

**Effect of Auricular Acupressure on Peri- and Early Post-Menopausal Women  
with Anxiety: A Double-Blinded, Randomized, and Controlled Pilot Study**

Ching-Ling Kao<sup>a,b</sup>, Chao-Hsun Chen<sup>c</sup>, Wei-Yun Lin<sup>b</sup>, Yu-Ching Chiao<sup>d</sup>, Ching-Liang  
Hsieh<sup>e,f,g\*</sup>

<sup>a</sup>Department of Adult Psychiatry , Tsao-Tun Psychiatric Center, Department of Health,  
Executive Yuan, Nan-Tou, 54249 ,Taiwan

<sup>b</sup>College of Chinese Medicine, Graduate institute of Integrated Medicine, China  
Medical University, Taichung, 40402, Taiwan

<sup>c</sup>Department of Chinese Medicine, Chang-Hua Hospital, Department of Health,  
Chang-Hua, 51341, Taiwan

<sup>d</sup>Department of Business Administration, National Chung Hsing University, Taichung,  
40227, Taiwan

<sup>e</sup>College of Chinese Medicine, Graduate Institute of Acupuncture Science, China  
Medical University, Taichung, 40402, Taiwan

<sup>f</sup>Acupuncture Research Center, China Medical University, Taichung, 40402, Taiwan

<sup>g</sup>Department of Chinese Medicine, China Medical University Hospital, Taichung,  
40402, Taiwan

\* Correspondence: Ching-Liang Hsieh M.D., Ph.D. College of Chinese Medicine,  
Graduate Institute of Acupuncture Science, China Medical University. 91 Hsueh-Shih  
Road, Taichung, 40402, Taiwan

Running title: Auricular acupressure improves women with menopausal anxiety

**Keywords:** Auricular acupressure; Menopause; Anxiety; Randomized controlled trial.

## **Abstract**

We tested effects of auricular acupressure on peri- and early post-menopausal women with anxiety (PPWA). Fifty PPWA were randomly assigned to the auricular acupressure group (AG) or the sham group (SG). After 3 meals and before sleep every day for 4 weeks, the AG received auricular acupressure on the bilateral ear shenmen and subcortex points for 3 min per point on alternating ears. The SG received sham auricular acupressure. The Alprazolam was reduced from 0.5 mg/day at baseline to 0.3 mg/day 4 weeks after auricular acupressure (4W) in the AG ( $P < .05$ ) whereas Alprazolam maintained at 0.5 mg/day in the SG ( $P > .05$ ). The Zolpidem was reduced from 3.0 mg/day at baseline to 1.5 mg/day at 4 W ( $P < .05$ ), whereas Zolpidem was reduced from 2.4 mg/day at baseline to 1.9 mg/day at 4W in the SG ( $P > .05$ ), suggesting auricular acupressure is helpful to PPWA.

## **Introduction**

In menopausal women, anxiety and accompanying insomnia generate a domino effect that can multiply symptoms associated with menopause and depression. These burdens last for more than a few months or even several years, and such conditions often affect quality of life. According to the American Psychiatric Association Diagnostic and Statistical Manual Fourth Edition (DSM-IV, TR) [1], anxiety is classified as an ongoing concern, worry, or sense of impending disaster, a feeling of tension, and an inability to relax. Anxiety disorders are a large group of conditions, including panic disorder, phobia, obsessive-compulsive disorder, generalized anxiety disorder, post-traumatic stress disorder, and anxiety secondary to general medical conditions. Insomnia is defined as difficulty falling asleep or maintaining sleep, early awakening, or not feeling rested after sleep along with fatigue, distress, or functional decline.

Menopause is when women permanently stop menstruating. Peri-menopause usually occurs in 5 to 7 years before menopause, and is the transitional phase from the regular ovarian menstrual cycle to complete cessation of ovarian functions. The epidemiology of natural menopause is defined as a lack of menstruation for 12 months in the absence of other causes such as pregnancy or breastfeeding [2]; however, no such standard exists for peri-menopause. Peri-menopause is

characterized by irregular menstrual cycles or less than 12 months without menstruation, but the only index in the first 2 or 3 days of the menstrual cycle is an elevation in the follicle stimulating hormone (FSH) [3]. According to Stages of Reproductive Aging Workshop (STRAW) criteria, FSH plasma concentrations of more than 2 standard deviations more than the normal 14 IU/ L above the early follicular phase concentration of FSH indicates peri-menopause.

