

Scalp cooling and chemotherapy: evaluation of quality of life and trichoscopy

Crioterapia capilar e quimioterapia: avaliação de qualidade de vida e tricoscopia

Enfriamiento del cuero cabelludo y quimioterapia: valoración de la calidad de vida y tricoscopia

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Abstract

Objectives: This study aimed to evaluate the quality of life (QoL) of patients undergoing scalp cooling during chemotherapy and to describe hair density data assessed by trichoscopy. **Background:** Hair loss during chemotherapy is a common and distressing side effect, and prevention can be done through scalp hypothermia. **Methods:** A prospective cohort study was conducted at a single oncology center in Brazil. Patients undergoing scalp cooling during chemotherapy were included. QoL and body image satisfaction (BIS) questionnaires were administered at the beginning and end of treatment. Data on alopecia were collected. Trichoscopy with a Fotofinder® device was performed at the beginning, before the second cycle, and at the end of treatment. STROBE guidelines were followed for the development of this study. **Results:** Twenty-seven patients were included. There was no difference in mean QoL or BIS scores in the comparison of patients with hair loss < 50% with those with hair loss ≥ 50%. Better outcomes in the QoL and BIS scales were found in patients treated with anthracyclines. Hair density described by trichoscopy showed a maximum reduction of up to 16.3%, and loss was more common in the frontal area. **Conclusions:** Thus, there is no clear evidence of better QoL in patients with a lower grade of alopecia after scalp cooling during chemotherapy. Validated scales can be useful for assessing QoL in this population.

Keywords: Alopecia; Breast neoplasms; Drug therapy.

Resumo

Objetivos: Este estudo teve como objetivo avaliar a qualidade de vida (QV) de pacientes submetidas ao resfriamento do couro cabeludo durante a quimioterapia e descrever os dados de densidade capilar avaliados por tricoscopia. **Introdução:** A queda de cabelo durante a quimioterapia é um efeito colateral comum e angustiante, e a prevenção pode ser feita através da hipotermia do couro cabeludo. **Métodos:** Foi realizado um estudo de coorte prospectivo em um único centro de oncologia no Brasil. Foram incluídos pacientes submetidos ao resfriamento do couro cabeludo durante a quimioterapia. Questionários de qualidade de vida e satisfação com a imagem corporal (SIC) foram aplicados no

início e no final do tratamento. Dados sobre alopecia foram coletados. A tricoscopia com aparelho Fotofinder® foi realizada no início, antes do segundo ciclo e ao final do tratamento. Para o desenvolvimento deste estudo foram seguidas as orientações do STROBE. Resultados: Vinte e sete pacientes foram incluídas. Não houve diferença na média dos escores de QV ou SIC na comparação de pacientes com perda de cabelo < 50% com aquelas com perda de cabelo \geq 50%. Melhores resultados nas escalas de QV e SIC foram encontrados em pacientes tratadas com antraciclina. A densidade capilar descrita pela tricoscopia apresentou redução máxima de até 16,3%, sendo a perda mais comum na região frontal. Conclusões: Não há evidências claras de que pacientes com menor grau de alopecia após o resfriamento do couro cabeludo durante a quimioterapia apresentem melhor qualidade de vida. Escalas validadas podem ser úteis para avaliar a qualidade de vida nessa população.

Palavras-chave: Alopecia; Neoplasias mamárias; Terapia medicamentosa.

Resumen

Objetivos: Este estudio tuvo como objetivo evaluar la calidad de vida (CV) de pacientes sometidas a enfriamiento del cuero cabelludo durante la quimioterapia y describir los datos de densidad del cabello evaluados por tricoscopia. **Antecedentes:** La pérdida de cabello durante la quimioterapia es un efecto secundario común y angustiante, y la prevención se puede realizar a través de la hipotermia del cuero cabelludo. **Métodos:** Se realizó un estudio de cohorte prospectivo en un solo centro de oncología en Brasil. Se incluyeron pacientes sometidas a enfriamiento del cuero cabelludo durante la quimioterapia. Se administraron cuestionarios de CV y de satisfacción con la imagen corporal (SIC) al principio y al final del tratamiento. Se recogieron datos sobre la alopecia. Se realizó tricoscopia con el dispositivo Fotofinder® al inicio, antes del segundo ciclo y al final del tratamiento. Para el desarrollo de este estudio se siguieron las pautas STROBE. **Resultados:** Se incluyeron a 27 pacientes. No hubo diferencia en las puntuaciones medias de CV o SIC en la comparación entre pacientes con pérdida de cabello < 50 % y aquellas con pérdida de cabello \geq 50 %. Se encontraron mejores resultados en las escalas CV y SIC en pacientes tratadas con antraciclina. La densidad capilar descrita por tricoscopia mostró una reducción máxima de hasta el 16,3%, siendo más frecuente la pérdida en la zona frontal. **Conclusiones:** No hay evidencia clara de una mejor CV en pacientes con menor grado de alopecia después del enfriamiento del cuero cabelludo durante la quimioterapia. Las escalas validadas pueden ser útiles para evaluar la CV en esta población.

