and moisturizing vaginal gel (containing Hyaluronic acid with high PM protective, moisturizing and lubricating; Allanotin, anti-irritant and protective; Betaine, restructuring and moisturizing; Beta-glucan, restorative, regenerating and protective; Zanthalene, anti-itching, soothing and calming; Defensil plus, soothing, calming, protective and anti-inflammatory) provided free of charge by an ONCOS cosmetic oncology specialist (ONCOS-QD Italia s.r.l.)

The CG used a placebo product as a dermatological treatment, ie demineralized gelled water, also provided free of charge by ONCOS-QD Italia s.r.l.

All patients were periodically contacted by telephone in order to verify that they had properly applied the product.

Measures

Gynecological Complaints. Four ad-hoc questions investigated gynecological-related symptoms, assigning a score from 0 to 10: vaginal pain (0= vaginal pain absent, 10= worst possible vaginal pain), vaginal burning (0= vaginal burning absent, 10= worst possible vaginal burning), vaginal itching (0= vaginal itching absent, 10= worst possible vaginal itching), vaginal dryness (0= vaginal dryness absent, 10= worst possible vaginal dryness).

Quality of Life. The Italian version of the World Health Organization Quality of Life Instruments[6-7] is a 26-item measure of perceived Quality of Life (QoL) during the past two weeks. The WHOQOL-BREF evaluates four domains related to QoL, namely physical health, psychological, social relationships and environment, which can be summed to provide an overall index of quality of life and general health. Items are rated on a 5-point Likert scale (1 = Not at all; 5 = Completely), with higher scores indicating a greater QoL. In the current study, the reliability of the total score at baseline was excellent (McDonald's ω = .91).

Psychological Distress. The Italian version of the Kessler Psychological Distress Scale 10 (K10)[10] is a 10-item measure of psychological distress experienced during the last 4-weeks. Items are rated on a 5-point Likert scale (1 = None of the time; 5 = All the time). Total scores range from 10 to 50, with higher scores indicating greater psychological distress. In the current study, the reliability of this measure at baseline was good (McDonald's ω = .84).

Statistical analysis

The data was initially screened through simple descriptive statistics, including means, standard deviations, frequencies, and percentages.

The differences between the groups at baseline were tested through independent sample *t*-tests or Chi-Squared tests. We finally tested our main hypothesis on the differences between the groups over time (from baseline [T0] to 42 days from enrolment [T2]) on both primary and secondary outcomes through a repeated-measure ANOVA, followed by Tukey's post-hoc tests. The within-factor was Time (T0, T1, and T2), while the between-factor was the grouping variable (Experimental or Control groups). All effect sizes were interpreted according to the guidelines[3]. All analyses were performed with a Statistical Package for Social Sciences (SPSS) version 26.0. All statistical tests were two-tailed, and a *p*-value ≤.05 was considered statistically significant.

Results

Preliminary Analyses

We first tested for normality assumptions and for the presence of univariate outliers. All variables were normally distributed, however we found few outliers in both groups for WHOQOL-BREF at T1 and T2, whose scores were brought into range[13].

Twenty-nine women were assigned to the experimental group (mean age: 53.03 ± 7.25), while the remaining 20 were assigned to the control one (mean age: 50.90 ± 5.35). Comparisons between the groups at baseline evidenced that those in the Experimental group were more educated and reported greater well-being (i.e., a lower score at K10 and a higher score at WHOQOL-BREF) than the patients in the Control group. From a clinical point of view, patients in the Control group were more frequently treated with Chemotherapy or with a Radiological treatment (see Table 1 for more details).

Descriptives and zero-order correlations for psychological, sociodemographic, and clinical variables are reported in Tables 1-3 and in Graphs 1.

Main Analyses

As for the primary outcomes, we found a statistically significant main effect of Time, as well as a significant interaction effect between Time and the Randomization Group, and both effects were large. Similarly, we found a statistically significant main effect of Time, as well as a significant interaction effect between Time and the Randomization Group for our secondary outcomes, and these effects were large.

That is, the treatment was associated with statistically significant decreases in vaginal pain, vaginal

Table 1 - Means, standard deviations, frequencies and percentages for the sociodemographic and psychological variables examined in this study, separately for each group.

