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# The effect of auricular acupressure on sleep in breast cancer patients undergoing chemotherapy: A single-blind, randomized controlled trial☆

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## 1. Introduction

According to the statistics in the 2012 Global Burden of Cancer (GLOBOCAN) database released by the World Health Organization (WHO), breast cancer is the most common female cancer diagnosed worldwide. > 1.7 million cases are diagnosed annually and incidence and mortality rates are increasing (Ferlay et al., 2015). The five-year survival rate was 91.3% in 2012, which was higher than that of other cancers, due to early screening and improvements in treatment quality for Korean patients with breast cancer (National Cancer Center, 2016). Various breast cancer treatments are available to prevent recurrence, such as postoperative chemotherapy and radiotherapy (Siegel et al., 2012). Among these, chemotherapy is a long-term and repetitive treatment that causes damage to normal cells as well as cancer cells; various side effects include fatigue, pain, nausea, vomiting, sleep disturbances, and depression (Hsu et al., 2017; Kim, Barsevick, Beck, & Dudley, 2012). Among these side effects, sleep problems are becoming increasingly important since sleep affects morbidity during and after treatment (Palesh et al., 2013).

The autonomic nervous system controls sleep in humans (Buckley & Schatzberg, 2005; Dowd, Goldman, & Weinstein, 2011; Roth, Roehrs, & Pies, 2007) and is also involved in the immune response. Sleep affects the ability of the immune system to control homeostasis; furthermore, when a person experiences stress, the autonomic nervous system is activated causing cytokines like interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α), among others, to be secreted from the vagus nerve (Alfaro et al., 2014; Irwin et al., 2014; Irwin, Olmstead, Ganz, & Haque, 2013). Patients with breast cancer and insomnia have higher levels of fatigue and a lower quality of life (Dirksen, Belyea, & Epstein, 2009); sleep disturbances remain unresolved even after the treatment phase ends, affecting the patient's recovery from the treatment and survival (Matthews et al., 2014). Sleep disturbances are characterized by shortened sleeping hours at night, difficulty sleeping, increased sleep latency, increased daytime sleepiness, and frequently interrupted sleep (Ancoli-Israel et al., 2014; Simeit, Deck, & Conta-Marx, 2004). Currently, many patients with cancer endure these sleep disorders; however, health personnel do not provide proper treatment or intervention (Palesh et al., 2013). Therefore, it is necessary to promote interventions that healthcare personnel can easily apply in clinical settings with fewer side effects.

Auricular acupuncture, a form of acupuncture therapy that stimulates certain areas of the ear canal (Oleson, 2013), was first introduced in 1950 (Wang, Peloquin, & Kain, 2001). Auricular pressure, which comes from the use of auricular acupuncture, uses seeds, magnets, and stones rather than needles to stimulate certain auricular reflective points. Practitioners believe auricular reflective points connect to the internal organs of the body (Oleson, 2013; Suen & Wong, 2007). Also, auricular therapy is convenient, noninvasive, and has few side effects (Kung, Yang, Chiu, & Kuo, 2011; Yeh, Chien, Glick, van Londen, & Bovbjerg, 2015).

Chemotherapy must be accompanied by interventions to counteract the side effects; healthcare practitioners in clinical settings can easily apply auricular therapy, which is a complementary alternative medicine. However, the effectiveness of auricular therapy in improving sleep quality for patients with breast cancer needs to be evaluated. Therefore, using objective assessment tools, such as blood count tests and sleep activity devices, in addition to a subjective questionnaire of patients with breast cancer who received chemotherapy, this study aimed to investigate the effects of auricular therapy on sleep quality in patients with breast cancer.

## 2. Materials and methods

### 2.1. Study design

This randomized clinical trial (RCT) was designed to assess the effectiveness of auricular acupressure on sleep in patients with breast cancer undergoing chemotherapy. Participants were randomized into two groups: (i) an experimental group that received auricular pressure on specific acupoints traditionally considered as beneficial for sleep

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disturbances, and (ii) a control group that received placebo auricular pressure on points not traditionally associated with improving sleep disturbance. The duration of the treatment was six weeks.

### 2.2. Participants and setting

This study was conducted at Ewha Womans University Hospital between May 1, 2016 and May 15, 2017. The criteria for participant selection were as follows: women aged 19 to 65 years who underwent anthracycline chemotherapy with a three-week cycle after breast cancer surgery, an Insomnia Severity Index (ISI) score of eight or more, and the absence of inflammatory lesions or external wounds on the ears of the patient. The ISI is an instrument measuring insomnia levels, developed by Morin (Morin & Benca, 2012). The Korean version of the ISI, the ISI-K, was used in our study (Cho, Song, & Morin, 2014). Individuals whose cancer had metastasized to other organs and patients who were taking sleeping pills or antidepressant drugs were excluded.

