# **ICTORES** Journal of Obstetrics Gynecology and Reproductive Sciences

Ahmed Elsadeek Radwan<sup>1</sup>. J Obstetrics Gynecology and Reproductive Sciences

## **Research Article**

**Open Access** 

## The Effect of Laser Acupuncture on Menopausal Symptoms

Ahmed Elsadeek Radwan<sup>1</sup>, Mohamed Amr Hussein Elnoury<sup>2</sup> and Sherif Fathi ElMekkawi<sup>3</sup>

<sup>1</sup>Department of Obstetrics & Gynecology, Suez Insurance Hospital,

<sup>2</sup>National Institute of Laser Enhanced Science, Cairo, Egypt,

<sup>3</sup>Department of Obstetrics and Gynecology, Ain Shams University, Abbassia, Cairo, Egypt

\*Corresponding Author: Ahmed Elsadeek Radwan– department of Obstetrics & Gynecology, Suez Insurance Hospital – Suez, Egypt. Email : ayman\_gyn007@yahoocom.

## Received date: January 14, 2017; Accepted date : February 23, 2017; Published date: March 27, 2017.

**Citation this Article:** Ahmed Elsadeek Radwan, The Effect of Laser Acupuncture on Menopausal Symptoms, J. Obstetrics Gynaecology and Reproductive Sciences, **Doi:** 10.31579/2578-8965/003

**Copyright** © 2017 Ahmed Elsadeek Radwan. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## Abstract:

#### Objective

Acupuncture is frequently utilized to manage climacteric symptoms and other gynecological conditions. Laser acupuncture has the advantages of being noninvasive, reproducible, and convenient. This study sought to explore the effectiveness of laser acupoint stimulation in relieving symptoms associated with menopause.

#### **Methods**

A randomized, double-blind, controlled study was conducted on 120 women diagnosed as menopausal patients (>1 year past last menstruation), aged 40 - 60 years with a Kupperman Menopause Index (KMI) equal or more than 15. women were randomized into Group A: Laser acupuncture (n=30), Group B: (HRT); Tibolone 2,5 mg/day (n=30) orally, Group C: Laser acupuncture and Tibolone 2,5 mg/day orally (n=30), Group D: Non interventional (self-care group) (n=30). Each patient was given a standard daily log and was required to record the frequency and severity of hot flashes and side effects of the treatment felt daily. The serum levels of follicle stimulating hormone (FSH), LH and E2 were detected before and after the treatment. **Results** 

120 woman

120 women with postmenopausal symptoms were divided randomly into four equal groups; After the treatment and the follow-up, in (Group A) there was no significant difference regarding FSH, LH and E2 level before treatment and after treatment with LASER acupuncture, as regard (Group B); there was statistically significant difference before and after treatment concerning hot flashes of KMI and he levels of FSH, LH decreased significantly and the level of E2 increased significantly. Combined treatment using hormonal replacement therapy with Laser Acupoints (Group C) showed dramatic improvement in study subjects and the improvement was more than that in group B. There were no significant differences were found regarding self-care group on either frequency of hot flashes, FSH, LH and E2 level.

#### Conclusions

Laser acupoints are effective and can be used as an alternative treatment to decrease the frequency and severity of postmenopausal hot flashes and postmenopausal symptoms especially if combined with Tibolone.

### **Key Words**

Laser acupoint stimulation, Acupuncture, Menopause, Hot flushes.

## Introduction

Menopause is a normal physiologic event that every woman who lives long enough will experience. Menopause is said to have occurred once a period of 12 months of amenorrhoea (no menstrual periods) has elapsed. Perimenopause is the era preceding menopause and finishes 12 months after the last menstrual period (1).

It can occur naturally as the consequence of aging or from surgical removal of the ovaries, radiotherapy, or chemotherapy.

Most ladies experience normal physiological menopause between 40 and 58 years of age (2-6). From perimenopause to late postmenopause, some ladies experience some difficulties "Menopausal symptom" which varies widely from mild to severe, and while many women transition through menopause with manageable symptoms, others experience more severe symptoms that include hot flashes and sweats (vasomotor instability) (7), new onset joint pain, vaginal dryness, sleep and mood disturbances (8).