The most common symptoms of menopause are hot flashes, night sweats, vaginal dryness, problems with decreased sexual function, sleep disorders, headaches, heart palpitations, inability to concentrate, and fatigue; in addition, weight gain, joint pain, short-term memory problems, urinary problems, skin itching, and intestinal discomfort are common symptoms [4]. For middle-aged women, numerous sources of stress may worsen the anxiety of the situation, such as "empty nest" syndrome, care for elderly parents, spouse death, or divorce. Epidemiological research shows that numerous menopausal women have more symptoms of irritability and depression, and are prone to mild to severe depression. A cohort study by a Harvard research team found that significant new depressive symptoms in menopausal women have at least twice the possibility of leading to depression than in the pre-menopausal stage [5]. Anxiety and insomnia can be predictors of depression for women in this period [6]. Anxiety can also predict vasomotor symptoms [7]. An increasing trend of hot flashes,

sleep disturbance, physical and mental symptoms, muscle and joint pain, and other symptoms at different stages of menopause may affect women's quality of life [8]; however, early treatment of anxiety can improve menopause-related symptoms, depression, and quality of life.

Although estrogen therapy has an effect on vasomotor symptoms, depression, anxiety, and insomnia in menopausal and postmenopausal women, the Women's Health Initiative (WHI) reported an increase in cases of coronary heart disease, stroke, venous thrombosis, and dementia cases after hormone therapy [9]. Although all these studies are conducted on post-menopausal women, and the time before termination of hormone treatment is at least 5 years, they have caused misgivings on the safety of long-term hormone therapy. Some studies show that the drugs of choice for insomnia in menopausal and post-menopausal women, such as the non-benzodiazepines Zolpidem and Eszopiclone, are effective for the short-term, and improve sleep, mood, quality of life, and menopause-related symptoms within 4 weeks [10, 11]; however, long-term use of these drugs may still cause psychological or physical dependence. Typical clinical anxiety disorders such as generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, and post-traumatic stress disorders require serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and other antidepressants to treat general anxiety states, or anxiety disorders related to general

physical condition are treatable with low doses of anti-anxiety agents.

As a treatment for generalized anxiety disorders, acupuncture has relatively similar effects as traditional medicine, and can be used in combination with traditional medicine to reduce the side effects of serotonin reuptake inhibitors. Acupuncture reduces anxiety through the regulation of neurotransmitters by reducing the platelet 5-hydroxytryptamine (5-HT) concentration and plasma adrenocorticotrophic hormone (ACTH) [12]. Some randomized controlled studies showed that ear acupuncture before surgery can reduce anxiety related to surgery [13], and can improve anxiety in everyday life for healthy participants [14]. As opposed to acupuncture focused on parts of the body, auricular acupuncture therapy can easily be mapped to the body's acupuncture points, and is convenient for patients because treatment does not require the removal of clothing. Acupuncture covers a variety of techniques. Apart from needle insertion, one approach is to paste magnetic beads on corresponding acupuncture points and pressing several times to reduce local congestion, redness, or heat. This approach is called acupressure.

We used evidence-based methods to review the history and research of the effects of ear acupuncture on anxiety [15-17]. No previous study has explored the therapeutic effect of a combination of auricular acupressure and drug treatment for women suffering from anxiety and insomnia during the menopausal stage; therefore,

we designed this protocol in an attempt to provide convenient and effective treatment and to reduce dependence on sedatives, thereby improving quality of life for participants.



## **Materials and methods**

### ***Participants***

Ninety-one peri- and early post-menopausal women with anxiety (PPWA) were recruited at the Department of Psychiatry, Chang-Hua Hospital, Department of Health from January 1, 2010 to December 31, 2010. Forty-one patients were excluded from the study prior to signing informed consent: 12 patients had experienced menopause for more than 10 years, 1 had a serious medical disease, 3 had major psychiatric illnesses, 2 had recently used hormones, 1 regularly used Chinese herbs, and 3 refused the trial. The inclusion criteria were 1) between 40 and 60 years of age; 2) irregular menstruation for less than 12 months or menopause for less than 10 years; 3) FSH plasma concentrations of  $\geq 14$  IU / L ; and 4) anxiety secondary to peri-menopause or early post-menopause. Participants provided written informed consent after a full explanation of the purpose and process of the study. Exclusion criteria were 1) serious medical disorders (for example, asthma; epilepsy; or heart, liver, or renal failure); 2) substance dependence or abuse (for example, alcohol, drugs, hypnotics, and analgesics); 3) contraindications to sedatives and hypnotic drugs; 4) contraindications to acupuncture treatment; 5) suicidal and violent tendencies; 6) existence of primary anxiety disorders and other major axis I psychiatric diagnoses (for example, schizophrenia, major depression, and bipolar disorders); 7) lack of fulfillment of the

standard type and dosage of the drugs set in this study; 8) use of hormone therapy for menopausal symptoms; 9) use of traditional Chinese medicine for mental conditions; and 10) refusal to sign the informed consent form. The plan was reviewed and approved before the trial by the China Medical University Hospital Institutional Review Board (CMUH IRB No. DMR98-IRB-291-1).