Variables	Experimental Group (n = 29)	Control Group (n = 20)	p-value
Age, mean (SD)	53.03 (7.25)	50.90 (5.35)	.268
Education, *n* (%)			.004
Middle schools	8 (27.6)	15 (75)	
High schools	16 (55.2)	3 (15)	
University (Bachelor, Master or Ph.D.)	5 (17.2)	2 (10)	
Work status, *n* (%)			.30
Part time	1 (3.6)	0 (0)	
Full time	22 (78.6)	18 (94.7)	
Unemployed\Housewife	5 (17.9)	1 (5.3)	
Civil status, *n* (%)			.51
Single\Divorced\Widowed	3 (10.7)	1 (5.3)	
Married\Engaged	25 (89.3)	18 (94.7)	
Chemotherapy, *n* (%)	19 (67.9%)	20 (100%)	.005
Radiological treatment, *n* (%)	12 (41.4%)	15 (75%)	.020
Surgical treatment, *n* (%)	23 (79.3%)	19 (95%)	.12
Hormonal treatment, *n* (%)	29 (100%)	20 (100%)	.99
Pain, mean (SD)	3.79 (2.98)	3.95 (2.01)	.83*
Pruritus, mean (SD)	3.59 (2.81)	3.95 (1.61)	.57*
Burning sensation, mean (SD)	3.41 (2.73)	3.50 (1.19)	.88*
Mucosal dryness, mean (SD)	5.00 (3.00)	3.95 (1.57)	.12*
K10 total score, mean (SD)	20.90 (6.47)	25.75 (2.53)	.001*
WHOQOL-BREF Total score, mean (SD)	85.59 (9.99)	72.65 (7.53)	< .001*

Note. = Kessler Distress Scale – 10; WHOQOL BREF = WHO Quality of Life Scale. * Degrees of Freedom were corrected to control for the violation of the assumption of equality of variances.

burning, vaginal itching, vaginal dryness and with a statistically significant increase in QoL. All effects -with their corresponding F, DFs, p-value and effect size- are reported in Table 4.

Discussion and conclusions

The current literature on oncology points out that hormone-sensitive tumors decrease the risk of recurrence and mortality[12], but have several side effects on the urogenital system. Multiple evidences in literature revealed that women diagnosed with cancer must fight various difficulties and challenges which can provide an indelible negative impact on their life[2]. About 63% of women with breast cancer report urogenital symptoms related to hormonal treatments[4]. The most common symptom is insufficient vaginal lubrication, followed by dyspareunia, itching or irritation, vaginal discharge, and urinary inflammation[4]. Urogenital symptoms negatively affect sexual function, the couple's quality of life, psychological distress[8] and, consequently, the women's perceived quality of life[9] .

The use of specific dermatological products could reduce the impact of side effects on the urogenital system. The aim of the study is to investigate the impact of secondary effects on the urogenital system resulting from hormone therapy on the quality of life of cancer women. In particular, we hypothesized that specific dermatological treatments could significantly improve women's wellbeing, decreasing the negative impact of urogenital symptoms and enhancing the women's sexuality and quality of life (QoL).

In our study, at the time of the first administration (T0), women in the experimental group (EG) showed a higher level of quality of life (QoL) and a lower pres-

Table 2 - Means and Standard Deviations for the entire sample (N = 49) of women with a diagnosis of hormone-sensitive breast cancer, and separately for each group (Experimental, n = 29; Control, n = 20), at each time point.

		T0	T1	T2
Variable(s)	Group	Mean (SD)	Mean (SD)	Mean (SD)
Pain	Total	3.86 (2.61)	2.96 (1.99)	2.88 (2.16)
	Exp	3.79 (2.98)	2.45 (2.08)	2.10 (2.09)
	Cont	3.95 (2.01)	3.70 (1.63)	4.00 (1.75)
Pruritus	Total	3.73 (2.38)	3.06 (2.28)	2.82 (2.10)
	Exp	3.59 (2.81)	2.52 (2.49)	1.93 (1.96)
	Cont	3.95 (1.61)	3.85 (1.69)	4.1 (1.59)
Burning sensation	Total	3.45 (2.22)	2.78 (2.02)	2.33 (1.91)
	Exp	3.41 (2.73)	2.21 (2.11)	1.48 (1.45)
	Cont	3.50 (1.19)	3.60 (1.60)	3.55 (1.85)
Mucosal dryness	Total	4.57 (2.55)	3.37 (2.20)	2.88 (1.94)
	Exp	5.00 (3.00)	3.10 (2.47)	2.21 (1.72)
	Cont	3.95 (1.57)	3.75 (1.71)	3.85 (1.87)
K10 Total score	Total	22.88 (5.72)	20.84 (5.96)	19.08 (6.13)
	Exp	20.90 (6.47)	17.83 (5.66)	15.62 (4.34)
	Cont	25.75 (2.53)	25.2 (2.93)	24.1 (4.73)
WHOQOL-BREF Total score	Total	80.31 (11.05)	82.59 (11.80)	85.20 (12.05)
	Exp	85.59 (9.99)	89.62 (8.41)	92.14 (8.28)
	Cont	72.65 (7.53)	72.40 (7.92)	75.15 (9.28)