While about 70% of women will seek symptom relief, some women will experience very mild symptoms and may not see the need to seek symptom relief from a health care provider (9). Vasomotor manifestations are exceptionally common crosswise over menopausal stages in many social orders (10).

Currently, menopausal women have an array of options for symptom management including hormone therapy, estrogen and/or progesterone(11), off label use of pharmaceutical agents such as antihypertensive or antidepressants (12), lifestyle changes, such as diet, exercise, alcohol and tobacco abstinence, and complementary and alternative therapies, such as herbs, meditation, or acupuncture (13).

For some women, such as estrogen receptor positive breast cancer survivors, estrogen therapy may be an absolute contraindication, and alternate pharmaceutical agents such as selective serotonin reuptake inhibitors (14),  $\alpha$ -1 adrenergic agents, (15) or may be used anticonvulsants (16). Unfortunately, a body of evidence suggests these pharmaceutical agents may only provide marginal symptom relief yet carry significant side effects (17).

In the past 10 years, new information from two large studies, the Heart and Estrogen/Progestin Replacement Study(18), and the Women's Health Initiative (19), have led women to consider the inherent safety of hormone therapy.

Both of these large, multi-center studies suggest risks of exogenous hormone therapy may outweigh benefits, has come under criticism after outcomes linking HRT specifically with an augmented risk of risks of breast cancer, stroke, heart disease or thrombosis (20).

For women who are not able to, or choose not to take hormones or pharmaceutical agents, alternative therapies may offer symptom relief with far fewer side effects (21).

Alternative therapies used by menopausal women may include herbs such as black cohosh, traditional Chinese herbs, exercise, mediation or paced respiration, and acupuncture (22).

However, to date, studies examining the effectiveness of complementary and alternative therapies for menopausal symptom relief have been small and yielded contradictory findings, which raise concerns regarding the efficiency of these therapies (23). This has driven ladies and healthcare staffs to search for alternative means of relieving the symptoms associated with menopause.

The executive summary identified several areas where further research is indicated: developing new methods for treating menopausal symptoms, attempting to increase the biologic and physiologic understanding of symptom etiology, and continuing to examine traditional and alternative, behavioral and non-pharmacologic therapies. Traditional Chinese medicine was specifically included in these recommendations (24).

## Patients and Methods

A randomized, double-blind, controlled study was conducted on 120 women diagnosed as menopausal patients (>1 year past last menstruation), aged 40 - 60 years with a Kupperman Menopause Index (KMI) equal or more than 15. Precipitants were selected randomly from Department of Medical Laser Application/ Laser Medical Center National Institute of Laser Enhanced science, Cairo University & Department of Gynecology, Ain Shams Gynecology and Obstetrics Hospital, Ain shams University and Department of Gynecology, Suez Health Insurance Hospital, Egypt. The study was done from October 2015 to May 2016. The participants divided into 4 groups (A&B&C&D):

- Group A: Laser acupuncture (n=30)
- Group B: (HRT); Tibolone 2.5 mg/day (n=30) orally.
- Group C: Laser acupuncture and Tibolone 2.5 mg/day orally (n=30)
- Group D: Non interventional (self-care group) (n=30)

spontaneous amenorrheic interval at least 6 months since the last regular menstruation. for those patients with an amenorrheic interval less than 12 months, the baseline level of e2 should not exceed 30 pg/ml. the level of thyroid-stimulating hormone (tsh) was normal and the serum fsh concentration was >50 miu/ml. kupperman menopause index at least 15. good general health; a gynecologic examination and laboratory tests showed that the patient did not suffer from other organic diseases of the reproductive system after the bilateral ovariectomy. written informed consent.