### ***Design and sample size***

The present study is a randomized double-blind control pilot study of a combination of modern medicine and complementary therapy of auricular acupressure to research the change in anxiety symptoms in peri-and early post-menopausal women.

Remission of anxiety is defined as a reduction in score on the Hamilton Anxiety Rating Scale (HAMA) [18]  $\geq 50\%$  and Clinical Global Impression-severity/Clinical Global Impression-Improvement/ (CGI-S/CGI-I)[19]  $\leq 2$ ; and improvement of menopausal symptoms is defined as a reduction in score on the Menopause Rating Scale (MRS)[20]  $\geq 50\%$ .

Because the present study was a pilot study, no basis existed on which to calculate power or sample size.

### ***Randomized and grouping***

Fifty peri- and early post-menopausal women with anxiety were assigned to 1 of 2 groups by a computerized random numbers table, as follows: 1) In the auricular acupressure group (AG), participants received ear adhesive tape with magnetic beads (200 Gauss, Xiang Yu International Co., Ltd., Taiwan) on the ear shenmen (MA-TF1) and subcortex (MA-AT1) points for both ears from a Chinese medicine physician with more than 8 years of experience in auricular acupressure. Acupressure was applied to each acupoint on alternating ears for 3 min at each point after 3 meals and before bedtime every day for 4 weeks. The ear adhesive tape with magnetic beads was changed twice a week; thus, they were changed 8 times in the 4 weeks; 2) In the sham acupressure group (SA), the methods were identical to AG, but the ear adhesive tape had no magnetic beads. All participants were allowed to receive doses of Alprazolam 0 to 2 mg/day and Zolpidem 0 to 10 mg/day, gradually tapering the dosage of each drug during the period of treatment.

### ***Assessment and outcome measure***

The assessment was performed by a psychiatric specialist who was blind to the group. The participants were evaluated at baseline (before auricular acupressure) and 4 weeks after auricular acupressure (4W). The type and dosage of medication were also recorded at each visit.

Primary outcome measures focused on the difference in dosage of Alprazolam or Zolpidem between the baseline and at 4W and the difference in HAMA, MRS, CGI-S, and CGI-I scores between baseline and at 4W. The secondary outcome measure was the difference in quality of life according to Short Form Health Survey (SF-36) scores and its sub-scores between baseline and at 4W.

The HAMA contains 14 items measured with a 5-point Likert scale. The score is from 0 (no symptoms) to 4 (extremely severe). The present study calculated only the total scores. The higher the total score was, the more serious the symptoms of anxiety.

The MRS includes 11 items that can be divided into 3 subscales: the urogenital, somatic, and psychological domains. It uses a 5-point Likert scale from 0 (no symptoms) to 4 (extremely severe). The study calculated only the total scores. The higher the total score, the more serious the symptoms of menopause are. The SF-36 contains 36 items to assess physical and mental health, divided into 8 subscales: physical function (PF), social function (SF), role limitations caused by physical problems (RP), role limitations caused by emotional problems (RE), mental health (MH), energy/vitality (VT), body pain (BP), and general perception of health (GH).

This study assessed each subscale; higher scores presented a better health status. The CGI-S contains 7 items from 1 to 7 points. A higher score indicates greater severity.

The CGI-I contains 7 items from 1 to 7 points. A lower score represents a higher

degree of improvement.

### ***Statistical Analysis***

The data were analyzed using statistical software SPSS 18.0 version. The categorical data was analyzed using Pearson  $\chi^2$  tests or Fisher's exact tests. Independent  $t$  tests (two-tailed) were used to analyze the variables between the AG and SG groups, and paired  $t$  tests (two-tailed) were used to analyze the intra-group variables. Significance of statistical difference was set to  $P < .05$ .

## **Results**

### ***Baseline characteristics of demographic data***

Of the 50 PPWA enrolled in the present study, 27 participants were assigned to the AG and 23 to the SG. Only 25 participants in the AG completed the trial. One stopped because of dizziness, and 1 stopped because of other reasons. Nineteen participants completed the trial in the SG; 2 stopped because they felt no effect, and 2 could not adhere to the times in the study. Therefore, 44 participants completed the trial (Fig. 1).

The baseline characteristics of the AG and SG participants, which comprised age, education, parity, age at menarche, marital status, menopausal status (peri-menopause and post-menopause), and levels of FSH were similar between the 2 groups (all  $P > .05$ ; Table 1). In addition, factors influencing anxiety investigated prior to the trial, namely use of herbal medicine, smoking habits, alcohol habits, caffeine habits, and Brief Symptom Rating Scale (BSRS), were similar between the AG and the SG (all  $P > .05$ ; Table 2). The exception was that prior use of FSH was greater in the SG than in the AG ( $P = .03$ ; Table 2).

