MORNING CHRONOTYPE IS A PROTECTIVE FACTOR AGAINST CHEMOTHERAPY-INDUCED HOT FLASHES IN PREMENOPAUSAL WOMEN WITH BREAST CANCER

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OBJECTIVE

- **Adjuvant chemotherapy in patients with breast cancer often causes hot flashes, impairing quality of life. However, the psychiatric factors associated with the development of chemotherapy-induced hot flashes (CIHF) remain undetermined.**
- **The purpose of this study was to investigate whether chronotype was associated with the incidence of CIHF.**

METHODS

- **A total of 119 premenopausal women with early-stage breast cancer awaiting adjuvant chemotherapy after surgery without hot-flashes were included.**
- **The presence of CIHF was defined as having moderate-to-high level of hot flashes symptom by the hot flashes subscale in the Menopause Rating Scale, at 6 months after the completion of chemotherapy.**
- **Chronotype (morning/intermediate/evening) was assessed with the Composite Scale of Morningness before adjuvant chemotherapy.**
- **To examine the association between chronotype and CIHF, we built logistic regression models, adjusting for age, body mass index, sleep quality, and radiation therapy.**

RESULTS

Table 1. Comparison of normal vs. hot-flashes group 6 months after completion of chemotherapy

Characteristics	Normal (n=59)	Hot-flashes (n=60)	<i>p</i> value
	Mean ± SD or N (%)	Mean ± SD or N (%)	
Age	43.1 ± 5.7	43.1 ± 6.1	0.964
Age ≥ 50 years	9 (15.3%)	13 (21.7%)	0.506
BMI, kg/m2	22.4 ± 2.7	22.5 ± 2.9	0.866
BMI ≥25 kg/m2	17 (30.9%)	24 (40.7%)	0.373
Married	48 (81.4%)	46 (76.7%)	0.687
College graduates or higher	34 (57.6%)	36 (60.0%)	0.939
Employment			0.713
Homemaker	30 (50.8%)	27 (45.8%)	
Work place	29 (49.2%)	32 (54.2%)	
One alcoholic drinks per week	10 (16.9%)	14 (23.3%)	0.523
History of smoking	6 (10.2%)	4 (6.7%)	0.720
Disease stage			0.269
I	18 (30.5%)	21 (35.0%)	
II	33 (55.9%)	36 (60.0%)	
III	8 (13.6%)	3 (5.0%)	
Operation			0.150
BCS	36 (61.0%)	45 (75.0%)	
TM	23 (39.0%)	15 (25.0%)	
Radiation therapy	41 (69.5%)	51 (85.0%)	0.072
Chemotherapy			0.935
AC.D	27 (45.8%)	26 (43.3%)	
FAC	32 (54.2%)	34 (56.7%)	
Hormone therapy	45 (76.3%)	45 (75.0%)	1.000
Chronotype			0.067
Intermediate	11 (18.6%)	16 (26.7%)	
Morning	26 (44.1%)	33 (55.0%)	
Evening	22 (37.3%)	11 (18.3%)	
PSQI	5.0 ± 2.9	6.6 ± 3.8	0.014
Good sleep	51 (89.5%)	44 (75.9%)	0.093
Poor sleep	6 (10.5%)	14 (24.1%)	
HADS-D	5.8 ± 3.8	6.8 ± 3.5	0.134
Not depressed	39 (66.1%)	39 (65.0%)	1.000
Depressed	20 (33.9%)	21 (35.0%)	
HADS-A	5.6 ± 3.3	6.5 ± 3.8	0.159
Not anxious	42 (71.2%)	42 (70.0%)	1.000
Anxious	17 (28.8%)	18 (30.0%)	

Abbreviations: AC-D, adriamycin/cyclophosphamide and docetaxel; BCS, breast-conserving surgery; BMI, body mass index; FAC, fluorouracil/adriamycin/cyclophosphamide; HADS, Hospital Anxiety and Depression Scale (HADS-D and HADS-A: subscales for depression and anxiety, respectively); PSQI, Pittsburgh Sleep Quality Index; TM, total mastectomy

Table 2. Univariate analyses of predictors for chemotherapy induced hot-flashes

Factors	Univariate analyses	
	OR (95% CI)	<i>p</i> value
Age at baseline		
< 50 years	1.00 (reference)	
≥ 50 years	1.54 (0.61-4.04)	0.370
BMI, kg/m2		
< 23 kg/m2	1.00 (reference)	
≥ 23 kg/m2	1.53 (0.71-3.36)	0.279
Stage of disease		
I	1.00 (reference)	
II	0.94 (0.42-2.06)	0.867
III	0.32 (0.06-1.30)	0.130
Operation		
BCS	1.00 (reference)	
TM	0.52 (0.23-1.13)	0.104
Radiation therapy		
No	1.00 (reference)	
Yes	2.49 (1.03-6.35)	0.047
Chemotherapy		
AC.D	1.00 (reference)	
FAC	1.10 (0.53-2.28)	0.790
Hormone Therapy		
No	1.00 (reference)	
Yes	0.93 (0.40-2.16)	0.872
Chronotype		
Intermediate	1.00 (reference)	
Morning	0.37 (0.16-0.94)	0.040
Evening	1.15 (0.46-2.94)	0.773
Sleep quality		
Good	1.00 (reference)	
Poor	2.70 (0.99-8.19)	0.060
Depression		
Not depressed	1.00 (reference)	
Depressed	1.05 (0.49-2.25)	0.899
Anxiety		
Not anxious	1.00 (reference)	
Anxious	1.06 (0.48-2.34)	0.887

Table 3. Multivariate analyses of predictors for chemotherapy induced hot-flashes

Factors	Multivariate analyses	
	OR (95% CI)	<i>p</i> value
Age at baseline		
< 50 years	1.00 (reference)	
≥ 50 years	2.58 (0.82-9.07)	0.117
BMI, kg/m2		
< 23 kg/m2	1.00 (reference)	
≥ 23 kg/m2	1.45 (0.60-3.55)	0.406
Radiation therapy		
No	1.00 (reference)	
Yes	2.69 (0.99-7.93)	0.060
Chronotype		
Intermediate	1.00 (reference)	
Morning	0.37 (0.13-0.96)	0.045
Evening	1.23 (0.44-3.54)	0.692
Sleep quality		
Good	1.00 (reference)	
Poor	1.95 (0.62-6.87)	0.060

- **CIHF occurred in 50.4% of participants.**
- **The morning type was inversely associated with CIHF (reference: intermediate type, odds ratio [OR], 0.37; 95% confidence interval [CI], 0.16–0.94; p = 0.040) in the univariate model.**
- **The association remained significant (OR, 0.37; CI, 0.13–0.96; p = 0.045) after adjusting for age, body mass index, sleep quality, and radiation therapy.**

DISCUSSION

- **The morning chronotype is a protective factor against the development of CIHF in patient with breast cancer.**
- **Chronotypes should be assessed and considered in the prediction and management of CIHF.**

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