

## ACUPUNCTURE IN THE TREATMENT OF MENOPAUSE-RELATED SYMPTOMS IN WOMEN TAKING TAMOXIFEN

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Fifteen patients were enrolled in a pilot study to evaluate the safety and efficacy of acupuncture for the treatment of menopausal symptoms in tamoxifen-treated patients. Patients were evaluated before treatment and after one, three and six months with the Greene Menopause Index and were treated according to the traditional Chinese medicine. Anxiety, de-

pression, somatic and vasomotor symptoms were improved by the treatment; libido was not modified. Acupuncture seems to be safe and effective for the treatment of menopausal symptoms in women with previous breast cancer taking tamoxifen. Confirmatory studies with a larger number of patients and with a placebo-treated group are warranted.

**Key words:** acupuncture, menopause, tamoxifen.

### Introduction

Tamoxifen is a cornerstone in the adjuvant treatment of primary breast cancer. It reduces recurrences and mortality<sup>1</sup> and the risk of osteoporotic fracture<sup>2</sup>, with a slight increase in the risk for endometrial cancer and venous thromboembolism<sup>1-3</sup>. Nevertheless, benefits far outweigh risks. Some reports, but not all, suggest a reduction in the incidence of coronary events in women treated with tamoxifen<sup>2-4</sup>.

Menopause-related symptoms, like hot flashes, night sweats and vaginal discharge, are frequently enhanced in patients taking tamoxifen, and more than half report one or more of these symptoms<sup>5</sup>. Several non-estrogenic agents have been employed to reduce the severity of menopausal syndrome with inconclusive results<sup>6</sup>.

Some authors have reported interesting results on the use of acupuncture in treatment of menopause-related symptoms<sup>7,8</sup>. Furthermore, acupuncture seems to be effective in the treatment of vasomotor symptoms in men affected by prostatic carcinoma receiving Gn-RH analogue<sup>9</sup>.

Based on these reports, we began a pilot study to evaluate the safety and efficacy of acupuncture in the treatment of menopause-related symptoms in tamoxifen-treated patients.

### Patients and methods

From January 1999 to June 2000, 15 patients (mean age, 51; range, 37-56) suffering from tamoxifen-related symptoms were enrolled in the study. All patients were treated with QUART (quadrantectomy with axillary dissection and radiotherapy), adjuvant chemotherapy (CMF, 1.8 q 28 for six courses) and are taking tamox-

ifen (20 mg/day) as adjuvant hormone therapy. The histologic specimen revealed a node negative, ductal or lobular carcinoma, and estrogen receptors positive in all patients. All patients were menopausal at least for one year and had never assumed drugs to treat menopausal symptoms. All patients were free of disease for at least 2 years. A research nurse administered the Greene Menopause Index to all patients before treatment (T0), after 1 month (T1), 3 (T2) and 6 months (T3) in the form of structured interview. After an informed consent, acupuncture was started with a weekly schedule for 3 months and was performed on a series of occupants according to traditional Chinese medicine. Later, patients were treated monthly with a maintenance intent. In particular, KI-6, SP-6, BL-23, CV-4, GB-35 and H-5 points were stimulated in all patients. Compliance with tamoxifen assumption and with the follow-up program was also recorded.

### Outcome measures

The Greene Menopause Index is structured in 21 items in order to obtain a comprehensive evaluation of menopausal status based on the appraisal of 21 symptoms (for each item: 0, absence of symptom; 1, symptom rarely present; 2, symptom often present; 3, symptom very often present). Items 1-6 (possible range, 0-18) are related to anxiety (A). Items 7-11 (possible range, 0-12) are related to depression (D). Somatic symptoms (S) are investigated by items 12-18 (possible range, 0-18). Items 19-20 (possible range, 0-6) are related to vasomotor symptoms (V), and item 21 (possible range, 0-4) is dedicated to reduction of libido (sex). The Greene Menopause Index was previously validated for an Italian population of postmenopausal women.

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### Statistical analysis

The Friedman test was used to evaluate the overall significance of differences among the four observation times for each dimension of the Greene Menopause Index. Pairwise comparisons (before treatment vs respectively one month, 3 months and 6 months) were performed using the Wilcoxon matched-pairs signed rank test when the Friedman test was significant. Since three comparisons were made, significance level was considered equal to 0.017, for each comparison, to assume a global significance level of 0.05.

### Results

All patients completed the programmed protocol of acupuncture; no side effects were recorded.

Friedman test analysis suggested that scores related to anxiety ( $P < 0.001$ ), depression ( $P < 0.001$ ), somatic ( $P < 0.001$ ) and vasomotor symptoms ( $P = 0.001$ ) were significantly improved by the treatment, whereas libido was not modified.