#### **Exclusion criteria**

- Recent use of systemic hormone therapy or hormonal contraceptives in last 8 weeks before study entry; (wash out period: 8 weeks for systemic and 4 weeks for local use), use of SSRI (wash out period: 8 weeks).
- Recent use of selective estrogen receptor modulators (SERMS) or aromatase inhibitors
- Known hypersensitivity or contraindications (reasons not to take) to estrogen, or progestins
- o contraindication of tibolone
- Pre-breast cancer or high-risk breast cancer condition; history of cancer within the past five years including use of tamoxifen
- Abnormal bleeding suggestive of endometrial pre-cancer or endometrial hyperplasia
- Abnormal screening blood tests; use of anticoagulant drugs.
- o More than eight years' amenorrhea
- $\circ$   $\;$  Thickness of postmenopausal endometrial thickness equal or more than 5 mm  $\;$
- Inability to complete the study procedures.
- Surgical menopause.
- Others; heart valve disease, poorly controlled hypothyroidism, hyperthyroidism, poorly controlled diabetes mellitus, tuberculosis, the body mass index (BMI) of the subject was more than 24, cigarette smoker, Organ transplant, psychological illness, overt drug or alcohol dependency.

#### Primary outcome measures:

 Change in a mean number of moderate to severe hot flushes per week combination of the mann whitney values (mwv) of the kupperman menopause index (kmi) and the frequency of adverse events at the end of treatment.

#### Secondary outcome measures:

- Menopausal symptoms and quality of life
- Hot flush weekly weighted score
- Kupperman menopause index (kmi)
- Assessments of adverse events
- Physical examinations
- Urogenital symptoms
- Laboratory tests (fsh, lh, estradiol, cholesterol).

#### Methods:

- After taking written consent from all patients, all patients subjected to:
- Full history.
- Full general examination.
- Hormonal profile.
- Routine blood examination, a routine uronoscopy, a liver function test and a renal function test, respectively, 1 day before the treatment started and 1 day after the treatment ended.

6

 Randomization lists were computer generated (block randomization, random block size).

 We measured the frequency of menopausal symptoms by Registration forms using a Kupperman Menopause Index (KMI).

#### Intervention

- The treatment program in the group (A) Laser acupuncture: It consisted of application of laser acupoints (Sanyinjiao (sp6), Hegu (LI.4), Quchi (LI.11), Fengchi (GB.20.), Guanyuan (CV 4.) and Fuliu (KI7)) of both sides for 6 weeks, three sessions /week, Infrared laser diode applied 90 Sec. / each point, with wave length 904 nm and power output 5 mill watts. The head of the machine was perpendicular, with direct contact to each point.
- The treatment program in the group (B) HRT Group: The patients were prescribed with oral Livial (Tibolone), in the dosage of one tablet a day (2.5 mg/tablet) for 12 consecutive weeks. One day before the treatment and at the end of the treatment, the levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH) were measured with enzyme- linked immunosorbent assay (ELISA) and the levels of E2 were measured with double antibiotic ELISA.
- Patients in Group (C) were treated with Laser acupuncture and Tibolone 2,5 mg/day orally;
- Patients in Self-care group were guided by the information leaflet on self-provided care for menopausal symptoms, the participants were free to use any over-the-counter medication and self-provided non- pharmaceutical interventions. No medical treatment for menopausal symptoms was prescribed to them within the study.
- **Hot flashes and sleep disturbances:** Participants received a diary in which they recorded frequency and severity of hot flashes and amount of sleep at night for 14 days.
- The severity of hot flashes was defined as follows:
  - o mild—a fleeting, warm sensation without sweating or disruption of normal activities;
  - moderate—a warm sensation associated with sweating, and disruption of normal activities;
  - severe—a hot sensation associated with sweating and the discontinuation of normal activities.
- The score of the hot flash severity for a particular day is calculated by adding  $1 \times$  the number of mild hot flashes  $+ 2 \times$  the number of moderate hot flashes  $+ 3 \times$  the number of severe hot flashes.
- The frequency of hot flashes is the total number of the mild, moderate and severe hot flashes occurred during 24 hours. Scoring: 0 = Absent: 1 = mild: 2 = moderate: 3 = Severe

Symptom	Frequency/day	Score
Hot flushes		
Light headaches		
Headaches		
Depression		
Irritability		
Unloved feelings		
Anxious feelings		
Anxious sleeplessness		
Unusual tiredness		
Backache		
Joint pains		
Muscle pains		
New facial hair		
Unusual dry skin		
Less sex drive		
Less sexual feelings		
Dry vagina		
Dyspareunia (painful intercourse)		
TOTAL SCORE:		

For analyses an average score is calculated. Scores over 15 correlate strongly with objective measures of oestrogen deficiency and are suggestive of (peri) menopause.

