Abstracts and Commentaries on Key Articles in the Literature

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Acupuncture for the treatment of hot flashes in patients with breast cancer receiving antiestrogen therapy: a pilot study in Korean women.

Jeong YJ, Park YS, Kwon HJ, Shin IH, Bong JG, Park SH. *J Altern Complement Med.* 2013;19(8):690–696.

RESearchers from the Catholic University of Daegu, and Daegu Haany University of Oriental Medicine, in Daegu, Korea, conducted this prospective single-armed observational study. This study was supported by a grant of the Ministry of Health and Welfare, Republic of Korea (Project No. 20-11-0-090-091-3000-3033-320).

This study was planned to evaluate the feasibility and safety of acupuncture for treatment of hot flashes in Korean women with breast cancer who were undergoing antiestrogen therapy. Ten Korean women with breast cancer were enrolled in the study.

Inclusion criteria were as follows: (1) pre- or postmenopausal status and presence of breast cancer treated with antiestrogen therapy using tamoxifen or anastrozole; (2) moderate or severe vasomotor symptoms according to the definition of the U.S. Food and Drug Administration; (3) an average of three or more hot flashes per week during the 1-week period before the trial; (4) a Karnofsky performance score of > 60 , which means the ability to participate in the trial for oneself or with occasional assistance; (5) voluntary participation; (6) follow-up for the duration of the study; (7) cessation of hormone-replacement therapy or other pharmacologic or alternative treatments for hot flashes at least 4 weeks before the trial, if such treatments were used.

Participants received 12 sessions of acupuncture, provided 3 times per week for 4 weeks. The severity of hot flashes was assessed via a visual analogue scale (VAS) and a total hot flash score. Patients were evaluated 1 week before treatment (baseline), once per week during treatment, and 4 weeks after the final acupuncture session. All sessions were 40 minutes long, and the acupuncture portion was 20 ± 5 minutes in duration. Acupuncture was applied at five acupuncture points: GV 20; M-HN-3; and bilaterally at three points, HT 8, KI 10, and LR 2. No

electrical stimulation or other interventions were used. Acupuncture was performed by a traditional Korean medicine (TKM) physician with a minimum of 3 years of experience.

The mean age at baseline was 46.6 years (standard deviation [SD]=4.93; range, 38–53).

Changes in mean VAS score from baseline to 4 weeks after the final acupuncture session showed a significant reduction in the average VAS score for hot-flash severity at the end of treatment ($F = 30.261$, $p < 0.001$). A repeated-measures analysis of variance revealed a significant reduction in the average frequency, severity, and total hot flash score at the end of treatment ($F = 3.719$, $p = 0.007$; $F = 21.698$, $p < 0.001$; $F = 3.825$, $p = 0.006$, respectively). Acupuncture was well-tolerated with few adverse events.

Results from this small study suggest that acupuncture is a useful alternative treatment for alleviating hot flashes in patients who have breast cancer and who are receiving antiestrogen therapy.

Continuous auricular electroacupuncture can significantly improve heart rate variability and clinical scores in patients with depression: first results from a transcontinental study.

Shi X, Litscher G, Wang H, et al. *Evid Based Complement Alternat Med.* 2013;2013:894096.

THIS STUDY WAS CONDUCTED by researchers from the People's Liberation Army General Hospital, Beijing, China, the Medical University of Graz, Graz, Austria, and a private clinic, Lassnitzhöhe, in Lassnitzhöhe, Austria. The study was supported by the Stronach Medical Group, the Austrian Federal Ministries of Science and Research and Health, the Eurasia-Pacific Uninet, and the German Academy of Acupuncture.

In this article, the researchers describe the results from continuous auricular electroacupuncture (EA) measurements in patients with depression using computer-based heart rate variability (HRV) recordings before, during, and

after long-lasting EA under standardized clinical conditions in Beijing, China.