### 2.3. Sample size

As this study was an exploratory study to assess the effects of auricular acupressure on sleep in breast cancer patients, a traditional sample size calculation was not performed. A total of 72 potential participants were recruited, though 26 were eliminated after screening, More speicifically, three patients were excluded because they were, 65 years old or older and eight had an ISI score of less than eight, for a total of 11 participants who were unsuitable for the selection criteria, and 15 dropped out due to personal reasons. Therefore, 46 participants remained at the beginning of the study. This study protocol and written informed consent were approved by the Institutional Review Board of Ewha Womans University Hospital (EUMC 2016-03-025-001). All participants provided written informed consent.

### 2.4. Randomization

To randomly sort patients into groups, a table of random numbers generated by the Random Allocation Software version 2.0.0 program was used. The participants were allocated to the experimental groups by stratified, block randomization, with a block size of two. After participant enrollment, patients were randomly assigned to the two groups in a 1:1 ratio. The investigator who generated the random number sequence had no contact with the participants in the trial. The participants were not informed of their group allocation.

### 2.5. Interventions

#### 2.5.1. Preliminary investigation

Study participants were patients with breast cancer receiving chemotherapy. A previous study showed that sleep disorders were further exacerbated following chemotherapy (Sanford et al., 2013).; hence, this preliminary investigation was performed on the day participants were hospitalized for chemotherapy, which was a day prior to chemotherapy administration. On the day of the preliminary investigation, insomnia levels were measured using a screening instrument (ISI-K) and participants were assessed to ensure they met the requirements for sleep quality, using the Pittsburgh Sleep Quality Index (PSQI). The primary outcome measurement, sleep quality rating, was assessed using the PSQI. Secondary outcomes included IL-6, TNF-α, cortisol, and C-reactive protein (CRP) values as well as sleep quantity measurements obtained using a Fitbit tracker device. The Fitbit tracker measured sleep activity and was worn by participants at the time of admission and removed after 24 h. To assess sleep quality and quantity, total sleep time, sleep efficiency, sleep latency, and number of awakenings during sleep were measured. Each patient wore a Fitbit Charge HR™ (FitBit® Inc., San Francisco, California, USA) on her wrist.

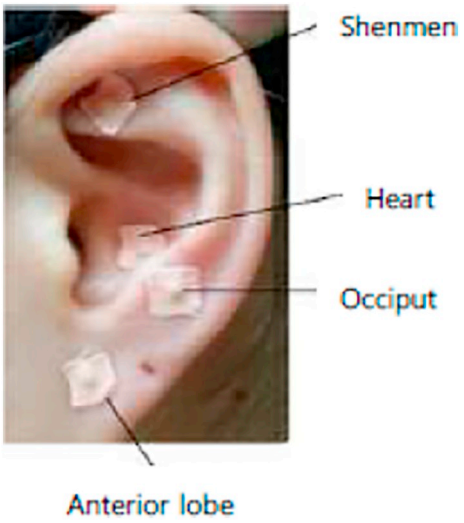


**Fig. 1.** Auricular points of the experimental group.

#### 2.5.2. Experimental intervention

Auricular therapy or placebo auricular pressure was applied to the experimental group and the control group, respectively, for a total of six weeks. The auricular therapy, consisting of vaccaria seeds, was administered to only one ear of each patient in the experimental group at a total of four points: the Shenmen, heart, anterior lobe, and occiput (Fig. 1), where the placebo control group received the therapy at four points of Helix located in the auricle (Fig. 2). These points were chosen for the placebo group because the auricle is clearly located far from the inner ear area and a previous study reported it was clearly located in a different area from the auricular points of the experiment group (Sjöling, Rolleri, & Englund, 2008). According to a study conducted by Sjöling et al. (2008) auricular therapy was performed on five reflective points at the auricle; however, in this study, the therapy was provided to four points—the same number of points offered to the experimental group—to maintain single blindness.

An auricular seal was applied for six days at a time because if the therapy is applied to only one ear, excessive pressure can be applied. Therefore, after an application, all seeds were removed and new seeds were alternately applied to the other ear (Li, Lee, & Suen, 2014). This therapy was performed six times a week for six weeks. Also, participants were asked to press the seed-applied areas with her hand for one minute before going to bed (Hughes, Towler, Storey, Wheeler, & Molassiotis, 2015).

#### 2.5.3. Interim investigation

The interim investigation for both experimental and control groups

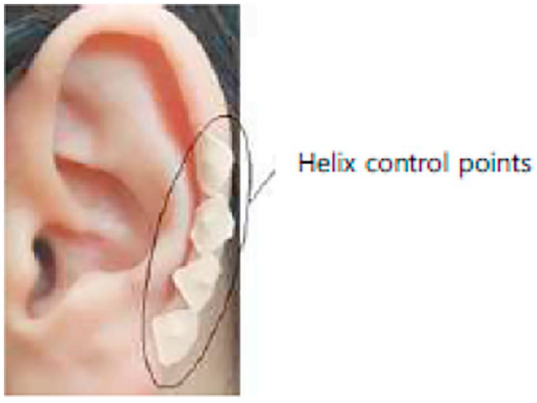


**Fig. 2.** Auricular points of the control group.

occurred during the third week of the experiment, when the patients began their three-week cycle of chemotherapy, in the same manner as the preliminary investigation. The amount of sleep was measured using the PSQI. Total sleep time, sleep efficiency, sleep latency, and number of awakenings during sleep were measured by a Fitbit tracker, worn for 24 h, as an objective measurement tool for sleep quality and quantity.