### ***Effect of auricular acupuncture on PPWA***

The HAMA scores at baseline and at 4W were similar between the AG and the SG (both  $P > .05$ ; Table 3). The HAMA scores were higher at baseline than at 4W in the

AG and in the SG (both  $P < .05$ ; Table 3), and the difference in HAMA score between baseline and 4W was similar between the 2 groups ( $P > .05$ ; Table 3).

The MRS scores at baseline and at 4W were similar for the AG and the SG (both  $P > .05$ ; Table 3). The MRS scores were higher at baseline than at 4W in the AG and in the SG (both  $P < .05$ ; Table 3), and the difference in MRS score between baseline and 4W was similar for the 2 groups ( $P > .05$ ; Table 3).

The CGI-S scores at baseline and at 4W were similar for the AG and the SG (both  $P > .05$ ; Table 3). The CGI-S scores were higher at baseline than at 4W in the AG and in the SG (both  $P < .05$ ; Table 3), and the difference between CGI-S score at baseline and at 4W was similar for the 2 groups ( $P > .05$ ; Table 3).

The CGI-I scores at baseline and at 4W were similar for the AG and the SG (both  $P > .05$ ; Table 3). The CGI-I scores were higher at baseline than at 4W in the AG and in the SG (both  $P < .05$ ; Table 3), and the difference between CGI-I score at baseline and at 4W was similar for the 2 groups ( $P > .05$ ; Table 3).

The Alprazolam doses at baseline and at 4W were similar for the AG and the SG (both  $P > .05$ ; Table 3). The Alprazolam doses were greater at baseline than at 4W in the AG (both  $P < .05$ ; Table 3), but not in the SG ( $P > .05$ ; Table 3). The difference in Alprazolam doses between baseline and 4W was similar for the 2 groups ( $P > .05$ ; Table 3).

The Zolpidem doses at baseline and at 4W were similar for the AG and the SG (both  $P > .05$ ; Table 3). The Zolpidem doses were higher at baseline than at 4W in the AG (both  $P < .05$ ; Table 3), but not in the SG ( $P > .05$ ; Table 3). The difference between Zolpidem doses at baseline and at 4W was similar for the 2 groups ( $P > .05$ ; Table 3).

#### ***Effect of auricular acupressure on sub-scores of SF-36 in PPWA***

The PF sub-score of SF-36 at baseline and at 4W were similar for the AG and the SG (both  $P > .05$ ; Table 4). The PF sub-scores of SF-36 were higher at 4W than at baseline in the AG (both  $P < .05$ ; Table 4), but not in the SG ( $P > .05$ ; Table 4). The difference between PF sub-scores of SF-36 at baseline and at 4W was similar for the 2 groups ( $P > .05$ ; Table 4).

The RP and RE sub-scores of SF-36 at baseline and at 4W were similar for the AG and the SG (both  $P > .05$ ; Table 4). The RP and RE sub-scores of SF-36 were greater at 4W than at baseline in the SG (both  $P < .05$ ; Table 4), but not in the AG (both  $P > .05$ ; Table 4). The difference between the RP and RE sub-scores of SF-36 at baseline and at 4W was similar for the 2 groups (both  $P > .05$ ; Table 4).

The VT, MH, BP, and GH sub-scores of SF-36 at baseline and at 4W were similar for the AG and the SG (all  $P > .05$ ; Table 4). The VT, MH, BP, and GH



sub-scores of SF-36 were greater at 4W than at baseline in the AG and in the SG (all  $P < .05$ ; Table 4), whereas the difference between VT, MH, BP, and GH sub-scores of SF-36 at baseline and at 4W were similar for the 2 groups (all  $P > .05$ ; Table 4).

The SF sub-score of SF-36 at baseline and at 4W were similar for the AG and the SG (both  $P > .05$ ; Table 4). The SF sub-score of SF-36 was similar at baseline and at 4W in the AG and in the SG (both  $P < .05$ ; Table 4). The difference in SF sub-score of SF-36 between baseline and 4W was similar for the 2 groups ( $P > .05$ ; Table 4).