Ten patients (7 females and 3 males; age range 29–59) who were depressed (Chinese diagnosis: Yu Zheng) and therefore receiving acupuncture treatment were investigated at the Chinese People's Liberation Army Hospital in Beijing.

The clinical evaluation of the patients, performed immediately before the first HRV data recording, used three main scales: the Hamilton anxiety rating scale (HAM-A); the Athens insomnia scale (AIS); and the Hamilton rating scale for depression (HRSD). The duration of R–R intervals was measured during a special time period (5 minutes), and, on a spectral-analysis basis. HRV (using a Medilog AR12 HRV [Huntleigh Healthcare, Cardiff, United Kingdom] system) was determined. Mean heart rate (HR), total HRV, and low-frequency/high-frequency (LF/H) ratio of HRV were chosen as evaluation parameters.

A method used for ear acupuncture is an electrical point-stimulation system (P-Stim; Biegler, Austria). Ultrathin permanent needles are applied at the ear. A generator, located behind the acupunctured ear, produces electrical stimulation impulses (using a constant alternating current of 1 mA, an impulse duration of 1 ms, and a stimulus frequency of 1 Hz; alternating 15 minutes of active stimulation with 15-minute breaks [no active stimulation]) in sessions conducted during a 3-day period. The following ear acupoints were chosen by an experienced Chinese acupuncturist for use in this study: *Shenmen*, Small Intestine, and Heart.

Patients came to the clinic on 3 consecutive days: On day 1, the subjects completed the questionnaires; then a first HRV measurement was performed, followed by application and activation of the P-Stim auricular stimulation equipment; immediately after that, a second HRV measurement was recorded. On day 2, with each patient still wearing the P-Stim device, the questionnaire was completed again and a third HRV measurement was recorded. Finally, on day 3, while still wearing the auricular punctual stimulation, a fourth HRV measurement was performed before the P-Stim device was removed. After a break of 30 minutes, a last HRV measurement was recorded, followed by completion of the questionnaire one final time.

There was a slight decrease in HR, but no significant change before, during, or after the stimulation sessions. In contrast, HRV was increased significantly ($p=0.041$) after continuous auricular EA over a 3-day period. Continuous HRV monitoring showed no significant alterations in the LF/HF ratio during or after ear acupuncture stimulation.

Significant reduction of the three scores investigated within this study (HAM-A, AIS; HRSD) were already noted after the first day of continuous EA with the P-Stim.

The researchers concluded that auricular stimulation resulted in positive, quantifiable clinical and physiologic alterations in parameters after continuous auricular acupoint stimulation in patients with depression.

Acupuncture in practice: investigating acupuncturists' approach to treating infantile colic.

Landgren K. Evid Based Complement Alternat Med. 2013;2013: 456712.

THIS REVIEW WAS CONDUCTED by a researcher from Lund University, in Lund, Sweden.

Infantile colic—in which an otherwise healthy infant cries and/or fusses for >3 hours per day, >3 days per week—affects 10%–40% of infants. Based on personal communications with internationally recognized pediatric acupuncture teachers and with experienced practitioners who also specialize in pediatrics, this article explores and discusses how acupuncturists trained in Traditional Chinese Medicine (TCM) regard and treat infantile colic.

At a major acupuncture conference in Europe in 2012 (one of the themes was pediatric acupuncture), nearly all of the speakers who lectured on pediatrics as well as acupuncturists with a wide experience of pediatric acupuncture were asked by the author of this article to share their experiences of treating infants with colic.

Twelve of 14 people asked to participate at the conference answered the questions asked by the article's author. However, not all informants answered all of the questions. Notes were made during these informal discussions. After the conference, a questionnaire was emailed to 10 additional acupuncturists who treat infants, asking if they would share their clinical experiences. Seven did so via e-mail. Later, a similar survey was sent to 6 acupuncturists with extensive knowledge of neurophysiology. Two of these answered.