#### 2.5.4. Post investigation

The post investigation for both experimental and control groups was performed during the sixth week of the experiment, on the day of hospitalization for chemotherapy treatment, in the same manner as the preliminary and interim investigations. The day before chemotherapy, the intervention (auricular therapy or placebo therapy) was administered. In the post investigation, the amount of sleep was measured using the PSQI whereas total sleep time, sleep efficiency, sleep latency, and number of awakenings during sleep was measured with a Fitbit tracker for 24 h. In addition, blood tests for IL-6, TNF-α, cortisol, and CR*P* values were conducted to further analyze sleep quality.

#### 2.5.5. Instruments

Sleep quality was assessed using PSQI-K (Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989; Sohn, Kim, Lee, & Cho, 2012); values were calculated based on patient responses to 19 questions evaluating sleep quality during the past month. The total PSQI score represents data from seven subcategories: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction ($p < .05$). At the time of each instrument's development, the reliability determined by the Cronbach's α rating was 0.83 (King et al., 2015) and 0.84 (Sohn et al., 2012) for the original PSQI instrument and the Korean version, PSQI-K, respectively. The Cronbach's α rating for the PSQI-K version used in this study was 0.81.

### 2.6. Statistical analysis

The collected data were analyzed using SPSS WIN 23.0 and statistical significance was set at $p < .05$. The homogeneity of the demographic characteristics and dependent variables between the two groups were examined using a chi-square test, a Fisher's exact test, and an independent *t*-test. Changes in the quality and amount of sleep between the two groups before, during, and after the experiment were evaluated using a repeated measures ANOVA. The difference in the quality of sleep on the third and sixth weeks compared to the quality of sleep before the experiment was assessed using an independent *t*-test. Variations in the amount of sleep on the third and sixth weeks compared to the amount of sleep before the experiment were measured using a nonparametric method: the Mann–Whitney *U* test.

The difference in blood test results for IL-6, TNF-α, cortisol, and CRP levels between the two groups was analyzed using the Mann–Whitney U test whereas the Wilcoxon signed ranks test was used to assess blood test changes within groups.

## 3. Results

### 3.1. Participant characteristics

The 46 participants available at the beginning of the study were randomly and evenly assigned to the experimental and control groups (23 each). Three patients in the experimental group and two in the control group dropped out during the study. Therefore, a total of 41 participants comprised the final experimental group (20) and control group (21) and completed study participation (Fig. 3).

### 3.2. Verification of homogeneity between the experimental and control group

The homogeneity test did not reveal statistically significant differences between the experimental and control groups (Table 1). Demographic and disease-related characteristics of the 46 original participants, including the five participants who left during the study, were examined before providing the intervention and their homogeneity was verified. Basic characteristics did not exhibit any differences; thus, selection bias did not affect study results.

### 3.3. Pittsburgh sleep quality index scores

The quality of sleep was statistically significant between the experimental and control groups ($F = 4.152$, $p = .048$), indicating a significant difference in average sleep quality between the groups. Also, a statistically significant difference was revealed in quality of sleep measured before intervention, three weeks after initiating the intervention, and six weeks following the intervention ($F = 12.891$, $p < .001$).

There was a statistically significant difference between groups depending on time change ($F = 5.104$, $p = .008$) (Table 2).

### 3.4. Fitbit data

No significant differences arose in total sleep time, sleep efficiency, sleep latency, or number of times awakened during sleep. Thus, we rejected the hypothesis that sleep quality and quantity in the experimental group would be different compared to the placebo control group.

### 3.5. Blood cytokines and cortisol

A significant difference in IL-6 level between the experimental and control group at the preliminary and post investigation was determined ($Z = -3.026$, $p = .002$). Also, there were significant differences in IL-6 and TNF-α. Nonetheless, no significant differences were found in cortisol and CRP levels (Table 3).

## 4. Discussion

Scientific studies must demonstrate treatment superiority over placebo effects (Aronson, 2011; Ernst, 2010) for them to be considered effective. The increased internal validity of this study due to its single blind, randomized design ensured a robust scientific analysis and more objective data. Our results confirmed that the quality of sleep for patients with breast cancer receiving chemotherapy was lower than patients not receiving chemotherapy. The average sleep quality during this study, 9.2 ± 4.1 according to the PSQI rating, was higher than the sleep quality rating before the intervention and higher than patients whose breast cancer treatment had been terminated for more than three months (Otte, Carpenter, Zhong, & Johnstone, 2011); however, it was similar to sleep quality data in cancer survivors before the intervention (Mustian et al., 2013). The PSQI score of the experimental group before the intervention was 11.50 ± 3.08; this is consistent with the reports from previous studies indicating that sleep disorders were more severe during while patients were receiving chemotherapy.