Palabras clave: Alopecia; Neoplasias mamarias; Farmacoterapia.

1. Introduction

Alopecia is one of the most common side effects of chemotherapy protocols used for treatment of malignant neoplasms. The negative impact on patient quality of life (QoL) has been described in several studies, with repercussions such as self-identity changes, modifications in social interactions, and image disorders (Haque et al., 2020).

Methods to prevent hair loss are widely used in several oncology centers, with scalp cooling being the most common and, to date, the most effective (Shin et al., 2015; Amarillo et al., 2022). Scalp cooling during chemotherapy causes vasoconstriction and temperature reduction in the scalp, leading to a decrease in transport and metabolism of chemotherapeutic drugs in the cells of hair follicles (Dunnill et al., 2018).

According to a systematic review and meta-analysis, scalp cooling can reduce grade 2 alopecia (hair loss \geq 50%) by 43% (Rugo & Voigt, 2018). Success rates in hair preservation are dependent on the chemotherapy regimen used, and scalp cooling is more effective in patients treated with taxanes than in those treated with anthracyclines (Villarreal-Garza et al., 2021). In addition, maintaining an appropriate scalp temperature, usually below 22°C, is important for the efficacy of this method (Komen et al., 2013).

This study aims to evaluate the QoL of patients undergoing scalp cooling to prevent hair loss caused by chemotherapy. Also, hair density data obtained by trichoscopy during the treatment of some patients are reported.

2. Methodology

This prospective cohort study (Pereira et al., 2018) was conducted at an oncology center between October 2018 and August 2020. Included patients were \geq 18 years old, had an indication for chemotherapy treatment, and underwent scalp cooling with the Orbis Paxman Hair Loss Prevention System as recommended by their attending physician. Patients who were

diagnosed with leukemia, cryoglobulinemia, melanoma, or scalp metastases, and those who had significant hepatic impairment (bilirubin > 1.5 mg/dL and/or liver enzyme level > 2.5 times the normal range) and a history of previous scalp irradiation were considered ineligible. Consecutive patients who met these criteria were invited to participate in this study.

The primary outcome was the association between grade of alopecia and QoL and body image satisfaction (BIS) of patients undergoing chemotherapy and scalp cooling. The secondary outcomes were QoL and BIS in the first and last cycles of chemotherapy, grade of alopecia according to the chemotherapy regimen used (with or without anthracycline), and hair density at the beginning and end of treatment based on trichoscopy.

Alopecia was classified according to the Common Terminology Criteria for Adverse Events 5.0 as grade 0 (G0) = without hair loss, G1 = hair loss < 50%, and G2 = hair loss \geq 50% (Department of Health and Human Services, 2017). For QoL assessment, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) was administered at the beginning and end of chemotherapy treatment, and was divided into 3 subscales, namely a global QoL subscale, a symptom subscale, and a functional subscale for comparison (Aaronson et al., 1993). Moreover, a BIS scale consisting of 18 questions was administered at those 2 time points (Ferreira & Leite, 2002).

Hair density changes were measured by trichoscopy using a Fotofinder® device and TrichoLAB tool before the start of treatment, before the second cycle of chemotherapy, and at the end of treatment. Scalp images were collected in 3 areas: frontal, temporal, and occipital.

Results were described using descriptive statistics with absolute and relative distributions and measures of central tendency and variability, with a study of symmetry by the Shapiro-Wilk test. The primary outcome was assessed using the Mann-Whitney U test together with data referring to QoL/BIS and use of anthracyclines. A general linear model (GLM) was used to compare the variations of mean QoL, BIS, and capillary density values, with Bonferroni post hoc evaluation. Two independent groups were compared using the Fischer exact test. For data analysis, SPSS version 25.0 (SPSS Inc., Chicago, IL, USA, 2018) for Windows was used. For statistical decision criteria, a significance level of 5% was adopted.

All included patients signed an informed consent form before the procedures were performed. This study was approved by an institutional human research ethics committee and was conducted in accordance with the Helsinki Declaration. STROBE guidelines were followed for the development of this study (Supplementary File 1).