Informants were asked about methods of diagnosis of infants with colic, points of frequent use, if the clinicians preferred using particular points for special symptoms (such as vomiting or frequency or absence of stooling), what points the clinicians considered to be inappropriate, stimulation of needles, treatment frequency, advice given to parents, and if the clinicians used acupuncture-related therapies.

In total, 23 professionals from five European and four non-European countries shared their experiences. The median experience of practicing acupuncture was 25 years.

Diagnosis: Several diagnostic methods were outlined, and they varied, based on the respondents' training. Some of these methods included palpating the abdomen to obtain important information about Excess or Deficiency conditions. Four acupuncturists based their diagnoses on pulse diagnosis, while most of the interviewed clinicians and teachers claimed that it was impossible to take the pulse of a 2–12-week-old infant. Another option for diagnosing infants mentioned was examination of the vein of the index finger (while this method provides information about pathogenic factors, it is unreliable). Another respondent mentioned that a blue vein on the bridge of the nose could signify “shock during pregnancy” (a blue vein suggests a

weak Spleen, while a greenish vein indicates a weak Spleen). According to TCM, both Excess and Deficiency can cause colicky symptoms.

None of the informants suggested that parents keep diaries to record how much the babies cried in order to assess the duration and intensity of their symptoms. Instead, these clinicians based their treatments on parents' subjective description of symptoms.

Syndromes: Most teachers and 2 clinicians based their point selections on syndromes or constitutions. Informants trained in Japanese acupuncture, Five-Elements, or Stems and Branches claimed that "there are no standard points and that one must take each baby's constitution into account." Among informants who differentiated patterns, the most frequently mentioned syndromes were "Stagnation of food" and "Spleen Qi Xu." Other less-common cited syndromes included "Cold," "Physical and psychological trauma," "pain with diarrhea," "pain with constipation," and "pain with Cold," while 1 clinician claimed that "Phlegm" was the most common pattern.

Acupoints. TCM acupuncturists claim that point specificity and choice of points according to patients' symptoms and signs are vital. According to TCM, children are more Yang than adults, which indicates a rapid changeability of their state. In addition, children's meridian systems are not fully developed. Among the respondents, twenty-three different points were claimed to have effect. The points that the teachers and clinicians used most frequently on infants were points used to address "Stagnation of food" or "Spleen Qi Xu." This could indicate that different points have different effects and that informants are adept at choosing optimal points for each baby on each specific treatment day. These responses could also simply indicate that acupuncture is nonspecific or that less-effective treatment is given in some cases. Both LI 4 and ST 36 were the most consistently used points for both "Stagnation of food" and "Spleen Qi Xu." Informants trained in Western medicine indicated the importance of choosing points in relevant segments to obtain neurologic connections between the points and the digestive organs. These clinicians emphasized that the purpose of the treatment was to stimulate the sympathetic system in order to reduce intestinal motility. According to this neurologic reasoning, ST 25, CV 12, and other points in segments relevant for intestinal functions could be useful for treating colic.

Informants reached a consensus about using fewer needles and mild, short-needle stimulation, compared to methods used for adult treatments. Most acupuncturists used 1–4 points per treatment with a range of 1–8 insertions. Retention time varied between "just in and out" and some minutes. A few teachers and 1 clinician stated that they stimulated the needle differently depending on Excess or Deficiency syndromes. The informants did not use electroacupuncture.

Most teachers recommended treatment 1–2 times per week. Clinicians treated at least twice a week, and 2 treated

daily. Infants were treated 1–8 times. Unilateral, bilateral, and diagonal treatments were equally common.

Six of the 14 teachers and 1 of the 7 clinicians rarely used needles on small children. These informants preferred the noninvasive massage techniques *Shonishin*, *Tu'ina*, and *Guasha* for treatment during early infancy. Eight recommended ordinary baby massage, while 1 stated that massage has no effect on visceral pain. Although some informants used moxa, often on CV 12, if Cold was present, others strongly discouraged using moxa on infants.

