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ORIGINAL ARTICLE

Evaluation of sleep pattern disorders in breast cancer patients receiving adjuvant treatment (chemotherapy and/or radiotherapy) using polysomnography

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Summary

Purpose: *To assess sleep disturbance patterns in breast cancer patients receiving adjuvant radiotherapy and/or chemotherapy in comparison to normal subjects, and their impact on quality of life.*

Methods: *Seventy-four histologically proven breast cancer patients of both genders, aged 30 to 65 years, were classified into 2 groups.*
First group: 26 patients with breast cancer before receiving any treatment.
Second group: 48 breast cancer patients, subdivided into group A (24 patients with adjuvant chemotherapy), and group B (24 patients with adjuvant radiotherapy).
A control group consisted of 24 healthy individuals matched in age and sex with patient groups.
Clinical assessment of sleep was done using the Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS) and one night Polysomnography (NPSG).

Results: *No statistically significant difference regarding age and sex was found compared to control group. The severity of insomnia (ISI) was 29.2%, 4.2%, 7.7% and 0% for patients who received chemotherapy and/or radiotherapy, and comparison of patients without treatment and the control group showed statistical significance. Excessive daytime sleepiness was 37.5%, 25%, 26.9% and 0% for patients who received chemotherapy and/or radiotherapy, before receiving treatment, and the control groups respectively, the difference been significant.*
Comparison of patients who received treatment with those who did not and the control groups showed significant shortening of total sleep time, decrease of sleep efficiency and lengthening of sleep latency.
Significant lengthening in stage 2 of non-rapid eye movement (NREM), while insignificant lengthening in stages 1, 3 and 4 of NREM sleep was noted. Significant reduction of rapid eye movement (REM) and total sleep time percentage were observed. Sleep apnea was insignificantly more common in breast cancer patients compared to healthy controls.

Conclusion: *Sleep-related changes in breast cancer patients should be used in planning best supportive care.*

Key words: *breast cancer, non-rapid eye movement, total sleep time, insomnia severity index*

Introduction

One of the major health problems in humans are sleep disturbances including insufficient sleep duration, poor sleep quality and failure to initiate sleep with resulting increase in health care costs. Sleep pattern disturbances with their drawbacks are more important in cancer patients [2-4].

Thirty to 93% of cancer patients suffer from sleep disturbances [5]. Breast cancer is a growing problem worldwide. The effect of diagnosis, chemotherapy, radiotherapy and hormonal treatment on sleep disturbances for better quality of life is attracting more research [6,7]. It is important to un-

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derstand cancer-related mental health symptoms in order to improve treatment and prevention efforts [6-8].

In cancer patients under chemotherapy, flattened diurnal cortisol slopes are frequently associated with sleep disturbances [9], while during radiotherapy, acute radiation sickness with its fatigue component occur and may persist for long time after radiotherapy resulting in sleep disturbances [10].

Sleep disturbances are a neglected problem in cancer, including breast cancer patients, contributing to administration of inadequate treatment. So, upgrading the significance of this major problem will indirectly help defining the right treatment.

The aim of this study was to assess sleep disturbance patterns in breast cancer patients receiving adjuvant radiotherapy and/or chemotherapy in comparison with normal subjects and evaluate their impact on quality of life.

Methods

This study was carried out in the Oncology and Neurology departments in Tanta University Hospital from February 2013 to June 2016, after taking written informed consent from the patients and/or 1st degree relatives.

Eligibility criteria included age more than 21 years, non-metastatic breast cancer according to TNM (8th Edn) [11], histopathologically proved breast cancer, adequate hematological, heart, liver and kidney functions with no serious medical problems.

Patients aged more than 75 years, body mass index (BMI) more than 30, presented with stage IV (metastatic) breast cancer, pregnancy, underlying serious medical problems were the main exclusion criteria. Patients who had dementia, altered mental status or any psychiatric condition that would prohibit the understanding test were also excluded.

The patients were collected before treatment and after either adjuvant chemotherapy or radiotherapy.

Seventy-four histologically confirmed breast cancer patients aged from 30 to 65 years of both genders and treated at the Oncology and Neurology Departments from February 2013 to June 2016 were classified into 2 groups:

First group: 26 patients with breast cancer before receiving any treatment.

Second group: 48 breast cancer patients subdivided into group (A) including 24 patients receiving chemotherapy and group (B) including 24 patients receiving radiotherapy.

Included were also 24 healthy individuals as control group matched in age and sex with the patient groups.

Patient demographic data were collected with special inquiry about vomiting, diarrhea, anxiety, pain, dyspnea, depression, and fatigue. Routine laboratory examinations including liver, renal, fasting postprandial blood sugar were done to exclude hepatic, renal and metabolic disease.

Metastatic work up including chest X ray, abdominopelvic ultrasound, bone scan, CA15.3 and CA 125 tumor markers and in some cases PET-CT scan were carried out.

