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Survival in women with breast cancer who used or did not use scalp cooling in the neoadjuvant/adjuvant setting

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ABSTRACT

Background: Scalp cooling can prevent chemotherapy-induced alopecia. Success varies according to the type of chemotherapy. A controversy exists regarding the use of scalp cooling because of the lack of safety data. No data are available regarding the impact on survival.

Purpose: To compare overall survival in women who used or did not use scalp cooling in the neoadjuvant/adjuvant setting.

Method: The survival of women treated in a specialized breast cancer centre (the Centre des Maladies du Sein Deschênes-Fabia) in Quebec City who all used scalp cooling was compared to that of a population-based random sample of women treated in other regions of the province of Quebec (Canada) where scalp cooling is not available. Cox proportional hazard models were used.

Results: Overall, survival was comparable (and possibly better although not at a conventionally statistically significant level: HR = 0.80, 95 % CI : 0.63-1.01, p=0.06) among the 553 women who used scalp cooling compared to the 817 who did not. An interaction was found between scalp cooling and treatment in the adjuvant vs. neoadjuvant setting (p-interaction=0.015). In the adjuvant setting (n=485 scalp cooling and 740 no scalp cooling), the crude HR (in favour of scalp cooling) was 0.66 (95% CI: 0.50-0.87, p=0.003). In the neoadjuvant setting (n=68 scalp cooling and 77 no scalp cooling), the HR was 1.40 (95% CI: 0.84-2.33, p=0.2). No interaction was found with stage.

Conclusion: This is the first study to compare survival of women who used scalp cooling to that of women who did not. Scalp cooling to prevent chemotherapy-induced alopecia had no negative effect on survival in women with breast cancer who used it.

BACKGROUND

Alopecia (hair loss) is associated with the vast majority of chemotherapy regimens used for breast cancer today. Hair loss starts 2-3 weeks after the initiation of chemotherapy and is usually reversible although recent data show that it might be irreversible in about 6% of patients using docetaxel[1], a drug commonly used in breast cancer.

Patients rank hair loss in the top three most troublesome side effects and this has not changed in decades[2]. Scalp cooling techniques to prevent hair loss exist but are rarely used in North America although they are more accepted in Europe. One reason is the absence of data on safety. When considering potential mechanisms for scalp cooling that involve reduced chemotherapy delivery and/or efficacy in the scalp, hypothetically cancer cells, if present in the scalp, might not be killed by chemotherapy if scalp cooling is used. Two questions can be asked in regard to safety: 1) Is scalp cooling is associated with an increase in scalp metastases? 2) Is scalp cooling associated with increased breast cancer relapse or decreased survival? Study on scalp metastases have shown that they can occur even when no scalp cooling is used. In the context of non-metastatic breast cancer, scalp metastasis incidence is between 0.4-1.8%[3] but they almost always occur when metastases are present in other sites. We published two case report of women who developed scalp metastases as the first site of recurrence but where scalp cooling has been used either only for one chemotherapy cycle or where the woman lost her hair, meaning that chemotherapy reached the scalp[4]. Overall, scalp metastases are very rare events and a direct link between scalp cooling and scalp metastases cannot be established.

No data on survival of women using scalp cooling vs. no scalp cooling are available. We have designed a study to compare overall survival in women with breast cancer who used or did not use scalp cooling in the neoadjuvant/adjuvant setting.

METHOD

Study population

This was a retrospective cohort study of 1370 women with breast cancer. All patients have received chemotherapy and were non-metastatic at diagnosis. The cohort of women who used scalp cooling were 553 women (diagnosed between June 1st 1998 and June 20th 2002) all treated at the Centre des Maladies du Sein Deschênes-Fabia (CMS) in Quebec City, were scalp cooling is offered routinely. Data on staging, pathology and treatment received were available in our breast cancer database. Details concerning use of scalp cooling were obtained by chart review. Data on survival were obtained through administrative databases of the provincial government. This group of women was compared with a cohort of 817 women (diagnosed between 1998 and 2003). This is a population-based random sample of women treated in other regions of the province of Quebec (Canada) where scalp cooling is not available. The data are provided by the Institut National de Santé Publique du Quebec (INSPQ). Women from the INSPQ cohort who were from the CMS were excluded from the INSPQ cohort. The median follow-up for scalp cooling group is 6.31 year (3.23-10.3) and 7.97 years (6.4-10.3) for non-scalp cooling group. Ethical Review Board approval was obtained.

Statistics

Kaplan-Meier survival curves were calculated to assess crude differences in survival according to use of scalp cooling , and the log rank statistic was used to assess statistical significance of observed differences. The Cox proportional hazards model was used to calculate HRs and their 95% CIs. Cox models were adjusted for the following variables: age, stage, grade, lymphovascular invasion, type of chemotherapy, hormonal receptors status and participation to a randomized controlled trial (RCT).
A HR of 1 indicates that the mortality rates in the two groups compared were the same, whereas a HR of >1 and <1 means a higher and lower death rate in the scalp cooling group respectively, compared with women in the non-scalp cooling group.