The Wilcoxon matched-pairs signed test analysis revealed a progressive improvement in anxiety, somatic and vasomotor symptoms, whereas depression did not ameliorate after the third month of treatment (Table 1).

All patients complied with treatment with tamoxifen and with the follow-up program.

### Discussion

Treatment of postmenopausal women with a history of breast cancer has two objectives: (i) prevention of osteoporosis, cardiovascular and Alzheimer's disease, and (ii) treatment of menopausal-related symptoms. Tamoxifen reduces the incidence of osteoporotic fractures<sup>2</sup>, and some studies have demonstrated a reduction in coronary events<sup>2,4</sup>. However, it exacerbates menopause-related symptoms such as hot flushes, night sweats and vaginal discharge, dryness and itching<sup>5</sup>.

Several drugs (vitamin E, megestrol acetate, fluoxetine, venlafaxine, paroxetine, clonidine, ergotamine, soy phytoestrogens) have been used to treat hot flushes. Results have been inconclusive, and a significant incidence of secondary effects related to the drug administered have been reported<sup>6</sup>.

Hormone replacement therapy (HRT) has been proposed to treat vasomotor symptoms in women taking tamoxifen<sup>10</sup>. We do not recommend this approach based on three considerations: (i) data on the safety of HRT in women with previous breast cancer are insufficient<sup>11</sup>; (ii) the consequences of the use of HRT on the beneficial effect of tamoxifen are unknown; (iii) women with a history of breast cancer are hesitant to receive estrogen-based therapy<sup>12,13</sup>.

The treatment of choice for menopausal symptoms in women taking tamoxifen has not been defined. In this group of patients, acupuncture seems to be effective

**Table 1 - Wilcoxon matched-pairs signed rank test analysis**

Domains	Treatment	M ± SD	Significance levels of comparisons with respect to $t_0$ $P <$
Anxiety	T <sub>0</sub>	8.07 ± 3.11	-
	T <sub>1</sub>	6.67 ± 3.07	0.002
	T <sub>2</sub>	4.80 ± 2.71	0.0001
	T <sub>3</sub>	3.40 ± 1.99	0.0001
Depression	T <sub>0</sub>	7.93 ± 3.98	-
	T <sub>1</sub>	6.00 ± 3.26	0.001
	T <sub>2</sub>	4.73 ± 2.84	0.001
	T <sub>3</sub>	3.07 ± 1.81	ns (0.035)
Somatic symptoms	T <sub>0</sub>	5.66 ± 3.46	-
	T <sub>1</sub>	3.60 ± 1.82	0.002
	T <sub>2</sub>	2.80 ± 1.64	0.001
	T <sub>3</sub>	2.13 ± 1.08	0.001
Vasomotor symptoms	T <sub>0</sub>	5.67 ± 0.69	-
	T <sub>1</sub>	3.33 ± 1.01	0.001
	T <sub>2</sub>	2.40 ± 0.95	0.0001
	T <sub>3</sub>	2.06 ± 1.18	0.0001

T<sub>0</sub> = before treatment, T<sub>1</sub> = after one month, T<sub>2</sub> = after three months, T<sub>3</sub> = after six months.

for treatment of vasomotor symptoms<sup>14</sup>. Our data confirm the safety and efficacy of acupuncture in the treatment of vasomotor symptoms in women treated with tamoxifen. At the same time, we recorded a significant improvement in the control of anxiety, depression and somatic symptoms, but libido was not modified. No secondary effects related to acupuncture were recorded.

Data on compliance to standard therapy of patients treated with acupuncture and/or with other alternative and complementary treatment modalities are contradictory<sup>15,16</sup>. In our experience, all patients were compliant with the treatment with tamoxifen and to the programmed follow-up. In order to avoid withdrawal of the standard treatment, we believe mandatory that the oncologist explain the role of acupuncture. We clearly inform our patients that acupuncture is "complementary" and not "alternative" to the standard treatment and that its aim is to treat menopausal symptoms and to improve quality of life, not to cure cancer. Our data, in accord with previous reports, suggest that the use of complementary or alternative medicine is not associated with poor compliance with standard treatment<sup>17,18</sup>.

Limitations of our study are related to the small number of patients and to the absence of a placebo-treated group. Menopausal symptoms are influenced by a series of behavioral components, and a placebo group is recommended. Nevertheless, our data are promising and offer a new choice for the treatment of menopausal symptoms in women taking tamoxifen, without secondary effects and with a good compliance to the standard treatment.

Further studies with a larger number of patients and with a control group are required to define the role of acupuncture in the treatment of menopause-related symptoms in women taking tamoxifen.

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