Note. Exp = Experimental Group; Cont = Control Group; K10 = Kessler Distress Scale – 10; WHOQOL BREF = WHO Quality of Life Scale

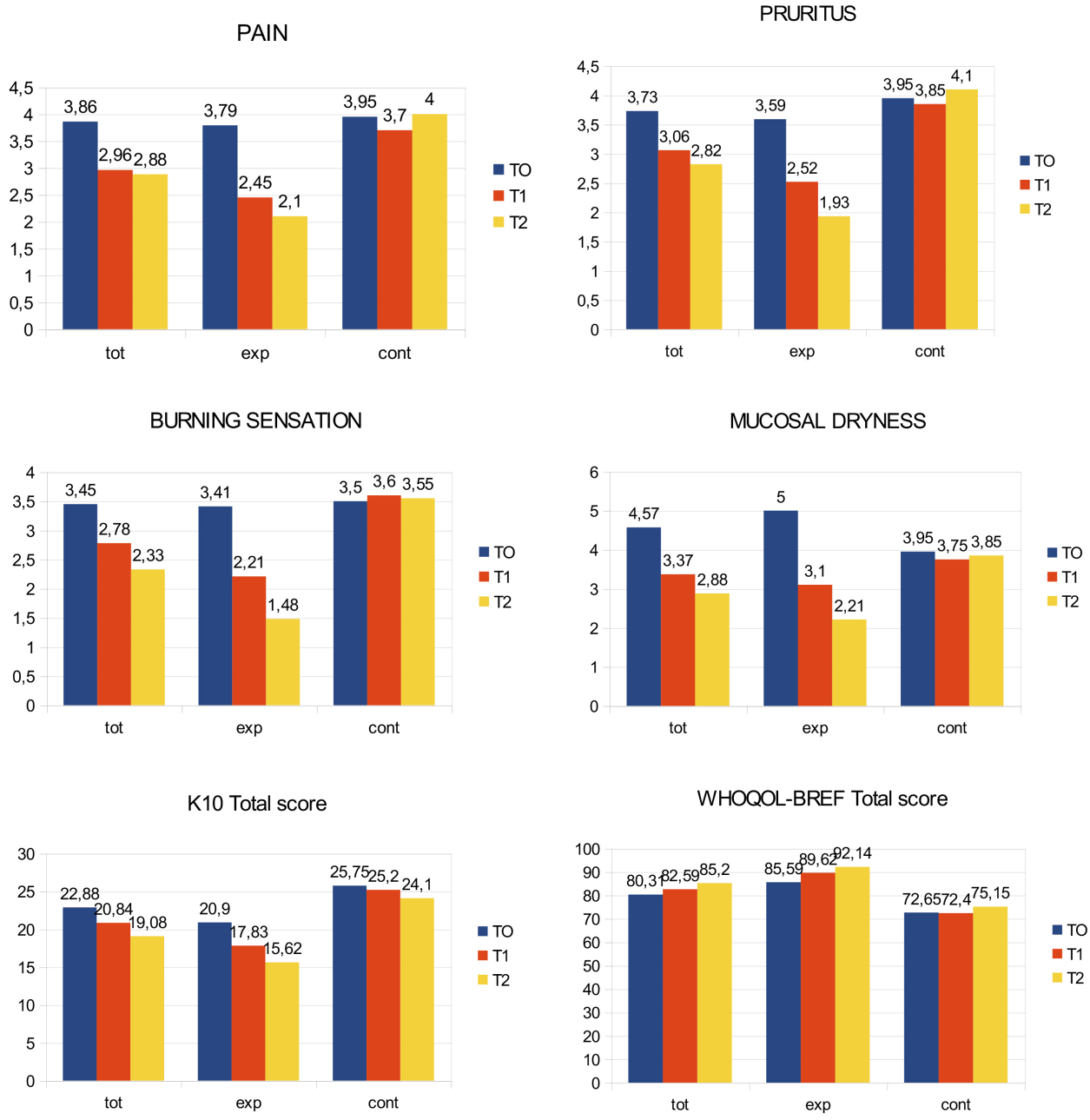
Table 3 - Zero-order correlations between all study variables in the complete sample of women with a diagnosis of hormone-sensitive breast cancer (n = 49).