## Discussion

The results of the present study indicate that the difference between HAMA, MRS, CGI-S, and CGI-I scores at baseline and at 4W was similar for the AG and the AG. The doses of Alprazolam and Zolpidem were reduced from baseline to 4W in the AG but not in the SG. Therefore, we suggest that auricular acupressure improved PPWA. Both Alprazolam and Zolpidem are sedative drugs widely used to treat PPWA or insomnia [10, 11], and HAMA, MRS, CGI-S, and CGI-I scores can be used to evaluate menopausal anxiety [20]. This is the first study showing that auricular pressure with low-dose Alprazolam and Zolpidem improves anxiety symptoms, menopausal symptoms, and quality of life in PPWA. The results also show that the dosage of drugs can be gradually reduced during the course of treatment to help avoid long-term drug use that could induce dependence. Adding auricular acupressure to a treatment of anti-anxiety drugs will not increase adverse side effects or decrease safety. However, participants in the AG and the SG could not predict which group would show significant improvements. The results are consistent with those of previous studies that found auricular pressure effective for treating anxiety [21] and anxiety before surgery [22] and for improving quality of life [23]. Evidence-based studies on the efficacy of acupuncture have compared the efficacy of real and control acupuncture for clinical conditions such as post-menopausal vasomotor symptoms in

women [24], including primary dysmenorrhea [25], insomnia [26], and weight loss [27], finding improvement in real and control acupuncture, and showing no statistical difference between the 2 groups. However, most of the studies did not design a treatment group without intervention as a control, instead using a noninvasive method as the control group; therefore, the placebo effect may have contributed to their results. Some scholars have indicated that sham acupuncture does not exist because true acupuncture and sham acupuncture could have similar effects on the central nervous or endocrine systems [28, 29].

The choice of the ear shenmen and subcortex acupoints was based on the meridian theory of traditional Chinese medicine with a sedative mechanism to regulate cortical excitation and inhibit brain function. Auricular acupressure on these acupoints may alleviate the stimulating effect of anxiety, which promotes blood circulation through the nerve channels. It may also stimulate the small myelinated nerve in the spinal cord, midbrain, pituitary, and hypothalamus, causing the release of endorphins into the bloodstream [30].

At the end of this study, the average Alprazolam dosage in the AG was 0.3 mg/day and in the SG was 0.5 mg/day. No statistically significant difference between the groups was reached; however, in the AG, the difference in drug use between the beginning and end of the study reached statistical significance. A previous study

showed that 1.5 to 3 mg of Alprazolam per day can improve moderate to severe anxiety and has antidepressant effects [31]. Our participants entered the study with mild to moderate anxiety. However, the average dosage remains lower than the general therapeutic dose in clinical use. Further research is required to adjust the experimental design using a fixed dosage of combination drugs to distinguish the difference between the 2 groups.

The present study has several limitations: 1) The sample size was small. With the first error set to 0.05 and the second error set to 0.2, the power of this study was 0.9; for the study to detect a significant difference in therapeutic effect, each group requires at least 30 participants; 2) The participants are all from a hospital in a rural area, and therefore, the results may not be representative of other areas; 3) If the participants were interested in auricular acupressure or held a positive view of it before the study, this was likely to affect the results of the study; 4) We had no untreated group as a control. As mentioned, sham acupuncture had a similar effect, but a design considering this cannot be a double-blind experimental design. Previous studies did not directly compare the efficacy of auricular acupressure with different methods such as rapeseed, Vaccaria seed, mustard seed, and magnetic beads in reducing anxiety; therefore, future studies might consider them; 5) The therapeutic relationship may provide a feeling of relaxation, causing participants to feel less

anxiety or less distressed, consciously or unconsciously driven by the hope of achieving clinical improvement; and 6) The timeframe for our study is only 4 weeks. We cannot predict whether the therapeutic effect would be maintained over a longer period. In the future, we could design a study that, after using a combination of drugs and auricular pressure for 4 weeks, uses auricular acupressure alone as treatment for a set time. This could avoid drug dependency and assess whether auricular acupressure alone can maintain beneficial effects.

In conclusion, no direct support was found for our hypothesis that auricular acupressure is better than sham acupressure for improving anxiety, menopausal symptoms, and quality of life. Participants improved whether receiving real or sham acupressure. The dosage of medication decreased significantly in the auricular acupressure group, but not the sham acupressure group. This may be indirect evidence of the benefit of such alternative therapy. Research to develop more safe and effective interventions using integrated complementary therapy and Western treatment should be encouraged. Further study with a larger sample size is necessary.

## **Acknowledgments**

This study is supported by a research fund from Chang-Hua hospital (CHH No. 94-4) ,  
and also is supported in part by the Taiwan Department of Health Clinical Trial and  
Research Center of Excellence (DOH100-TD-B-111-004).