## Results

In this study, 120 women with postmenopausal hot flashes were divided randomly into four equal groups (**A & B & C & D**):

**Group A**: Laser acupuncture (n=30); the mean age and BMI were  $(49.4\pm5.38)$  years and  $(26.69\pm2.45)$  Kg/m2.

**Group B**: (HRT); Tibolone 2,5 mg/day (n=30) orally were included in this group; the mean age and BMI were  $(49.13\pm4.97)$  years and  $(26.88\pm2.52)$  Kg/m2.

**Group C**: Laser acupuncture and Tibolone 2,5 mg/day orally (n=30) were included in this group; the mean age and BMI were  $(50.37\pm4.97)$  years and  $(26.17\pm2.50)$  Kg/m2.

**Group D**: Non interventional (self-care group) (n=30) were included in this group; the mean age and BMI were ( $50.70\pm5.74$ ) years and ( $26.53\pm2.60$ ) Kg/m2.

a	b	e	(2)	):	Comparison	between	groups	according	to age(yea	rs)
---	---	---	-----	----	------------	---------	--------	-----------	------------	-----

Ana (vaars)	Group A		Group B		Group C		Group D		Chi-square test	
Age (years)	No.	%	No.	96	No.	96	No.	%	x2	p-value
40-46 y	10	33.3%	16	53.3%	11	36.7%	9	30.0%		0.303
47-54 y	10	33.3%	10	33.3%	14	46.7%	12	40.0%	7,193	
55-60 y	10	33.3%	4	13.3%	5	16.7%	9	30.0%		
Total	30	100.0%	30	100.0%	30	100.0%	30	100.0%		

This table shows no statistically significant difference between groups according to age (years).

able (3): comparison of the 4 groups as regard the hot flus
---

Hot flashes	Group A	Group B	Group C	Group D
Before	4.77±1.28	4.90±1.40	4.90±1.40	4.87±1.31
After	3.17±1.46	2.30±1.70	1.40±0.86	4.67±1.47
Paired Diff.	1.60	2.60	3.50	0.20
Paired sample t-test	0.05	3.697	8.776	0.345
p-value	0.823	0.037	< 0.001	0.559

This table shows statistically significant difference between before and after treatment according to hot flashes of KMI in group A and B.

 Table (4): comparison of KMI among the 4 groups

KMI	Group A	Group B	Group C	Group D	F	p-value
Before						
Mean±SD	29.50±3.69	29.50±3.69	30.50±3.81	30.50±3.81	1 679	0.149
Range	24-35	22-37	25-36	23-38	1.0/8	0.148
After						
Mean±SD	26.90±3.38ª	17.50±2.19 <sup>b</sup>	19.00±2.38 <sup>b</sup>	27.30±3.44ª	11 207	<0.001
Range	21-33	15-20	16-22	19-36	11.38/	<0.001

\*\* All common characters have no differences

This table shows highly statistically significant difference between groups according to after of KMI.

6

6

## Discussion

An earlier study showed that the transition from reproductive to nonreproductive years in women is characterized by increased reporting of psychological, somatic, vasomotor and urogenital symptoms (25).

Menopause is a natural biological process, not a medical illness that defined as the permanent end of menstruation and fertility that occurs 12 months after last menstrual period. It caused by the natural decline of reproductive hormones, that ovaries start making less estrogen and progesterone.

Vasomotor episodes with hot flashes and night sweating are the most prevalent complaints related to menopause. A hot flash is described as a feeling of intense heat in the face, neck and chest. It lasts on average four minutes, with a range from a few seconds up to 10 minutes or more (26).

Although menopause is associated with changes in the hypothalamic and pituitary hormones that regulate the menstrual cycle, menopause is not a central event, but rather primary ovarian failure. As the hypothalamic-pituitary-ovarian axis remains intact during the menopausal transition, FSH levels rise in response to ovarian failure and the absence of negative feedback from the ovary (27).