Variables	1.	2.	3.	4.	5.
1. Pain	\				
2. Pruritus	.787**	\			
3. Burning sensation	.408**	.469**	\		
4. Mucosal dryness	.254	.194	.433**	\	
5. K10 total score	.074	.025	-.019	-.164	\
6. WHOQOL-BREF Total score	-.058	-.040	.068	.172	-.624**

Note. K10 = Kessler Distress Scale – 10; WHOQOL BREF = WHO Quality of Life Scale.
** = the correlation was significant at $p < .001$

ence of anxiety-depressive symptoms than the women in the control group (CG); this could be related to the higher frequency of chemotherapy and radiotherapy treatments within the control group (CG). There were no significant differences in the presence and intensity of urogenital symptoms in the two groups (EG and CG).

After 21 days of treatment, the experimental group (EG) showed a reduction in urogenital symptoms, unlike the control group (CG), which showed no improvement.After 42 days of treatment with the dermatological products, the experimental group (EG) showed a significant reduction in vaginal pain, vaginal burning, vaginal itching and vaginal dryness. The



Note. Exp = Experimental Group; Cont = Control Group; K10 = Kessler Distress Scale – 10; WHOQOL BREF = WHO Quality of Life Scale.

Graphs 1 - Means for the entire sample (N = 49) of women with a diagnosis of hormone-sensitive breast cancer, and separately for variables, for each group (Experimental, n = 29; Control, n = 20), at each time point.

Table 4 - Results from the Repeated Measures ANOVA, with the grouping variable as a between-subjects factor, on the primary and secondary outcomes on our sample of women with hormone-sensitive breast cancer.

Variable	Effect	DF	Error DF	*F*	*p*-value	partial η^2
Pain	Time	2	46	8.629	.001	.27
	Time * Rand Group	2	46	5.396	.008	.19
Pruritus	Time	2	46	4.584	.015	.17
	Time * Rand Group	2	46	9.470	< .001	.29
Burning sensation	Time	2	46	6.579	.003	.22
	Time * Rand Group	2	46	6.880	.002	.23
Mucosal dryness	Time	2	46	12.495	< .001	.35
	Time * Rand Group	2	46	11.437	< .001	.33
K10 total score	Time	2	46	15.862	< .001	.41
	Time * Rand Group	2	46	4.470	.017	.16
WHOQOL-BREF total score	Time	2	46	13.428	< .001	.37
	Time * Rand Group	2	46	4.999	.011	.18

Note. Rand = Randomization; K10 = Kessler Distress Scale – 10; WHOQOL BREF = WHO Quality of Life Scale.

quality of their sexual functions and overall quality of life (Qol) were, as a result, significantly increased. The control group (CG) showed no significant differences in the reduction of urogenital symptoms and quality of life after 42 days after their enrollment.

Our results confirmed how the use of specific dermatological products is a key factor in reducing urogenital symptoms resulting from hormone therapy and, consequently, increase women's quality of life (QoL). The daily use of dermatological products has led women to experience less pain and discomfort, improving self-esteem, social relationships, and couple sexual relationship. Therefore, the change in quality of life (QoL) seems to be influenced by the improvement of urogenital symptoms resulting from hormone therapy. This is congruent with the fact that good health represents not only the absence of the physical disease, but also a condition of physical and psychosocial well-being.

Ultimately, the decreased side effects on the urogenital system and improved QoL could lead to better adherence to therapy, as it is well known that side effects of therapies decrease the patient's will to comply to them.

The limitations of this study are that women in the control group (CG) were more likely to receive chemotherapy and radiotherapy treatments than the experimental group (EG), and this may have resulted in the difference in quality of life detected at baseline (T0) and could have an effect on the improvement in QoL over time. In conclusion, it is desirable for dermatologists to collaborate with oncologists to prevent and alleviate side effects on the urogenital system resulting from hormone therapy and to improve the quality of the sexual functions and quality of life of patients.

Conflicts of interest: There is no conflict of interest.

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