## References

- [1] American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision. : Washington, DC, 2000.
- [2] N.E. Avis and S.M. McKinlay, “A longitudinal analysis of women's attitudes toward the menopause: results from the Massachusetts Women's Health Study,” *Maturitas*, vol. 13, no. 1, pp. 65-79, 1991.
- [3] N.E. Avis and S.M. McKinlay, “The Massachusetts Women's Health Study: an epidemiologic investigation of the menopause,” *Journal of the American Medical Women's Association*, vol. 50, no. 2, pp. 45-49, 63, 1995.
- [4] C.A. Morse, A. Smith, L. Dennerstein, A. Green, J. Hopper, and H. Burger, “The treatment-seeking woman at menopause,” *Maturitas*, vol. 18, no. 3, pp. 161-173, 1994.
- [5] L.S. Cohen, C.N. Soares, A.F. Vitonis, M.W. Otto, and B.L. Harlow, “Risk for new onset of depression during the menopausal transition: the Harvard study of moods and cycles,” *Archives of General Psychiatry*, vol. 63, no. 4, pp. 385-390, 2006.
- [6] A.F. Polisseni, D.A. de Araújo, F. Polisseni, C.A. Mourão Junior, J. Polisseni, E.S. Fernandes, and O. Guerra Mde, “Depression and anxiety in menopausal women: associated factors,” *Revista brasileira de ginecologia e obstetrícia : revista da*

*Federação Brasileira das Sociedades de Ginecologia e Obstetrícia*, vol. 31, no. 1, pp. 28-34, 2009.

[7] M.S. Hunter, P. Gupta, A. Papitsch-Clark, and D.W. Sturdee, “Mid-Aged Health in Women from the Indian Subcontinent (MAHWIS): a further quantitative and qualitative investigation of experience of menopause in UK Asian women, compared to UK Caucasian women and women living in Delhi,” *Climacteric*, vol. 12, no. 1, pp. 26-37, 2009.

[8] H. Waidyasekera, K. Wijewardena, G. Lindmark, and T. Naessen, “Menopausal symptoms and quality of life during the menopausal transition in Sri Lankan women,” *Menopause (New York, N.Y.)*, vol. 16, no. 1, pp. 164-170, 2009.

[9] J.E. Rossouw, G.L. Anderson, R.L. Prentice, A.Z. LaCroix, C. Kooperberg, M.L. Stefanick, R.D. Jackson, S.A. Beresford, B.V. Howard, K.C. Johnson, J.M. Kotchen, and J. Ockene, “Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial,” *JAMA : the journal of the American Medical Association*, vol. 288, no. 3, pp. 321-333, 2002.

[10] C.M. Dorsey, K.A. Lee, and M.B. Scharf, “Effect of zolpidem on sleep in women with perimenopausal and postmenopausal insomnia: a 4-week, randomized, multicenter, double-blind, placebo-controlled study,” *Clinical*



*therapeutics*, vol. 26, no. 10, pp. 1578-1586, 2004.

[11]C.N. Soares, H. Joffe, R. Rubens, J. Caron, T. Roth, and L. Cohen,

“Eszopiclone in patients with insomnia during perimenopause and early postmenopause: a randomized controlled trial,” *Obstetrics and Gynecology*, vol. 108, no. 6, pp. 1402-1410, 2006.

[12] Q. Yuan, J.N. Li, B. Liu, Z.F. Wu, and R. Jin, “Effect of Jin-3-needling therapy

on plasma corticosteroid, adrenocorticotrophic hormone and platelet 5-HT levels in patients with generalized anxiety disorder,” *Chinese Journal of Integrative Medicine*, vol. 13, no. 4, pp. 264-268, 2007.

[13]M. Karst, M. Winterhalter, S. Münte, B. Francki, A. Hondronikos, A. Eckardt, L.

Hoy, H. Buhck, M. Bernateck, and M. Fink, “Auricular acupuncture for dental anxiety: a randomized controlled trial,” *Anesthesia and Analgesia*, vol. 104, no. 2, pp. 295-300, 2007.

[14]S.M. Wang and Z.N. Kain, “Auricular acupuncture: a potential treatment for

anxiety,” *Anesthesia and Analgesia*, vol. 92, no. 2, pp. 548-553, 2001.

[15]L. Gori and F. Firenzuoli, “Ear acupuncture in European traditional medicine,”

*Evidence-based Complementary and Alternative Medicine : eCAM*, vol. 4, no. Suppl 1, pp. 13-16, 2007.