Atresia of the follicular apparatus, in particular the granulosa cells, results in the reduced production of estrogen and inhibin, which leads to the reduced inhibin levels and the elevated FSH levels, a cardinal sign of menopause (28).

Correlations between endocrine levels and symptom severity ratings over time revealed that hot flash severity was sig- nificantly and positively related to FSH (29).

Menopausal symptoms affect about 70% of women approaching menopause. Common menopausal symptoms are menstrual irregularities that periods may come more frequently, shorten or lengthen, and become light or heavy, hot flash which is sudden feeling of warmth or heat that spreads over the body creating redness particularly noticeable in face and upper body, mood swing that the mood one minute up and another minute down, insomnia, vaginal dryness that vagina loss usual moist and may be associated with irritation, fatigue, weight gain especially in abdomen and depression (30).

Vasomotor, somatic, and psychological symptoms associated with menopause are often treated with hormone replacement therapy (HRT), but the role of non-pharmacological interventions has received little attention. As hot flashes are the most common problem for post-menopausal women and the potential health risks of HRT, it is important to find out an effective, safe and non-pharmacological treatments to relieve their menopausal hot flashes (*31*).

It is well known that acupuncture is associated with homeostatic regulation, and possess effects such as buffering hormonal disturbance, modulating ovulation, as well as improving psychological or behavioral abnormity (32).

Acupuncture in specific acupoints has been found to significantly increase blood concentrations of E2 in the ovariectomized rats (33), while reducing the elevated plasma LH due to ovariectomy; in addition, acupuncture also restored the number of gonadotropin-releasing hormone (GnRH) neurons in the ovariectomized rats (34).

Laser acupuncture is the irradiation of acupuncture points with low intensity laser which is alternative to invasive acupuncture needling. Laser acupuncture is advantageous in terms of side effects compared to classical acupuncture techniques and studies showed that there are positive effects can be assumed in myofascial pain syndromes of the neck, back and shoulder (35).

Laser acupoints were found to assist in the alleviation of postmenopausal hot flashes frequency and intensity (36).

This study was carried out to study the effect of laser acupuncture on menopausal symptoms. This prospective study was conducted in Suez Insurance Hospital, Ain Shams University Maternity Hospital and National Institute of Laser at the period starting October 2015 to May 2016 and included 120 postmenopausal women.

In the current study (**Group A**) women treated with LASER acupoints found to show improvement of symptoms associated with menopause especially the daily frequency of hot flushes.

also there was a little decrease in FSH and LH but there was no significant difference regarding FSH, LH and E2 level before treatment and after treatment with LASER acupuncture (P-value >0.05).

This agrees with *another study* which found that; laser acupoint stimulation using acupoints chosen from a limited set of acupoints is not efficacious in reducing symptoms associated with menopause (*37*).

Another study did not recommend laser acupuncture for relief of menopause symptoms (38). However, this disagrees with the finding of *a study which stated that* acupuncture and auricular acupressure significantly relieve the severity and frequency of menopausal hot flashes (39)

In another study, acupuncture was found to improve the reproductive disorders induced by ovariectomy in rats through modulating the blood E2 levels (40). Acupuncture may improve the function of the hypothalamic-pituitary-ovarian axis, increase blood adrenogenous androgen level and facilitate its transformation into estrogen by an aromatic enzyme in the brain, liver and fat tissues.

In another study, were comparison of laser-on versus laser- off acupuncture, laser-on treatments were ineffective in altering menopausal symptoms, over 3 months; the women documented their menopause symptoms (41).

During this time, 23 had laser-on and 17 had laser-off (sham) acupuncture to 10 specific body points every 14 days. On average, the laser-on and laser-off groups, respectively, reported about 37 and 33 percent fewer daytime and about 30 and 39 percent fewer nighttime hot flashes. They suggested further studies of laser acupuncture in menopausal women focus on alternative acupuncture points (41).

In (**Group A**) there was no significant difference regarding FSH, LH and E2 level before treatment and after treatment with LASER acupuncture (P-value >0.05).