Previous studies have reported scores of 14.5 ± 3.4 points in hemodialysis patients who were diagnosed with insomnia before the application of auricular therapy (Wu, Zou, Liu, Wu, & Lin, 2014) and 13.7 ± 0.4 points in postmenopausal women diagnosed with insomnia (Kung et al., 2011). Since our study included patients with borderline insomnia and excluded patients taking sleeping pills, we believe patients with severe insomnia were omitted.

According to a meta-analysis of the effects of acupressure, auricular therapy, and reflexology on insomnia treatment, the difference in

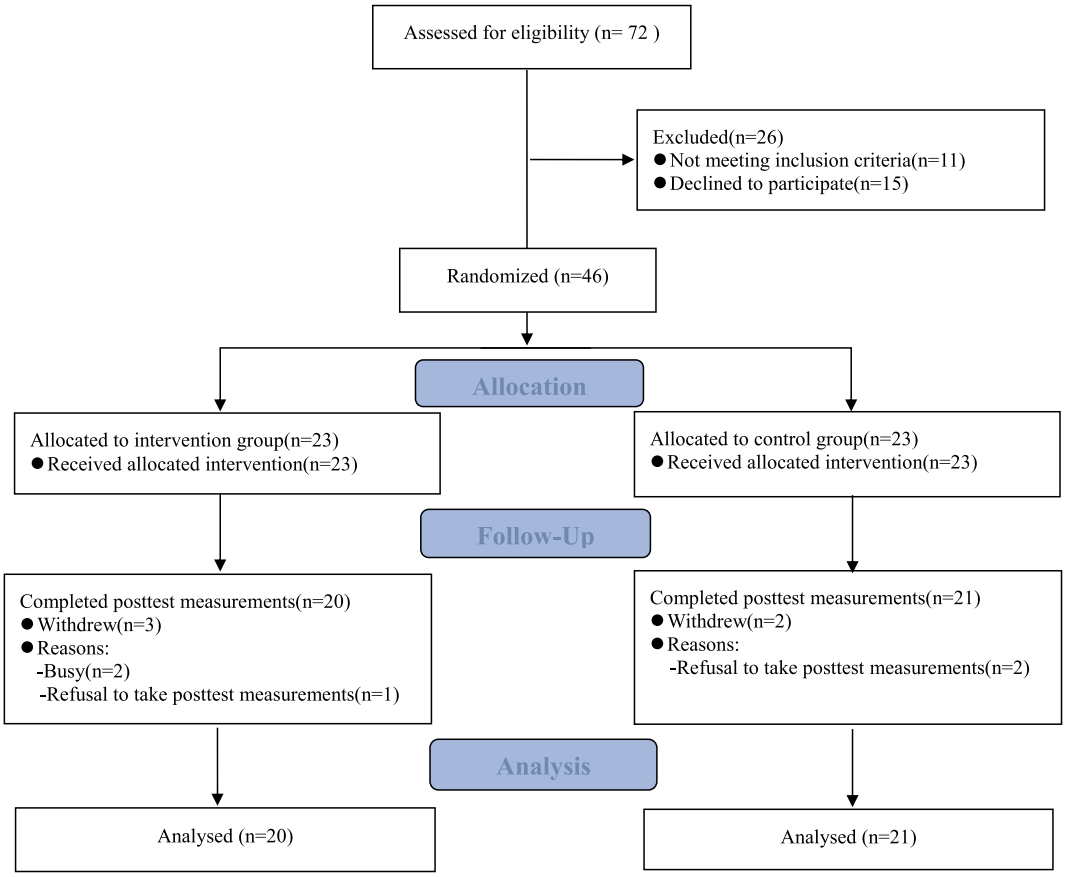


**Fig. 3.** CONSORT diagram: flow of participants through the study.

efficacy between the experimental and control group was evident, but not significant (Yeung et al., 2012). In the study by King et al., war veterans in the experimental group who were diagnosed with post-traumatic stress disorder received auricular therapy for five weeks and the control group did not receive any treatment (King et al., 2015); the average PSQI rating of the experimental group decreased by 3.3 points while the control group only decreased by 1.2 points; after six weeks of treatment, the average score for the experimental group decreased by 3.8 points and by 0.85 points for the control group. However, the King et al. study did not control the use of sleeping pills and the control group did not take any treatment to evaluate the placebo effect (King et al., 2015). Our study was more rigorous, since it was a single-blind study that accounted for the placebo effect and excluded patients taking sleeping pills or antidepressants. In the control group, however, no difference in sleep quality arose in the third week, but the decrease of 0.85 points in the PSQI-K rating for the sixth week implies that the placebo effect was not completely prevented. In addition, environmental factors should be also considered, as control group patients' rooms were quiet, relaxing, or provided psychologically relaxing music. Therefore, future researchers should control environmental factors.

Results from a previous study in which involving patients with breast cancer receiving chemotherapy, auricular therapy was applied for four weeks to five areas the shenmen, sympathetic point, back of the head, subcortex, and nervous breakdown points; the auricular therapy showed an effect in fatigue recovery, sleep disturbance, and pain (Yeh, Chien, Lin, Bovbjerg, & Van Londen, 2016). Nonetheless, in that study, the type of anticancer drug administered was not controlled and the age distribution of participants ranged from 29 to 84 years, which may have been impacted results due to the higher incidence of sleep disorders among elderly patients (Feinsilver, 2003; Kryger, Roth, & Dement, 2011). In contrast to that study, which failed to control for age and type of anticancer drugs, the present study had a smaller age range, from 19 to 65 years, and controlled the potential influence of different drug types by including only breast cancer patients receiving anthracycline chemotherapy.