3. Results

Patients

Twenty-seven patients, all female and diagnosed with breast cancer, were included. Mean age was 47.4 (standard deviation, 10.3) years. Of those patients, 85% had clinical stage I or II cancer at diagnosis. Regarding chemotherapy regimens, 40.7% of patients were treated with anthracyclines. Thirteen women (81.25%) received docetaxel in combination with cyclophosphamide (9 patients) or carboplatin (4 patients) as the treatment of choice. Fourteen patients had comorbidities and 12 reported continuous use of at least one medication. Other baseline data are described in Table 1.

Table 1 - Patient characteristics.

Variable	Total sample (n = 27)
Age	
Mean ± SD	47.4 ± 10.3
Smoking status	
Smoker	4
Nonsmoker	22
Unknown	1
Comorbidities (n = 14)	
Hypothyroidism	4
Hypertension	2
Depression	2
Diabetes mellitus	1
Others	6
Medications (n = 12)	
Levothyroxine	4
Antidepressants	4
Vitamin D	2
Beta-blockers	1
Others	13
Clinical stage	
I	12
II	11
III	2
IV	1
Unknown	1
Cycles of chemotherapy	
4	12
6	5
8	10
Alopecia grade	
0-1	20
2	7
Chemotherapy protocol	
A+T	11
T+C	13
t	3

SD, standard deviation; A+T, anthracyclines plus taxanes; T+C, docetaxel plus carboplatin or cyclophosphamide; t, paclitaxel. Table 1 describes the characteristics of the study population, showing that most women were non-smokers, received 6 or more cycles of chemotherapy and the most common treatment protocol was TC. Source: Authors.

Quality of life and body image

Seven patients had G2 alopecia at the end of treatment. There were no differences in QoL or BIS when those were compared with patients with G0 and G1 alopecia (Table 2).

Table 2 - Mean EORTC QLQ-C30 and BIS scores in relation to grades of alopecia and chemotherapy regimen (with or without anthracycline).

	EORTC QLQ-C30 (mean ± SD)						BIS (Mean ± SD)	
	Global QoL		Functional†		Symptoms‡		Start	End
	Start	End	Start	End	Start	End		
Alopecia								
Grade 0-1 (n = 20)	75.4 ± 16.8	71.6 ± 21.7	74.4 ± 15.4	67.7 ± 26.1	13.9 ± 10.5	26.8 ± 24.3	66.6 ± 11.8	64.5 ± 11.7
Grade 2 (n = 7)	78.6 ± 15.9	76.2 ± 10.1	84.4 ± 12.6	76.8 ± 15.3	9.9 ± 11.1	15.8 ± 9.8	65.0 ± 9.4	56.4 ± 12.8
p§	0.652	0.675	0.158	0.618	0.244	0.471	0.803	0.184
Anthracycline								
Yes	73.5 ± 19.3	81.1 ± 21.4	82.2 ± 15.6	83.6 ± 16.2	11.2 ± 11.4	12.6 ± 13.1	68.9 ± 10.6	64.3 ± 11.5
No	78.1 ± 14.2	67.0 ± 15.9	73.4 ± 14.3	60.7 ± 24.1	14.0 ± 10.3	31.7 ± 23.5	68.0 ± 13.9	58.5 ± 9.6
p§	0.706	0.015	0.145	0.014	0.310	0.021	0.256	0.043

BIS, body image satisfaction; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life; SD, standard deviation.

† Score from 0 to 100 = higher means describe a better functional level

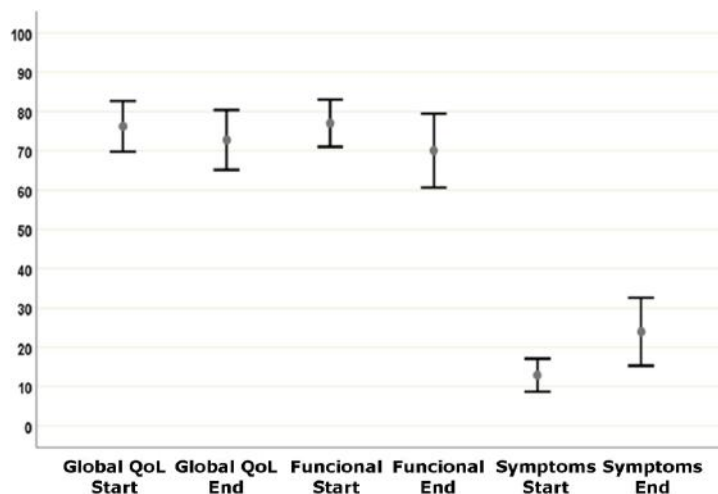
‡ Score from 0 to 100 = higher means describe more symptoms

§ Mann-Whitney U test

There was no difference in QoL when patients were stratified by grade of alopecia during treatment. Interestingly, QoL scores were better in patients who received anthracyclines. Source: Authors

There was no statistically significant difference in the global QoL or functional subscales when comparing the EORTC QLQ-C30 data of 27 patients at the beginning and end of treatment. Only the symptom subscale showed a significant difference in the analysis ($p = 0.002$), with a worse score at the end of treatment (Figure 1). In the BIS scale, no differences were detected in both evaluations ($p = 0.246$).