Table 1. Main characteristics of all 74 breast cancer patients

Characteristics	*Control*	*Before treatment*	*Chemotherapy*	*Radiotherapy*	*F test*	*p value*	*Post Hock test*			
Age (yrs)										
Range	35-60	30-59	33-65	32-59	1.282	0.285				
Mean	46.58	45.50	42.67	43.50						
SD	7.92	8.80	6.81	7.47						
Sex, n(%)										
Male	9 (37.5)	9 (34.6)	4 (16.7)	1 (4.2)	10.026	0.018				
Female	15 (62.5)	17 (65.4)	20 (83.3)	23 (95.8)						
Stage 1 NREM										
Range	3-8	4-15	3-23	4-16	2.752	0.047	P1	0.255	P4	0.773
Mean	5.79	7.58	8.50	7.79			P2	0.035	P5	0.996
SD	1.50	2.86	5.29	2.86			P3	0.182	P6	0.888
Stage 2 NREM										
Range	49-59	45-70	49-85	44-72	17.458	0.001	P1	0.001	P4	0.003
Mean	53.67	60.88	67.63	59.92			P2	0.001	P5	0.956
SD	2.58	5.69	10.53	5.54			P3	0.009	P6	0.001
Stage 3 NREM										
Range	14-20	10-26	9-26	11-27	1.048	0.375				
Mean	17.79	16.27	15.79	17.04						
SD	1.91	4.02	5.63	4.46						

P1: Control & cancer before treatment, P2: Control & chemotherapy (A), P3: Control & radiotherapy (B), P4: Cancer before treatment & chemotherapy (A), P5: Cancer before treatment & radiotherapy (B), P6: Chemotherapy (A) & radiotherapy (B), NREM: non rapid eye movement

Clinical assessment for sleep was done to assess the severity of both nighttime and daytime components of insomnia. Nature, severity, and impact of insomnia were evaluated using the insomnia severity index (ISI). This index evaluates 7 items including sleep onset, maintainace, awakening early in the morning, sleep discomfort, daytime functional activities due to sleep problem, detection of the problem by other persons and psychomotor disturbance due to sleep disturbance during the last month. Each item scored as follows: 0=no problem; 4=very severe problem, producing a final score ranging from 0 to 28. Mild, moderate and severe insomnia were 0-7, 15-21 and 22-28, respectively [12].

Epworth Sleepiness Scale (ESS) is also used for measuring excessive daytime sleepiness (EDS). The scale is formed from 8 items. To detect the different degree of somnificity, patients were asked to report their usual chances of falling asleep in 8 different situation e.g. 'sitting and reading' or 'watching TV' on a 4-point scale. The scale points were 0, 1, 2, 3, 4 to indicate would never doze and slight, moderate or severe opportunity of dozing, respectively. The results are summed to produce final score from 0 to 24, with higher scores indicating greater daytime sleepiness. Excessive daytime sleepiness for scores ≥11 is generally considered abnormal [13].

All patients underwent full night polysomnography (NPSG). Filmmaking from 17 channels were used to record the electric activity of brain (EEG) , ocular, and cardiac muscular activity of chin and lower extremity , nasooral airflow across the nasal and oral cavity, chest and abdominal muscle exertion and plus oximeter for measuring oxygen saturation [14].

Accredited sleep laboratory in the Neurology Department, Tanta University Hospital, was used to evaluate all the patients enrolled in the study.

The electroencephalograph (EEG) was divided in REM and NREM. The latter is subdivided into 4 stages [15].

Sleep was scored according to American Academy of Sleep Medicine criteria. We also evaluated the total sleep time, sleep onset latency (SOL), sleep efficiency (SE) and time spent in sleep wakefulness (WASO) [16].

Statistics

Statistical analyses of the present study were conducted using the mean, standard deviation and chi-square test using SPSS V.19 statistical software package [17]. Independent sample t-tests and also x^2 and Fisher's exact tests were used to evaluate differences in demographic and clinical characteristics between breast cancer patients before and after treatment with the control group. P<0.05 was considered statistically significant.

Results

No statistically significant difference was noted regarding age and sex between treatment groups compared to control group. Significant lengthening in stage 2 NREM in breast cancer patients was seen, while insignificant lengthening in stages 1 and stage 3 of NREM sleep was reported, as can be seen in Table 1.

In breast cancer patients, significant shortening of total sleep time, decrease of sleep efficiency, lengthening of sleep latency and rise of wakefulness after sleep onset as compared to healthy controls were registered (p=0.001). Significant reduction of REM and total sleep time percentage was

Table 2. Correlation of control group and breast cancer patients with TST, REM , REM latency and SL