The impact of auricular therapy on the blood index of patients with breast cancer was further analyzed by measuring cytokines IL-6 and TNF-α; these cytokine levels significantly decreased in the experimental group but there was no change in the control group after the intervention. Such a result is consistent with previous studies that reported increased cytokine levels in cases of sleep disorders (Doong et al., 2015; Irwin, Olmstead, & Carroll, 2016; Liu et al., 2012). In the Liu et al. study, IL-6 levels were 2.9 ± 3.9 pg/ml before chemotherapy and increased to 4.2 ± 3.1 pg/ml by the fourth chemotherapy session, which was approximately 12 weeks after the auricular therapy intervention (Liu et al., 2012). IL-6 levels decreased from 2.25 ± 1.81 pg/ml before applying auricular therapy to 0.98 ± 0.66 pg/ml at the sixth week of the intervention, demonstrating the effect of auricular therapy on sleep.

The CRP values of the experimental and control groups before the intervention were low— 0.28 mg/dl and 027 mg/dl, respectively—and did not change during the study; patients with severe sleep disturbances were not included and our six-week intervention period was shorter than other studies. Another study found a difference in TNF-α, IL-4, and IL-6 values depending on the fatigue level in the morning and afternoon (Dhruva et al., 2015), reaffirming the necessity to collect data in the same time frame to derive significant values.

In a study that examined cytokine changes among patients with breast cancer who incorporated Tai Chi into their treatment for 12 weeks, IL-6 and TNF-α levels significantly decreased in the experimental group, but CRP levels did not change (Irwin et al., 2014). Moreover, a study that assessed the prevalence of sleep disturbances, IL-6, and TNF-α levels in patients with breast cancer reported significantly

**Table 1**
Characteristics of the study participants at baseline (Study entry).

| Characteristics | Total($N$ = 41) | Intervention($n$ = 20) | Control($n$ = 21) | $P$ value |
|---|---|---|---|---|
| | n(%) | n(%) or M ± SD | n(%) or M ± SD | |
| Age(yr) | | | | |
| ≤39 | 10(24.4) | 4(9.8) | 6(14.6) | 0.852[b] |
| 40–49 | 19(46.3) | 10(24.4) | 9(22.0) | |
| 50–65 | 12(29.3) | 6(14.6) | 6(14.6) | |
| | 44.81 ± 8.34 | 45.05 ± 8.33 | 44.57 ± 8.34 | 0.855[a] |
| Educational level | | | | |
| ≥College graduate | 20(48.8) | 11(26.8) | 9(22.0) | 0.538 |
| ≤High school graduate | 21(51.2) | 9(22.0) | 12(29.3) | |
| Family structure | | | | |
| Nuclear family | 35(85.4) | 17(41.5) | 18(43.9) | 1.000[b] |
| Other | 6(14.0.6) | 3(7.3) | 3(7.3) | |
| Occupation status | | | | |
| Yes | 21(51.2) | 11(26.8) | 10(24.4) | 0.758 |
| No | 20(48.8) | 9(22.0) | 11(26.8) | |
| AC CTx cycle | | | | |
| 1–2 cycle | 37(90.2) | 19(46.3) | 18(43.9) | 0.606[b] |
| 3–4 cycle | 4(9.8) | 1(2.4) | 3(7.3) | |
| Type of surgery | | | | |
| Breast conserving | 30(73.2) | 16(39.0) | 14(34.1) | 0.484 |
| Mastectomy | 11(26.8) | 4(9.8) | 7(17.1) | |
| TNM stage | | | | |
| StageIA | 9(22.0) | 4(9.8) | 5(12.2) | 0.855[b] |
| Stage IIA | 13(31.7) | 7(17.1) | 6(14.6) | |
| Stage IIB | 9(22.0) | 5(12.2) | 4(9.8) | |
| Stage IIIA | 7(17.1) | 2(4.9) | 5(12.2) | |
| Stage IIIB | 1(2.4) | 1(2.4) | 0(0.0) | |
| Stage IIIC | 2(4.8) | 1(2.4) | 1(2.4) | |
| ER | | | | |
| Negative | 10(24.4) | 5(12.2) | 5(12.2) | 1.000[b] |
| Positive | 31(75.6) | 15(36.6) | 16(39.0) | |
| PR | | | | |
| Negative | 12(29.3) | 6(14.6) | 6(14.6) | 1.000 |
| Positive | 29(70.7) | 14(34.1) | 15(36.6) | |
| HER2 | | | | |
| Negative | 14(34.1) | 6(14.6) | 8(19.5) | 0.744 |
| Positive | 27(65.9) | 14(34.1) | 13(31.7) | |

[a]t-test. [b]Fisher's exact test.
Abbreviations: AC CTx, anthracycline cyclophosphamide chemotherapy; TNM, tumor, node, metastasis; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

higher cytokine levels in patients with sleep disorders; also, our findings concerning the relationship between sleep quality and IL-6 were similar to the results in that study (Doong et al., 2015). In the meta-analysis of sleep disturbances and cytokine-related relationships, changes in IL-6 and CRP levels were observed during sleep disturbances. Overall, the average effect size of IL-6 was greater than CRP, thus IL-6 triggers change in CRP levels during sleep disturbances; also, CRP levels increased during severe and persistent sleep disturbances (Irwin et al., 2016).