Figure 1 - Mean European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 scores in the general population (95% confidence interval). Global quality of life (QoL) subscale, functional subscale, and symptom subscale were analyzed at the start and end of treatment.



Only the comparison of symptom subscale scores in both evaluations showed a significant difference ($p = 0.002$), according to a generalized linear model with Bonferroni post hoc test. Source: Authors

Among 11 patients who received anthracycline-based chemotherapy, 4 had G2 alopecia at the end of the study (36.37%). Among the remaining 16 patients, only 3 had G2 alopecia (18.75%). There were no differences between chemotherapy regimens with or without anthracyclines for G2 alopecia ($p = 0.17$). Global QoL subscale, functional subscale, symptom subscale, and BIS scale scores were significantly better in patients treated with anthracycline (Table 2).

Trichoscopy

Eight patients underwent trichoscopy with a Fotofinder® device at the 3 predetermined time points. The examinations were performed by 2 dermatologists together at each medical visit. In all scalp areas analyzed, there was a reduction in mean hair density per cm² over time, although none of the evaluated sites showed any significant differences. Hair density reduction was more substantial in the frontal area at the end of treatment (16.3%), followed by the temporal area (15.5%) and the occipital area (9.7%). All mean hair density values are available in Table 3. Figure 2 shows macroscopic and microscopic trichoscopy examinations in 2 patients included in this study.

Table 3 - Mean hair density per cm² measured in three areas before the first cycle of chemotherapy (T1), before the second cycle (T2), and at the end of treatment (T3).

	Hair density (n = 8)			
	Mean	SD	p†	Change from baseline (%)
Frontal area			0.101	
T1	193.8	32.5		
T2	170.2	39.0		-12.2%
T3	162.2	51.2		-16.3%
Temporal area			0.116	
T1	144.3	31.4		
T2	143.3	21.0		-0.7%
T3	121.9	30.0		-15.5%
Occipital area			0.315	
T1	165.7	40.3		
T2	156.8	29.6		-5.4%
T2	149.7	27.2		-9.7%

SD, standard deviation.

† Generalized linear model with Bonferroni post hoc test

Mean hair density seemed to be mostly affected in the frontal area in this study population. As the sample analyzed was very small, it was not possible to identify significant differences. Source: Authors.

Figure 2 - Comparison of hair density in 2 patients who wore a scalp cooling device during chemotherapy. Patient 1 was treated with anthracycline/taxane-based chemotherapy and patient 2 received only paclitaxel. Macroscopic evaluation of hair density is shown before the first cycle (A1, A2) and after the last cycle of chemotherapy (B1, B2). Microscopic trichoscopy images of the frontal area pre- (C1, C2) and posttreatment (D1, D2) and of the temporal area before the first (E1, E2) and after the last cycle (F1, F2) of chemotherapy are shown.