As regard **Group B**; Tibolone administration relieves climacteric complaints. There was statistically significant difference before and after treatment concerning hot flashes of KMI. Also it shows highly significant statistically difference before and after treatment according to FSH, LH and E2 level.

This agrees with a previous study which found that tibolone exerts encouraging effects on climacteric symptoms. These effects have been attributed to its unique molecular profile and to the tissue-related metabolism into estrogenic, progestogenic, and androgenic metabolites (42).

In **Group B**; the levels of FSH, LH decreased significantly and the level of E2 increased significantly (P-value <0.001). Same as **Group B**, Combined treatment using hormonal replacement therapy with Laser Acupoints (**Group: C**) it showed dramatic improvement in study subjects and the improvement was more than that in group B; as showed in Result chapter.

Studies compared electro acupuncture, or acupuncture plus auricular acupressure, versus hormonal therapy and reported hot flush frequency or severity, found that; acupuncture was associated with significantly more hot flushes per day than hormonal therapy (43).

## Conclusion

We conclude that the protocol of treatment in HRT group alone (**Group B**) and the group of a combination of laser acupoints in addition to HRT protocol of treatment (**Group C**) led to significant improvements in hot flash frequency and intensity and improvement the menopausal symptoms according to a score of KMI before and after treatment.

Also improvement of the levels of FSH and LH which decreased significantly while the level of E2 increased significantly. In the present study, laser acupoints was found to improve the postmenopausal symptoms and may improve the function of the hypothalamic-pituitary-ovarian axis, increase blood adrenogenous androgen level and facilitate its transformation into estrogen by aromatic enzyme in the brain, liver and fat tissues but it found to be highly effective if combined with HRT; we recommend to be used as alternative treatments to relieve menopausal symptoms.

Finally, laser acupoints are effective and can be used as an alternative treatment to decrease the frequency and severity of postmenopausal hot flashes and postmenopausal symptoms especially if combined with Tibolone.

#### References

- Perry, John R.B., Tanguy Corre, Tõnu Esko, Daniel I. Chasman, Krista Fischer, et al. (2013): "A Genome-Wide Association Study of Early Menopause and the Combined Impact of Identified Variants." Human Molecular Genetics 22(7): 1465–72.
- NIH. (2005): "NIH State-of-the-Science Conference Statement on Management of Menopause-Related Symptoms." NIH consensus and state-of-the-science statements 22(1): 1–38.
- Woods, Nancy Fugate, Kathleen Smith-Dijulio, Donald B Percival, Eunice Y Tao, Heather J Taylor, and Ellen Sullivan Mitchell. (2007): "Symptoms during the Menopausal Transition and Early Postmenopause and Their Relation to Endocrine Levels over Time: Observations from the Seattle Midlife Women's Health Study." Journal of women's health (2002) 16(5): 667–77.
- 4. Abernethy, Kathy. (2009): "Multidisciplinary Working: The Need for Competence." Menopause international 15(4): 140–41.
- Ader, R. (2000): "The Placebo Effect: If It's All in Your Head, Does That Mean You Only Think You Feel Better?" Advances in mindbody medicine 16(1): 7–11.
- Aiello, Erin J, Yutaka Yasui, Shelley S Tworoger, Cornelia M Ulrich, Melinda L Irwin, et al. (2004): "Effect of a Yearlong, Moderate-Intensity Exercise Intervention on the Occurrence and Severity of Menopause Symptoms in Postmenopausal Women." Menopause (New York, N.Y.) 11(4): 382–88.
- Bungay, G T, M P Vessey, and C K McPherson. (1980): "Study of Symptoms in Middle Life with Special Reference to the Menopause." British medical journal 281(6234): 181–83.
- Burger, Henry G., G. E. Hale, D. M. Robertson, and L. Dennerstein. (2007): "A Review of Hormonal Changes during the Menopausal Transition: Focus on Findings from the Melbourne Women's Midlife Health Project." Human Reproduction Update 13(6): 559–65.
- Burke, Adam, Dawn M Upchurch, Claire Dye, and Laura Chyu. (2006): "Acupuncture Use in the United States: Findings from the National Health Interview Survey." Journal of alternative and complementary medicine (New York, N.Y.) 12(7): 639–48.
- Freedman, Robert R. (2005): "Pathophysiology and Treatment of Menopausal Hot Flashes." Seminars in Reproductive Medicine 23(2): 117–25.
- Freeman, Ellen W., Mary D. Sammel, Hui Lin, and Deborah B. Nelson. (2006): "Associations of Hormones and Menopausal Status With Depressed Mood in Women With No History of Depression." Archives of General Psychiatry 63(4): 375.