Additionally, cortisol, a primary biomarker secreted from the hypothalamic pituitary–adrenal axis, is released during stress and sleep disturbances (Buckley & Schatzberg, 2005; Roth et al., 2007). Since its normal level varies depending on the examination time, cortisol samples were consistently collected between 4 pm and 8 pm, thereby controlling the data collection time. Nonetheless, this study did not show significant changes in cortisol. Cortisol is rapidly secreted approximately once an hour, due to the ultradian rhythm, and changes in cortisol are highly variable depending on individual personality characteristics (Clow, Hucklebridge, Stalder, Evans, & Thorn, 2010). Therefore, it is necessary to control psychological and environmental factors, when possible, and the time interval should be narrow and consistent when investigating differences in cortisol levels.

## 5. Conclusion

Patients with breast cancer receiving chemotherapy are often

**Table 2**
PSQI scores.

| | Intervention(n = 20) | Control(n = 21) | Source | F | $p$ |
|---|---|---|---|---|---|
| | M ± SD | M ± SD | | | |
| PSQI total score | | | | | |
| Baseline | 11.50 ± 3.08 | 11.42 ± 2.69 | Group | 4.152 | 0.048* |
| Week 3 | 9.75 ± 3.09 | 11.42 ± 2.48 | Time | 12.891 | < 0.001* |
| Week 6 | 7.70 ± 2.77 | 10.57 ± 3.23 | G*T | 5.104 | 0.008* |

Abbreviations: PSQI, pittsburgh sleep quality index.
* $p < .05$, G*T: Group*Time.

**Table 3**
Blood cytokines, and cortisol associated with 6-week outcome at baseline and after intervention with auricular acupressure.

| Variables | Group | Baseline | Week 6 | *p* value | Mean(SD) change | *p* value |
|---|---|---|---|---|---|---|
| | | Mean(SD) | Mean(SD) | | Mean(SD) | |
| IL-6(pg/ml) | Intervention | 2.25 ± 1.81 | 0.98 ± 0.66 | 0.004 | 1.27 ± 2.13 | 0.002* |
| | Control | 2.14 ± 0.76 | 2.16 ± 2.17 | 0.179 | −0.01 ± 2.31 | |
| TNF-α(pg/ml) | Intervention | 0.92 ± 0.34 | 0.66 ± 0.35 | 0.114 | 0.25 ± 0.54 | 0.029* |
| | Control | 1.01 ± 0.18 | 0.94 ± 0.35 | 0.200 | 0.06 ± 0.39 | |
| Cortisol(μg/ml) | Intervention | 4.68 ± 2.10 | 3.42 ± 1.94 | 0.048 | 1.26 ± 2.88 | 0.826 |
| | Control | 3.53 ± 1.60 | 3.60 ± 2.05 | 0.792 | −0.06 ± 2.25 | |
| CRP(mg/dl) | Intervention | 0.28 ± 0.37 | 0.16 ± 0.27 | 0.055 | 0.12 ± 0.29 | 0.649 |
| | Control | 0.27 ± 0.59 | 0.24 ± 0.37 | 0.836 | 0.02 ± 0.49 | |

Abbreviations: IL-6, interleukin-6; TNF-α, tumor necrosis factor alpha; CRP, c-reactive protein.
* $p < .05$.

experience lower sleep quality but are reluctant to take medication, such as sleeping pills, because of the chemotherapy side effects. Six-weeks of auricular therapy using vaccaria seeds effectively reduced cytokine levels and improvements in sleep quality were similar to those acquired using auricular acupuncture. In contrast to auricular acupuncture, auricular therapy is noninvasive, simple, and safe to apply without causing pain. However, auricular therapy is a safe and easy-to-apply intervention that can be used in clinical practice, especially since few side effects have been reported while some study participants reported no side effects at all.

## References


Alfaro, E., Dhruva, A., Langford, D. J., Koetters, T., Merriman, J. D., West, C., ... Hamolsky, D. (2014). Associations between cytokine gene variations and self-reported sleep disturbance in women following breast cancer surgery. *European Journal of Oncology Nursing, 18*(1), 85–93.

Ancoli-Israel, S., Liu, L., Rissling, M., Natarajan, L., Neikrug, A. B., Palmer, B. W., ... Maglione, J. (2014). Sleep, fatigue, depression, and circadian activity rhythms in women with breast cancer before and after treatment: A 1-year longitudinal study. *Supportive Care in Cancer, 22*(9), 2535–2545.