RESULTS

A total of 1370 women were included in the study. Among these, 553 used scalp cooling at least once in the neoadjuvant or adjuvant setting and 817 did not. Baseline characteristics are presented in table 1. The median age was around 52 years old. Overall, more women in the scalp cooling arm participated to a RCT; 18.6% in the scalp cooling arm and 10.4% in the non-scalp cooling arm. In the neoadjuvant subgroup, there were differences in the proportion of women with stage III (63.2% in the scalp cooling arm and 36.4% in the non-scalp cooling arm) and who used taxanes (23.5% in the scalp cooling arm and 35.1% in the non-scalp cooling arm).

Results on overall survival are presented in table 2. Overall, survival was comparable ($HR_{ajusted}$ = 0.89, 95 % CI: 0.68-1.17, p=0.4) among the 553 women who used scalp cooling compared to the 817 who did not. An interaction was found between scalp cooling and treatment in the adjuvant vs. neoadjuvant setting (p-interaction = 0.1487). In the adjuvant setting (n=485 scalp cooling and 740 no scalp cooling), the $HR_{ajusted}$ (in favour of scalp cooling) was 0.80, 95% CI: 0.59-1.10, p=0.17. In the neoadjuvant setting (n=68 scalp cooling and 77 no scalp cooling), the $HR_{ajusted}$ was 1.84, 95% CI: 0.92- 3.68, p=0.08. No interaction was found with stage.

DISCUSSION

In summary, there is no negative impact on survival among women treated with adjuvant chemotherapy. However, there is little available information on effects of scalp cooling among women getting neoadjuvant chemotherapy since subgroups were very small (68 scalp cooling and 77 no scalp cooling) and further studies are needed in that setting. We believe that data we have amassed are reassuring and that we can continue investigation of scalp cooling in **adjuvant chemotherapy**.

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Table 1. Baseline characteristics of the population

Characteristics	Global (N = 1370) (% except for age in year)			With adjuvant chemotherapy (N= 1225) (% except for age in year)			With neoadjuvant chemotherapy (N= 145) (% except for age in year)		
	No scalp cooling (N=817)	Scalp cooling (N=553)	P values	No scalp cooling (N=740)	Scalp cooling (N=485)	P values	No scalp cooling (N=77)	Scalp cooling (N=68)	P value
Age at diagnosis (years)	52.5 ± 10.9	51.8 ± 9.6	0.24	52.6±10.8	52±9.6	0.25	50.9±11.5	49.5±9.8	0.0031
Stage*[1]			<0.0001			0.0004			
I/	25.2	20.8		26.9	23.5		9.1	1.5	
II	63.2	66.4		64.7	70.9		48.1	33.8	
III	8.2	12.6		5.3	5.6		36.4	63.2	
Unknown	3.4	0.2		3.1	0		6.5	1.5	
Grade			<0.0001			<0.0001			0.62
I	17.5	15.4		18.1	16.5		11.7	7.4	
II	39.8	32.0		40.7	30.7		31.2	41.2	
III	37.8	39.8		37	39.6		45.5	41.2	
Unknown	4.9	12.8		4.2	13.2		11.7	10.3	
Lymphovascular invasion			<0.0001			<0.0001			0.0003
Yes	36.1	38.3		35.6	36.5		41.6	51.5	
No	36.7	61.7		37.3	63.3		31.2	45.6	
Unknown	27.2	0.5		27.2	0.2		27.3	2.9	
Hormone receptors			<0.0001			<0.0001			0.0021
Positive	64.3	72.5		64.1	74.9		66.2	58.8	
Negative	32.6	27.1		33.5	24.9		23.4	41.2	
Unknown	3.2	0.4		2.4	0.2		10.4	0	
Type of chemotherapy			<0.0001			<0.0001			0.023
AC or CMF	41.5	61.1		43.8	66.8		19.5	20.6	
CEF, CE, FEC or FAC	36.7	29.5		36.6	25.8		37.7	55.9	
Taxane-based/other	10.5	9.4		8	7.4		35.1	23.5	
Unknown	11.3	0		11.6	0		7.8	0	
Hormone therapy			<0.0001			<0.0001			0.73
Yes	60.3	70.9		59.9	71.3		64.9	67.6	
No	39.7	29.1		40.1	28.7		35.1	32.4	
Participation in a clinical trial			<0.0001			<0.0001			0.3806
Yes	10.4	18.8		10	18.6		14.3	20.6	
No	89.6	81.2		90	81.4		85.7	79.4	

*[1] According to the American Joint Committee on Cancer Staging (Version 5)

Table 2. Hazard ratio for overall survival in scalp-cooling vs. no scalp-cooling groups

	HR_{crude}	95% CI	P value	$HR_{adjusted}$ *[2]	95% CI	P value
Global (n= 1370)	0.80	(0.63-1.01)	0.063	0.89	(0.68-1.17)	0.405
Adjuvant (n= 1225)	0.66	(0.50-0.87)	0.003	0.80	(0.59-1.10)	0.17
Neoadjuvant (n= 145)	1.40	(0.84-2.33)	0.203	1.84	(0.92-3.68)	0.08
Interaction group neoaduvant treatment		0.015			0.149	

*[2] Adjusted for age, stage, grade, lymphovascular invasion, chemotherapy, hormones receptors, and participation to clinical trial. The global model is also adjusted for neoadjuvant treatment.