- 12. Friedman, Elliot M, Mary Hayney, Gayle D Love, Burton H Singer, and Carol D Ryff. (2007): "Plasma Interleukin-6 and Soluble IL-6 Receptors Are Associated with Psychological Well-Being in Aging Women." Health psychology : official journal of the Division of Health Psychology, American Psychological Association 26(3): 305–13.
- Gaab, J., N. Rohleder, U. M. Nater, and U. Ehlert. (2005): "Psychological Determinants of the Cortisol Stress Response: The Role of Anticipatory Cognitive Appraisal." Psychoneuroendocrinology 30(6): 599–610.
- George, Sharon A. (2002): "The Menopause Experience: A Woman's Perspective." Journal of Obstetric, Gynecologic & Neonatal Nursing 31(1): 77–85.
- Gold, Ellen B. (2011): "The Timing of the Age at Which Natural Menopause Occurs." Obstetrics and Gynecology Clinics of North America 38(3): 425–40.
- Guthrie, Janet R, Lorraine Dennerstein, John R Taffe, Philippe Lehert, and Henry G Burger. (2005): "Hot Flushes during the Menopause Transition: A Longitudinal Study in Australian-Born Women." Menopause (New York, N.Y.) 12(4): 460–467.
- Hardy, Rebecca, and Diana Kuh. (2002): "Change in Psychological and Vasomotor Symptom Reporting during the Menopause." Social Science and Medicine 55(11): 1975–1988.
- Harlow, Siobán D., and Pangaja Paramsothy. (2011): "Menstruation and the Menopausal Transition." Obstetrics and Gynecology Clinics of North America 38(3): 595–607.
- Harlow, Siobán D, Margery Gass, Janet E Hall, Roger Lobo, Pauline Maki, et al. (2013): "NIH Public Access." 19(4): 387– 395.
- HARMAN, S.MITCHELL, FREDERICK NAFTOLIN, ELIOT

   A. BRINTON, and DEBRA R. JUDELSON. (2005): "Is the Estrogen Controversy Over? Deconstructing the Women's Health Initiative Study: A Critical Evaluation of the Evidence." Annals of the New York Academy of Sciences 1052(1): 43–56.
- Kuczmarski, R J, M D Carroll, K M Flegal, and R P Troiano. (1997): "Varying Body Mass Index Cutoff Points to Describe Overweight Prevalence among U.S. Adults: NHANES III (1988 to 1994)." Obesity Research 5(6): 542–548.
- 22. Kumar, V, AK Abas, and N Fausto. (2004): 12 Robbins and Cotran Pathologic Basis of Disease.
- Lee, M M, S S Lin, M R Wrensch, S R Adler, and D Eisenberg. (2000): "Alternative Therapies Used by Women with Breast Cancer in Four Ethnic Populations." Journal of the National Cancer Institute 92(1): 42–47.
- Lekander, Mats, Stig Elofsson, Ing-Marie Neve, Lars-Olof Hansson, and Anna-Lena Undén. (2004): "Self-Rated Health Is Related to Levels of Circulating Cytokines." Psychosomatic medicine 66(4): 559–563.
- Lewis, Vivian. (2009): "Undertreatment of Menopausal Symptoms and Novel Options for Comprehensive Management." Current medical research and opinion 25(11): 2689–2698.
- Lewith, George T., Peter J. White, and Ted J. Kaptchuk. (2006): "Developing a Research Strategy for Acupuncture." The Clinical Journal of Pain 22(7): 632–638.
- Liu, Rui Hai. (2004): "Potential Synergy of Phytochemicals in Cancer Prevention: Mechanism of Action." The Journal of nutrition 134(12 Suppl): 3479S–3485S.
- Lobo, R L. (1987): "Absorption and Metabolic Effects of Different Types of Estrogens and Progestogens." Obstet.Gyn.Clin.N.A. 14(1): 143–168.
- 29. Long, Cheng-Yu, Cheng-Min Liu, Shih-Cheng Hsu, Chin-Hu Wu, Chiu-Lin Wang, and Eing-Mei Tsai. (2006): "A Randomized Comparative Study of the Effects of Oral and Topical Estrogen Therapy on the Vaginal Vascularization and Sexual Function in Hysterectomized Postmenopausal Women." Menopause (New York, N.Y.) 13(5): 737–743.