Aronson, D. (2011). *Evidence-based technical analysis: Applying the scientific method and statistical inference to trading signals.* NewJersey: John Wiley & Sons.

Buckley, T. M., & Schatzberg, A. F. (2005). On the interactions of the hypothalamic-pituitary-adrenal (HPA) axis and sleep: Normal HPA axis activity and circadian rhythm, exemplary sleep disorders. *The Journal of Clinical Endocrinology & Metabolism, 90*(5), 3106–3114.

Buysse, D. J., Reynolds, C. F., III, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research, 28*(2), 193–213.

Cho, Y. W., Song, M. L., & Morin, C. M. (2014). Validation of a Korean version of the insomnia severity index. *Journal of Clinical Neurology, 10*(3), 210–215.

Clow, A., Hucklebridge, F., Stalder, T., Evans, P., & Thorn, L. (2010). The cortisol awakening response: More than a measure of HPA axis function. *Neuroscience & Biobehavioral Reviews, 35*(1), 97–103.

Dhruva, A., Aouizerat, B. E., Cooper, B., Paul, S. M., Dodd, M., West, C., & Merriman, J. D. (2015). Cytokine gene associations with self-report ratings of morning and evening fatigue in oncology patients and their family caregivers. *Biological Research for Nursing, 17*(2), 175–184.

Dirksen, S. R., Belyea, M. J., & Epstein, D. R. (2009). Fatigue-based subgroups of breast cancer survivors with insomnia. *Cancer Nursing, 32*(5), 404.

Doong, S. H., Dhruva, A., Dunn, L. B., West, C., Paul, S. M., Cooper, B. A., & Leutwyler, H. (2015). Associations between cytokine genes and a symptom cluster of pain, fatigue, sleep disturbance, and depression in patients prior to breast cancer surgery. *Biological Research for Nursing, 17*(3), 237–247.

Dowd, J. B., Goldman, N., & Weinstein, M. (2011). Sleep duration, sleep quality, and biomarkers of inflammation in a Taiwanese population. *Annals of Epidemiology, 21*(11), 799–806.

Ernst, E. (2010). Homeopathy: What does the "best" evidence tell us. *The Medical Journal of Australia, 192*(8), 458–460.

Feinsilver, S. H. (2003). Sleep in the elderly. What is normal? *Clinics in Geriatric Medicine, 19*(1), 177–188.

Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., … & Bray, F. (2015). Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer, 136(5), E359-E386.

Hsu, H. T., Lin, K. C., Wu, L. M., Juan, C. H., Hou, M. F., Hwang, S. L., & Dodd, M. J. (2017). Symptom cluster trajectories during chemotherapy in breast cancer outpatients. *Journal of Pain and Symptom Management, 53*(6), 1017–1025.

Hughes, J. G., Towler, P., Storey, L., Wheeler, S. L., & Molassiotis, A. (2015). A feasibility study of auricular therapy and self-administered acupressure for insomnia following cancer treatment. *European Journal of Integrative Medicine, 7*(6), 623–627.

Irwin, M. R., Olmstead, R., Breen, E. C., Witarama, T., Carrillo, C., Sadeghi, N., & Bower, J. E. (2014). Tai chi, cellular inflammation, and transcriptome dynamics in breast cancer survivors with insomnia: A randomized controlled trial. *Journal of the National Cancer Institute Monographs, 2014*(50), 295–301.

Irwin, M. R., Olmstead, R., & Carroll, J. E. (2016). Sleep disturbance, sleep duration, and inflammation: A systematic review and meta-analysis of cohort studies and experimental sleep deprivation. *Biological Psychiatry, 80*(1), 40–52.

Irwin, M. R., Olmstead, R. E., Ganz, P. A., & Haque, R. (2013). Sleep disturbance, inflammation and depression risk in cancer survivors. *Brain, Behavior, and Immunity, 30*, S58–S67.

Kim, H. J., Barsevick, A. M., Beck, S. L., & Dudley, W. (2012). Clinical subgroups of a psychoneurologic symptom cluster in women receiving treatment for breast cancer: A secondary analysis. *Oncology Nursing Forum, 39*(1), E20–E30.

King, H. C., Spence, D. L., Hickey, A. H., Sargent, P., Elesh, R., & Connelly, C. D. (2015). Auricular acupuncture for sleep disturbance in veterans with post-traumatic stress disorder: A feasibility study. *Military Medicine, 180*(5), 582–590.

Kryger, M. H., Roth, T., & Dement, W. C. (2011). *Principles and practice of sleep medicine* (5th ed.). St. Louis: Elsevier Saunders.

Kung, Y. Y., Yang, C. C., Chiu, J. H., & Kuo, T. B. (2011). The relationship of subjective sleep quality and cardiac autonomic nervous system in postmenopausal women with insomnia under auricular acupressure. *Menopause, 18*(6), 638–645.

Li, M. K., Lee, T. D., & Suen, K. L. (2014). Complementary effects of auricular acupressure in relieving constipation symptoms and promoting disease-specific health-related quality of life: A randomized placebo-controlled trial. *Complementary Therapies in Medicine, 22*(2), 266–277.