[16]K. Pilkington, G. Kirkwood, H. Rampes, M. Cummings, and J. Richardson,

- “Acupuncture for anxiety and anxiety disorders--a systematic literature review,” *Acupuncture in Medicine : Journal of the British Medical Acupuncture Society*, vol. 25, no. 1-2, pp. 1-10, 2007.
- [17]K. Pilkington, “Anxiety, depression and acupuncture: A review of the clinical research,” *Autonomic Neuroscience : Basic & Clinical*, vol. 157, no. 1-2, pp. 91-95, 2010.
- [18]M. Hamilton, “The assessment of anxiety states by rating,” *The British Journal of Medical Psychology*, vol. 32, no. 1, pp. 50-55, 1959.
- [19]W. Guy, *ECDEU Assessment Manual for Psychopharmacology*. Rockville, MD, USA: US Department of Health, Education, and Welfare. 1976.
- [20]L.A. Heinemann, P. Potthoff, and H.P. Schneider, “International versions of the Menopause Rating Scale (MRS) ,” *Health and Quality of Life Outcomes*, vol. 1, pp. 28, 2003.
- [21]A. Kober, T. Scheck, B. Schubert, H. Strasser, B. Gustorff, P. Bertalanffy, S.M. Wang, Z.N. Kain, and K. Hoerauf, “Auricular acupressure as a treatment for anxiety in prehospital transport settings,” *Anesthesiology*, vol. 98, no. 6, pp. 1328-1332, 2003.
- [22] S.M. Wang, I. Maranets, M.E. Weinberg, A.A. Caldwell- Andrews, and Z.N. Kain, “Parental auricular acupuncture as an adjunct for parental presence during

- induction of anesthesia,” *Anesthesiology*, vol. 100, no. 6, pp. 1399-1404, 2004.
- [23] S.H. Maa, M.F. Sun, K.H. Hsu, T.J. Hung, H.C. Chen, C.T. Yu, C.H. Wang, and H.C. Lin, “Effect of acupuncture or acupressure on quality of life of patients with chronic obstructive asthma: a pilot study,” *Journal of Alternative and Complementary Medicine (New York, N.Y.)*, vol. 9, no. 5, pp. 659-670, 2003.
- [24] L. Venzke, J.F. Calvert Jr., and B. Gilbertson, “A randomized trial of acupuncture for vasomotor symptoms in post-menopausal women,” *Complementary Therapies in Medicine*, vol. 18, no. 2, pp. 59-66, 2010.
- [25] M.C. Wang, M.C. Hsu, L.W. Chien, C.H. Kao, and C.F. Liu, “Effects of auricular acupressure on menstrual symptoms and nitric oxide for women with primary dysmenorrhea,” *Journal of Alternative and Complementary Medicine (New York, N.Y.)*, vol. 15, no. 3, pp. 235-242, 2009.
- [26] M. Sjöling, M. Rolleri, and E. Englund, “Auricular acupuncture versus sham acupuncture in the treatment of women who have insomnia,” *Journal of Alternative and Complementary Medicine (New York, N.Y.)*, vol. 14, no. 1, pp. 39-46, 2008.
- [27] C.H. Hsieh, “The effects of auricular acupressure on weight loss and serum lipid levels in overweight adolescents,” *The American Journal of Chinese Medicine*, vol. 38, no. 4, pp. 675-682, 2010.

- [28] I. Lund and T. Lundeberg, “Are minimal, superficial or sham acupuncture procedures acceptable as inert placebo controls?,” *Acupuncture in Medicine : Journal of the British Medical Acupuncture Society*, vol. 24, no. 1, pp. 13-15, 2006.
- [29] T. Lundeberg, I. Lund, J. Näslund, and M. Thomas, “The Emperors sham - wrong assumption that sham needling is sham,” *Acupuncture in Medicine : Journal of the British Medical Acupuncture Society*, vol. 26, no. 4, pp. 239-242, 2008.
- [30] K.K. Hui, J. Liu, N. Makris, R.L. Gollub, A.J. Chen, C.I. Moore, D.N. Kennedy, B.R. Rosen, and K.K. Kwong, “Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects,” *Human Brain Mapping*, vol.9, no. 1, pp. 13-25, 2000.
- [31] K. Davison, R.G. Farquharson, M.C. Khan, and A. Majid, “A double blind comparison of alprazolam, diazepam and placebo in the treatment of anxious out-patients,” *Psychopharmacology*, vol. 80, no. 4, pp. 308-310, 1983.

**Figure 1. Flowchart**

**Table 1. Demographic characteristics at baseline**

	AG (n=25)	SG (n=19)	<i>P-value</i>
Age (years)	53.56±4.63	54.42±6.42	.607 <sup>t</sup>
Education(years)	8.92±3.71	9.47±4.58	.660 <sup>t</sup>
Parity	2.71±1.31	3.12±1.36	.360 <sup>t</sup>
Menarche (years)	14.25±1.77	13.67±1.24	.267 <sup>t</sup>
Marital status			.179 <sup>c</sup>
married	24(96%)	17(89.5%)	
single	1(4%)	0(0.0%)	
divorced	0(0.0%)	2(10.5%)	
Menopausal status			.986 <sup>c</sup>
Peri-menopause	5(20.9%)	4(21.1%)	
Post-menopause	19(79.1%)	15(78.9%)	
FSH	58.7±28.2	66.2±35.6	.45 <sup>t</sup>

Data are expressed as mean ± standard deviation (SD). AG: auricular acupressure group; SG: sham group; FSH: follicle stimulating hormone; t: Student's *t* test; c: Pearson chi-square or Fisher's exact test.