 Loprinzi, Charles L., Vered Stearns, and Debra Barton. (2005): "Centrally Active Nonhormonal Hot Flash Therapies." American Journal of Medicine 118(12 SUPPL. 2): 118–123.

6

- Low Dog, Tieraona. (2005): "Menopause: A Review of Botanical Dietary Supplements." American Journal of Medicine 118(12 SUPPL. 2): 98–108.
- 32. Scheid, Volker. (2007): "Traditional Chinese Medicine-What Are We Investigating?. The Case of Menopause." Complementary Therapies in Medicine 15(1): 54–68.
- 33. Schilling, C, L Gallicchio, S R Miller, P Langenberg, H Zacur, and J A Flaws. (2007): "Relation of Body Mass and Sex Steroid Hormone Levels to Hot Flushes in a Sample of Mid-Life Women." Climacteric : the journal of the International Menopause Society 10(1): 27–37.
- Schwingl, P J, B S Hulka, and S D Harlow. (1994): "Risk Factors for Menopausal Hot Flashes." Obstetrics and gynecology 84(1): 29–34.
- 35. Shapiro, Sander. (2001): "Addressing Postmenopausal Estrogen Deficiency." Medscape General Medicine.
- Shelton, Tamara Venit. (2013): "Curiosity or Cure? Chinese Medicine and American Orientalism in Progressive Era California and Oregon." Oregon Historical Quarterly 114(3):266.
- Sherwood, Andrew, Joel W. Hughes, Cynthia Kuhn, and Alan L. Hinderliter. (2004): "Hostility Is Related to Blunted β-Adrenergic Receptor Responsiveness Among Middle-Aged Women." Psychosomatic Medicine 66(4): 507–513.

- Shifren, Jan L., Susan R. Davis, Michele Moreau, Arthur Waldbaum, Celine Bouchard, et al. (2006): "Testosterone Patch for the Treatment of Hypoactive Sexual Desire Disorder in Naturally Menopausal Women." Menopause 13(5): 770–779.
- 39. Takeo, Chikari, Etsuko Negishi, Aya Nakajima, Koichi Ueno, Ichiro Tatsuno, et al. (2005): "Association of Cytosine-Adenine Repeat Polymorphism of the Estrogen Receptor-?? Gene with Menopausal Symptoms." Gender Medicine 2(2): 96–105.
- Tang, Jin Ling, Bao Yan Liu, and Kan Wen Ma. (2008): "Traditional Chinese Medicine." The Lancet 372(9654): 1938– 40.
- 41. Thomson, Angus W., and Michael T. Lotze. (2003): The Cytokine Handbook, Two-Volume Set. Elsevier.
- Thurston, Rebecca C., Joyce T. Bromberger, Hadine Joffe, Nancy E. Avis, Rachel Hess, et al. (2008): "Beyond Frequency: Who Is Most Bothered by Vasomotor Symptoms?" Menopause 15(5): 841–47.
- 43. Zhao, Hong, Zhan Zhuang Tian, and Bo Ying Chen. (2003): "An Important Role of Corticotropin-Releasing Hormone in Electroacupuncture Normalizing the Subnormal Function of Hypothalamus-Pituitary-Ovary Axis in Ovariectomized Rats." Neuroscience Letters 349(1): 25–28.