Safety: While acupuncture seems to be a safe treatment for infants, some of the points suggested by informants may be less appropriate for safety reasons. For example, needling in CV17 is inappropriate because of its location on the thorax, and TE 16's location on the neck could be risky for a wriggling baby. Ear acupuncture points may require head restraining.

Conclusions: The author of this article, who is highly experienced in treating infants, shares the results of this practitioners' survey. Acupuncturists from nine countries representing many traditions shared their experiences and clinical expertise, which were compared with information provided in textbooks to deepen the understanding of how colic is treated in TCM.

The results of this study exemplify the diversity of methods in used TCM. The extent to which the treatment was individualized varied, ranging from none at all to fully individualized treatment protocols that focused on specific needs and symptoms. The TCM patterns commonly described by informants matched the textbooks to a great extent.

Chemotherapy-induced peripheral neuropathy in cancer patients: a four-arm randomized trial on the effectiveness of electroacupuncture.

Rostock M, Jaroslowski K, Guethlin C, Ludtke R, Schröder S, Bartsch HH. *Evid Based Complement Alternat Med.* 2013; 2013:349653.

THIS RANDOMIZED, CONTROLLED TRIAL (RCT), with a group sequential adaptive design, was conducted by researchers from seven different institutions in Freiburg, Hamburg (two institutions), Frankfurt-am-Main, and Essen, all in Germany and in Zurich, Switzerland. This study was supported by the Fördergesellschaft Forschung Tumorbologie, in Freiburg, Germany, and the Karl and Veronica Carstens Foundation, in Essen, Germany.

In German-speaking countries, vitamin B supplements and/or hydroelectric baths (HBs) are traditionally used in many rehabilitation centers for treating peripheral neuropathy. However, the effectiveness of these approaches has not been proven via controlled studies. In this RCT, researchers compared the effects of electroacupuncture (EA) with placebo, HBs, and vitamin B-complex.

The study was conducted as a randomized, placebo-controlled trial comparing EA with HBs, high doses of vitamins B₁ and B₆ (VitB), and a placebo for the treatment of chemotherapy-induced peripheral neuropathy (CIPN). Patients and physicians were blinded to the VitB and placebo but not to EA or HBs. The trial was planned according to a group sequential adaptive design with one interim analysis. Patients were allocated to one of the four treatment groups by nonstratified block randomization with randomly varying block lengths. Treatment protocols spanned 3 weeks.

Electroacupuncture. For this group, 8 ± 1 sessions of EA were conducted to treat the patients' affected extremities with the following point combination: LR 3 (*Taichong*); SP 9 (*Xiongxiang*); GB 41 (*Zulingqi*); and GB 34 (*Yanglingquan*) for legs in patients with CIPN symptoms in the lower extremities; and LI 4 (*Hegu*); LI 11 (*Quchi*); SI 3 (*Houxi*); and HT 3 (*Shaohai*) for arms in patients with CIPN symptoms in the upper extremities. Patients with CIPN symptoms in both upper and lower extremities were treated with the complete point combination. Acupuncture needles were deeply inserted bilaterally until De Qi was triggered. Each session included 15 minutes of electrostimulation (50 Hz), consisting of a combination of rectangular currents and high-amplitude waves.

Hydroelectric baths (HBs). For this group, 8 ± 1 sessions of HB were conducted to treat the affected extremities. Patients dipped their arms up to a hand's width above the elbow and their feet up to a hand's width above the ankle into a special water basin with water at a temperature of $\sim 35^\circ\text{C}$. Each treatment lasted for 15 minutes, with crossgalvanization of each individual extremity by a low-frequency (50 Hz) faradic current (direct current impulses) up to the individual's sensitive threshold.

Vitamin B complex. The treatment for this group consisted of 3 capsules of high-dosage vitamins B₁ and B₆ (the capsules contained 100 mg of thiamine nitrate and 100 mg of pyridoxine hydrochloride) per day for 3 weeks.