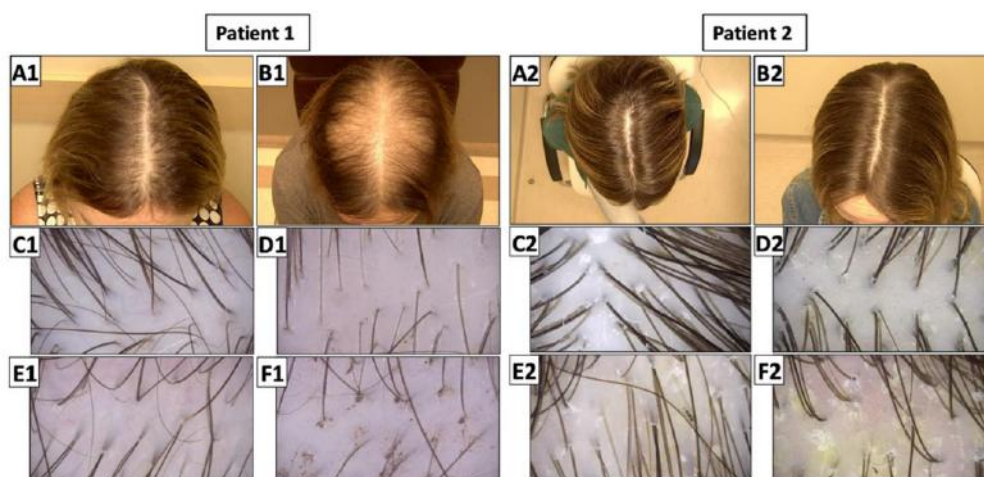


Figure 2 shows that patient 1, treated with anthracycline, had little hair loss compared with data from studies where scalp cooling was not used. Patient 2 was treated only with taxanes and virtually had no hair loss. Scalp cooling currently appears to be the best treatment option to prevent hair loss in patients undergoing chemotherapy. Source: Authors.

4. Discussion

In this single-center study, hair preservation (loss < 50%) with a scalp cooling device during chemotherapy was not associated with better QoL and BIS outcomes. Regardless of the grade of alopecia, a worse score in the QoL symptom subscale was observed at the end of treatment, with no significant differences in other scores.

In a systematic review of 13 studies, Marks et al. (2019) concluded that scalp cooling was not consistently associated with QoL improvements on the EORTC QLQ-C30 and -BR23 scales. The authors mention that more than one-third of the studies included did not compare QoL between successfully and unsuccessfully scalp-cooled patients. In the present study, G2 alopecia was not associated with worse QoL.

If effective scalp cooling is defined as hair loss < 50%, the present study found an efficacy of 63.63% when patients were treated with anthracyclines. Nangia et al. (2017) described an efficacy of 16% with the Orbis Paxman Hair Loss Prevention System in patients treated with anthracyclines. In the same setting, Vasconcelos et al. (2018) found a greater efficacy for that device, with hair loss < 50% in up to 76% of patients. A systematic review and meta-analysis of 27 studies showed an effectiveness rate of 61% (Wang et al., 2021). As shown in our study, scalp cooling prevented G2 alopecia even in patients receiving anthracyclines, although efficacy seems smaller than with regimens without this drug, as observed in other studies as well (Carbognin et al., 2022; Kate et al., 2021).

Since QoL and BIS scores were better in patients treated with anthracyclines despite no differences in the grade of alopecia, other associated factors influencing QoL should be considered. Among patients who did not use anthracyclines, 56% were treated with a combination of docetaxel and cyclophosphamide (TC). Ntellas, Spathas, Agelaki, and Zintzaras (2019) assessed the toxicity profile of sequential anthracycline and taxane chemotherapy regimens compared to TC regimen in 5 studies, demonstrating that allergy, rash, skin toxicity, and myalgia are more common with TC. These adverse events may have contributed to the differences found in both QoL and BIS favoring anthracyclines in the present study.

Trichoscopy is an important clinical method for the diagnosis of alopecia (Jain et al., 2013). Kanti et al. (2014) described a prospective cohort of patients with breast cancer treated with chemotherapy and evaluated the frontal and occipital areas with trichoscopy. In their study, mean hair density decreased 76% in the frontal area and 60% in the occipital area. In the present study, hair density losses were smaller: 16.3% in the frontal area and 9.7% in the occipital area. Despite the low number of patients undergoing trichoscopy, these results corroborate the good efficacy found in this population.

As this is a noncomparative study, it is not possible to determine whether scalp cooling alone is a factor for improving or maintaining QoL in patients. A comparison with a control group would help elucidate this question. Several factors may contribute to distress in patients treated for breast cancer and affect QoL and body image perception in addition to alopecia or other adverse events of chemotherapy. According to some studies, worse scores in the questionnaires are related to extent of surgery, age, depression/anxiety symptoms, and economic burden of the disease, and these aspects must be considered during evaluation of QoL (Delgado-Sanz et al., 2011; Syrowatka et al., 2017; Park et al. 2020).

Moreover, the scores most commonly used to measure QoL, such as the EORTC QLQ-C30, might not be fully adequate for the purpose of this study. Administration of a more specific scale, like the one proposed by Cho et al. (2014) to evaluate distress caused by alopecia during chemotherapy, would probably provide more reliable measures of QoL in these patients; however, it has not yet been translated into Portuguese language and validated.

5. Conclusion

In conclusion, the present analysis demonstrated similar QoL and BIS scores for all included patients, regardless of the grade of alopecia ($< 50\%$ and $\geq 50\%$), after scalp cooling treatment during chemotherapy. More appropriate scales for measuring QoL in this population should be used in future studies to determine the impact of preventing alopecia during breast cancer treatment.

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