	Control	*Before treatment*	*Chemotherapy*	*Radiotherapy*	*F test*	*p value*	*Post Hock test*			
							p value		*p value*	
TST										
Range	420-482	299-454	280-470	301-471	10.565	0.001	P1	0.001	P4	0.324
Mean	451.71	403.08	381.46	404.83			P2	0.001	P5	0.999
SD	18.97	43.62	61.57	43.92			P3	0.003	P6	0.273
REM										
Range	20-25	14-25	7-27	13-25	30.377	0.001	P1	0.001	P4	0.001
Mean	22.83	17.69	12.71	17.83			P2	0.001	P5	0.999
SD	1.61	3.28	5.41	3.41			P3	0.001	P6	0.001
REM latency										
Range	65-403	68-257	59-333	68-257	2.023	0.116				
Mean	97.17	116.42	139.79	125.54						
SD	67.35	48.81	74.55	52.82						
SL										
Range	15-29	12-73	8-123	12-75	6.671	0.001	P1	0.042	P4	0.264
Mean	21.33	38.62	50.43	38.92			P2	0.001	P5	0.999
SD	4.67	18.35	37.10	18.76			P3	0.043	P6	0.303

TST: total sleep time, REM: rapid eye movement, SL: sleep latency. For P1-P6 see footnote of Table 1

observed. Sleep apnea was insignificantly more common in breast cancer patients as compared to healthy controls (p=0.001; Tables 2 and 3.

Table 4 shows that the severity of insomnia (ISI) was 29.2%, 4.2%, 7.7% and 0% in chemotherapy and radiotherapy in breast cancer patients before treatment and the control group respectively (p=0.004).

Epgrowth sleepiness scale (ESS) was 37.5%, 25% and 26.9%, 0% in chemotherapy and radiotherapy of breast cancer patients without treatment and the control group respectively (p=0.0115).

Discussion

Between 20 and 70% of breast cancer patients suffer of insomnia [18]. Insomnia continues to be a serious problem affecting quality of life even after the end of treatment [19].

The aim of this study was to evaluate sleep pattern disorders in breast cancer patients before treatment and after adjuvant chemotherapy and/or radiotherapy. Sleep disorders were more pronounced among breast cancer patients compared to control group in our study.

In this study, the mean age of the studied groups was not different, and was similar to that reported by Julie et al. in 2008 [20], but it differed from that reported by Davidson et al. in 2002 [21].

In our study, ISI showed that the frequency of insomnia in breast cancer patients was significantly higher than in controls. According to treatment groups insomnia was more common in patients after adjuvant chemotherapy than patients who did not receive chemotherapy, and this was in concordance with the reports of other authors [22-25].

Among breast cancer patients the evaluation of ESS scores showed that EDS was markedly higher

Table 3. Correlation of control group and breast cancer patients with WASO, SE, apnea and ISI

	Control	*Before treatment*	*Chemotherapy*	*Radiotherapy*	*F test*	*p value*	*Post Hock test*	
WASO								
Range	15-30	24-68	22-95	26-75	25.414	0.001	P1	0.001
Mean	23.08	46.85	58.25	50.88			P2	0.001
SD	5.07	13.75	22.26	12.88			P3	0.001
SE								
Range	85-92	68-89	49-88.6	70-89	13.622	0.001	P1	0.006
Mean	87.79	81.69	76.03	81.00			P2	0.001
SD	1.86	5.06	10.49	5.12			P3	0.002
Apnea								
Range	2-6	3-6	2-9	2-9	1.116	0.346		
Mean	3.88	4.27	4.67	4.21				
SD	0.99	1.04	2.08	1.67				
ISI								
Range	1-9	4-15	3-23	3-15	13.024	0.001	P1	0.002
Mean	4.46	8.58	11.42	7.21			P2	0.001
SD	2.32	3.13	5.82	3.66			P3	0.080

WASO: wakefulness after sleep onset, SE: sleep efficiency, ISI: insomnia severity index. For P1-P3 see footnote of Table 1

Table 4. Correlation of control group and breast cancer patient with ISI and ESS

			Control	*Before treatment*	*Chemotherapy*	*Radiotherapy*	x^2	*p value*
ISI	≤ 14	N	24	24	17	23	13.279	0.004
		%	100.0	92.3	70.8	95.8		
	> 14	N	0	2	7	1		
		%	0	7.7	29.2	4.2		
ESS	< 11	N	24	19	15	18	10.459	0.015
		%	100.0	73.1	62.5	75.0		
	> 11	N	0	7	9	6		
		%	0	26.9	37.5	25.0		

ISI: insomnia severity index, ESS: Epworth Sleepiness Scale

among all breast cancer groups and it was especially higher in the chemotherapy group than other similar studies reported by other authors [22-25].

Polysomnography study showed marked reduction in total sleep time, sleep efficiency and REM sleep in breast cancer patients than in controls. In addition, they had significant prolonged sleep onset latency and WASO when compared to control group. Significant lengthening in stage 2 NREM in breast cancer patients was noted, while insignificant lengthening in stages 1 and 3 NREM sleep were reported and this was similar to what many authors have reported [22-25]. Also there was insignificantly increased sleep apnea in breast patients as compared to healthy controls [26].

Sleep problems are underestimated in breast cancer patients, and this study highlighted the need of more research on this topic that directly or indirectly impacts the quality of life and survival of patients. Actigraphy, a non-invasive method of monitoring human rest/activity cycles instead of polysomnography in studying sleep disturbances allows the free movement of patients and also longer duration of the study.

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Conflict of interests

The authors declare no conflict of interests.

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