Placebo. The placebo consisted of 3 lactose capsules per day; these capsules were identical in form, taste, and odor to the VitB capsules.

Enrollment. The study enrolled male and female adult patients with cancer, who were in remission after chemotherapy with taxanes, platinum derivatives, or vinca alkaloids, and who presented with symptoms of CIPN. Patients were recruited at the Albert Ludwig's University of Freiburg, in Freiburg, Germany.

Primary outcome. A detailed questionnaire was administered before the start of the therapy (day 0), after treatment on day 21, and during follow-up on day 84, about the extent and intensity of the patients' CIPN complaints. In addition, patients were asked to describe how intensely they suffered at the respective point in time from CIPN complaints altogether and to rate the severity of neuropathic symptoms on a numerical rating scale (NRS)—ranging from 0 (no com-

plaints) to 10 (highest imaginable complaints). The change from day 0 to day 21 on this patient-reported NRS was the primary outcome of the study.

Secondary outcomes. Patients were examined by an independent neurologist before the start of the study (day 0) and after completion of the treatment (day 21). The neurologist ascertained a neuropathy score for each patient and performed electroneurographic tests. The neuropathy score (0–15 points) was based on sensory symptoms (0–3 points), pin sensibility (0–3 points), vibratory threshold (0–3 points), strength (0–3 points), and deep-tendon reflexes (0–3 points). The electroneurographic tests included sensible nerve-conduction studies of the median (upper extremities) and the sural nerve (lower extremities). Finally, the neurologist evaluated the intensity of the CIPN complaints by classification according to the National Cancer Institute's common toxicity criteria (CTC). A follow-up interview at day 84, was done in writing, via a questionnaire sent to each patient's home.

Quality of life. The study participants' quality of life (QoL) was examined at day 0, day 21, and day 84 by means of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (also known as the EORTC QLQ-C30).

Demographics. Sixty patients were randomized into one of the four treatment groups. Nine patients withdrew or were lost to follow-up. The majority of patients were female (78%) and, overall, the groups were balanced with regard to demographic characteristics, health status, and comorbidities. The underlying cancer diagnoses as well as the cancer treatments were very heterogeneous within the study cohort. Although statistically not significant ($p=0.263$), mean baseline symptoms varied considerably between groups and ranged from 4.0 ± 1.7 in the EA to 5.5 ± 2.6 in the HB group. At study entry, subjective CIPN complaints of the included patients differed—while every patient in the EA and HB groups had paresthesia, only 75% in the vitB group and 88% in the placebo group did so. In the placebo group, fewer patients reporting having painful neuropathy, compared to the patients in treatment groups. Subjective impairment in fine-motor skills was nearly equal in all four groups.

Results. Symptoms were reduced similarly in all groups during the 3 weeks of treatment and remained at this lower level for another 9 weeks, except in the HB group, in which some deterioration was observed. At day 21, symptom reduction was best in the HB and the VitB groups. Compared to placebo (1.3 ± 1.3), EA produced worse effects (0.8 ± 1.2) resulting in a group difference of $d = -0.3$ (confidence interval: -1.4 to 0.8 ; $p=0.705$). As the p -value exceeded the predefined threshold of $\alpha = 0.05$, the study was stopped early at the first interim analysis.

The neuropathy scores decreased in all groups during treatment to a similar degree. Group differences were not significant between any two groups. There were no statistically significant differences among the treatment groups

according to electroneurographic test results and NCI common toxicity criteria classification. Sensory neuropathy symptoms were reduced similarly in all four groups. Health-related QoL was also moderately improved in all groups, but without any statistically significant group differences at day 21.

Conclusions: The researchers observed no therapeutic advantage of EA over an orally administered placebo control. In addition, no effects of HBs and vitamins B₁ and B₆ were demonstrated.

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