Liu, L., Mills, P. J., Rissling, M., Fiorentino, L., Natarajan, L., Dimsdale, J. E., … & Ancoli-Israel, S. (2012). Fatigue and sleep quality are associated with changes in inflammatory markers in breast cancer patients undergoing chemotherapy. Brain, Behavior, and Immunity, 26(5), 706–713.

Matthews, E. E., Berger, A. M., Schmiege, S. J., Cook, P. F., McCarthy, M. S., Moore, C. M., & Aloia, M. S. (2014, May). Cognitive behavioral therapy for insomnia outcomes in women after primary breast cancer treatment: A randomized, controlled trial. *Oncology Nursing Forum, 41*(3), 241–253.

Morin, C. M., & Benca, R. (2012). Chronic insomnia. *The Lancet, 379*(9821), 1129–1141.

Mustian, K. M., Sprod, L. K., Janelsins, M., Peppone, L. J., Palesh, O. G., Chandwani, K., … & Morrow, G. R. (2013). Multicenter, randomized controlled trial of yoga for sleep quality among cancer survivors. Journal of Clinical Oncology, 31(26), 3233–3241.

National Cancer Center (2016). Cancer incidence in Korea, 2014. Retrieved from http://www.cancer.go.kr/mbs/cancer/jsp/.

Oleson, T. (2013). *Auriculotherapy manual: Chinese and Western systems of ear acupuncture* (4th ed.). Los Angeles: Elsevier Health Sciences.

Otte, J. L., Carpenter, J. S., Zhong, X., & Johnstone, P. A. (2011). Feasibility study of acupuncture for reducing sleep disturbances and hot flashes in post-menopausal breast cancer survivors. *Clinical Nurse Specialist CNS, 25*(5), 228–236.

Palesh, O., Aldridge-Gerry, A., Ulusakarya, A., Ortiz-Tudela, E., Capuron, L., & Innominato, P. F. (2013). Sleep disruption in breast cancer patients and survivors. *Journal of the National Comprehensive Cancer Network, 11*(12), 1523–1530.

Roth, T., Roehrs, T., & Pies, R. (2007). Insomnia: Pathophysiology and implications for treatment. *Sleep Medicine Reviews, 11*(1), 71–79.

Sanford, S. D., Wagner, L. I., Beaumont, J. L., Butt, Z., Sweet, J. J., & Cella, D. (2013). Longitudinal prospective assessment of sleep quality: Before, during, and after adjuvant chemotherapy for breast cancer. *Supportive Care in Cancer, 21*(4), 959–967.

Siegel, R., DeSantis, C., Virgo, K., Stein, K., Mariotto, A., Smith, T., & Lin, C. (2012). Cancer treatment and survivorship statistics, 2012. *CA: a Cancer Journal for Clinicians, 62*(4), 220–241.

Simeit, R., Deck, R., & Conta-Marx, B. (2004). Sleep management training for cancer patients with insomnia. *Supportive Care in Cancer, 12*(3), 176–183.

Sjöling, M., Rolleri, M., & Englund, E. (2008). Auricular acupuncture versus sham acupuncture in the treatment of women who have insomnia. *The Journal of Alternative and Complementary Medicine, 14*(1), 39–46.

Sohn, S. I., Kim, D. H., Lee, M. Y., & Cho, Y. W. (2012). The reliability and validity of the Korean version of the Pittsburgh sleep quality index. *Sleep and Breathing, 16*(3), 803–812.

Suen, L. K., & Wong, E. M. (2007). Auriculotherapy with magnetic pellets produces longitudinal changes in sleep patterns of elderly patients with insomnia. *The Journal*

*of Alternative and Complementary Medicine, 13*(3), 306–307.
Wang, S. M., Peloquin, C., & Kain, Z. N. (2001). The use of auricular acupuncture to reduce preoperative anxiety. *Anesthesia & Analgesia, 93*(5), 1178–1180.
Wu, Y., Zou, C., Liu, X., Wu, X., & Lin, Q. (2014). Auricular acupressure helps improve sleep quality for severe insomnia in maintenance hemodialysis patients: A pilot study. *The Journal of Alternative and Complementary Medicine, 20*(5), 356–363.
Yeh, C. H., Chien, L. C., Glick, R. M., van Londen, G., & Bovbjerg, D. H. (2015). Auricular point acupressure (APA) to manage a symptom cluster of pain, fatigue, and disturbed sleep in breast cancer patients: A pilot study. *Journal of Pain & Relief, 4*(5), 1–7.
Yeh, C. H., Chien, L. C., Lin, W. C., Bovbjerg, D. H., & Van Londen, G. J. (2016). Pilot randomized controlled trial of auricular point acupressure to manage symptom clusters of pain, fatigue, and disturbed sleep in breast cancer patients. *Cancer Nursing, 39*(5), 402–410.
Yeung, W. F., Chung, K. F., Poon, M. M. K., Ho, F. Y. Y., Zhang, S. P., Zhang, Z. J., & Wong, V. T. (2012). Acupressure, reflexology, and auricular acupressure for insomnia: A systematic review of randomized controlled trials. *Sleep Medicine, 13*(8), 971–984.