**Table 2. Influencing factors at baseline**

	AG (n=25)	SG (n=19)	<i>P- value</i>
Prior use of hormone	9(36%)	13(68.4%)	.03
Herbal medicine	11(44%)	4(21%)	.11
Smoking habit	1(4%)	0(0%)	.38
Alcohol habit	1(4%)	0(0%)	.38
Caffeine habit	6(24%)	2(11%)	.23
BSRS	7.6±4.1	8.0±3.2	.76 <sup>t</sup>

AG: auricular acupressure group; SG: sham group; BSRS: Brief Symptom Rating

Scale.

t: Student's *t* test.

**Table 3. Effect of auricular acupressure on peri-menopausal and early post-menopausal women with anxiety**

	AG(n=25)		SG (n=19)	
	Baseline	4W	Baseline	4W
HAMA	17.8(6.2) <sup>a</sup>	8.0(5.5) <sup>a,b</sup>	19.6(5.5)	11.0(6.3) <sup>b</sup>
MRS	11.8(5.9) <sup>a</sup>	6.4(5.8) <sup>a,b</sup>	14.5(6.1)	8.2(4.9) <sup>b</sup>
CGI-S	3.8(0.7) <sup>a</sup>	2.3(0.9) <sup>a,b</sup>	4.1(0.7)	2.7(1.0) <sup>b</sup>
CGI-I	4.4(0.5) <sup>a</sup>	2.0 (0.9) <sup>a,b</sup>	4.5(0.5)	2.6(1.1) <sup>b</sup>
Alprazolam (mg/day)	0.5(0.4) <sup>a</sup>	0.3(0.3) <sup>a,b</sup>	0.5(0.6)	0.5(0.6) <sup>c</sup>
Zolpidem (mg/day)	3.0(4.0) <sup>a</sup>	1.5(3.1) <sup>a,b</sup>	2.4(2.6)	1.9(3.4) <sup>c</sup>

AG: auricular acupressure group; SG: sham group; Baseline: prior to auricular acupressure; 4W: at 4 week after auricular acupressure; HAMA: Hamilton Anxiety Rating Scale; MRS: Menopause Rating Scale; CGI-S: Clinical Global Impression-Severity; CGI-I: Clinical Global Impression-Improvement;

a No significant difference between AG and SG groups ( $P > .05$ ).

b Significant difference between baseline and 4W ( $P \leq .05$ ).

c No significant difference between baseline and 4W ( $P > .05$ ).



**Table 4. Effect of auricular acupressure on sub-scores of SF-36 in peri-menopausal and early post-menopausal women with anxiety**

	AG(n=25)		SG(n=19)	
	Baseline	4Ws	Baseline	4W
PF	80.2(15.0) <sup>a</sup>	87.8(14.9) <sup>a,b</sup>	73.4(21.9)	79.7(20.8) <sup>c</sup>
RP	59.0(42.6) <sup>a</sup>	75.0(36.1) <sup>a,c</sup>	46.1(47.3)	75.0(37.3) <sup>b</sup>
RE	52.0(44.2) <sup>a</sup>	68.0(41.4) <sup>a,c</sup>	49.1(43.6)	82.5(32.1) <sup>b</sup>
VT	54.6(22.4) <sup>a</sup>	65.2 (19.6) <sup>a,b</sup>	49.2(20.6)	61.3(20.7) <sup>b</sup>
MH	54.4(18.4) <sup>a</sup>	65.3(19.4) <sup>a,b</sup>	50.7(15.5)	64.4(16.6) <sup>b</sup>
SF	73.0(19.3) <sup>a</sup>	79.0(17.2) <sup>a,c</sup>	68.4(19.7)	76.3(16.6) <sup>c</sup>
BP	69.1(15.7) <sup>a</sup>	76.7(13.5) <sup>a,b</sup>	60.7(14.2)	73.8(19.7) <sup>b</sup>
GH	45.8(16.8) <sup>a</sup>	62.2(22.1) <sup>a,b</sup>	36.6(19.6)	55.8(23.2) <sup>b</sup>

AG: auricular acupressure group; SG: sham group; Baseline: prior to auricular acupressure; 4W: at 4 week after auricular acupressure; SF-36: Short Form Health Survey; PF: physical function; SF: social function; RP: role limitations due to physical problems; RE: role limitations due to emotional problems; MH: mental health; VT: energy/ vitality; BP: body pain; GH: general perception of health;

a No significant difference between AG and SG groups ( $P > .05$ ).

b Significant difference between baseline and 4W ( $P \leq .05$ ).

c No significant difference between baseline and 4W ( $P > .05$ ).

**Figure 1.**

