Abstracts and Commentaries on Key Articles in the Literature

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The long-term effect of acupuncture for migraine prophylaxis: a randomized clinical trial.

Zhao L, Chen J, Li Y, Sun X, Chang X, Zheng H, Gong B, Huang Y, Yang M, Wu X, Li X, Liang F. *JAMA Intern Med.* 2017;177(4):508–515.

THIS STUDY WAS PERFORMED by researchers from different universities in China. Long-term prophylactic effects of acupuncture for migraine are still uncertain. The objective of this trial was to investigate the long-term effects of true acupuncture compared with sham acupuncture and being placed in a waiting list control group for migraine prophylaxis. It was a 24-week randomized clinical trial (4 weeks of treatment followed by 20 weeks of follow-up). Participants were randomly assigned to true acupuncture, sham acupuncture, or a waiting list control group. The trial was conducted from October 2012 to September 2014 in outpatient settings at 3 clinical sites in China. The trial included a total of 249 participants aged 18–65 years with migraine without aura based on the criteria of the International Headache Society, with migraine occurring 2–8 times per month. Participants in the true acupuncture and sham acupuncture groups received treatment 5 days per week for 4 weeks for a total of 20 sessions. Participants in the waiting list group did not receive acupuncture but were informed that 20 sessions of acupuncture would be provided free of charge at the end of the trial.

Participants used diaries to record migraine attacks. The primary outcome was the change in the frequency of migraine attacks from baseline to week 16. Secondary outcome measures included the migraine days, average headache severity, and medication intake every 4 weeks within 24 weeks. A total of 249 participants aged 18–65 years were enrolled, and 245 were included in the intention-to-treat analyses. One hundred eighty-nine (77.1%) were women. Baseline characteristics were comparable across the 3 groups. The mean (standard deviation; SD) change in frequency of migraine attacks differed significantly among the 3 groups at 16 weeks after randomization ($P < 0.001$); the mean (SD) frequency of attacks decreased in the true acupuncture group by 3.2 (2.1), in the sham acupuncture group by 2.1 (2.5), and

the waiting list group by 1.4 (2.5); a greater reduction was observed in the true acupuncture than in the sham acupuncture group (difference of 1.1 attacks; 95% confidence interval [CI]: 0.4–1.9; $P = 0.002$) and in the true acupuncture versus waiting list group (difference of 1.8 attacks; 95% CI: 1.1–2.5; $P < 0.001$). Sham acupuncture was not statistically different from the waiting list group (difference of 0.7 attacks; 95% CI: –0.1 to 1.4; $P = 0.07$). Among patients with migraine without aura, true acupuncture may be associated with long-term reduction in migraine recurrence compared with sham acupuncture or assigned to a waiting list.

The feasibility of matching on a propensity score for acupuncture in a prospective cohort study of patients with chronic pain.

Johnson ES, Dickerson JF, Vollmer WM, Rowley AM, Ritenbaugh C, Deyo RA, DeBar L. *BMC Med Res Methodol.* 2017; 17(1):42.

SEVEREN RESEARCHERS FROM THE UNITED STATES investigated the feasibility of matching on a propensity score for acupuncture in a prospective cohort study of patients with chronic pain. Propensity scores are typically applied in retrospective cohort studies. The authors describe the feasibility of matching on a propensity score derived from a retrospective cohort and subsequently applied in a prospective cohort study of patients with chronic musculoskeletal pain before the start of acupuncture or usual care treatment and enrollment in a comparative effectiveness study that required patient reported pain outcomes.

The authors assembled a retrospective cohort study using data from 2010 to develop a propensity score for acupuncture versus usual care, based on electronic healthcare records and administrative data (e.g., pharmacy) from an integrated health plan, Kaiser Permanente Northwest. The propensity score's probabilities allowed matching acupuncture-referred and non-referred patients prospectively in 2013–2014 after a routine outpatient visit for pain. Among the matched patients, they collected patient-reported pain before treatment and

during follow-up to assess the comparative effectiveness of acupuncture. They assessed balance in patient characteristics with the post-matching c-statistic and standardized differences. Based on the propensity score and other characteristics (e.g., patient-reported pain), they were able to match all 173 acupuncture-referred patients to 350 non-referred (usual care) patients. They observed a residual imbalance (based on the standardized differences) for some characteristics that contributed to the score; for example, age (−0.283) and the Charlson comorbidity score (−0.264) had the largest standardized differences. The overall balance of the propensity score appeared more favorable according to the post-matching c-statistic (0.503).

The propensity score matching was feasible statistically and logistically and allowed approximate balance on patient characteristics, some of which will require adjustment in the comparative effectiveness regression model. By transporting propensity scores to new patients, healthcare systems with electronic health records can conduct comparative effectiveness cohort studies that require prospective data collection, such as patient-reported outcomes, while approximately balancing numerous patient characteristics that might confound the benefit of an intervention. The approach offers a new study design option.

Case report: fainting during acupuncture stimulation at acupuncture point LI4.

Kwon OS, Choi KH, Kim J, Cho SJ, Kang SY, Moon JY, Ryu YH. *BMC Complement Altern Med.* 2017;17(1):147.

THIS STUDY WAS PERFORMED at the KM Fundamental Research Division, Korea Institute of Oriental Medicine, Daejeon, in Korea. Fainting is one of the major adverse events that can occur as a result of acupuncture treatment. However, the observation of changes in biological parameters is rarely available when fainting occurs. In this case report, the authors observed changes in the electroencephalogram (EEG) in a participant who fainted while participating in a clinical trial aiming to observe a relationship between acupuncture stimulation at LI4 acupuncture point and EEG in healthy adults. The EEG pattern of the participant changed twice. The first change was in response to the acupuncture needle insertion, and the second change occurred during fainting. Both changes consisted of a burst in EEG amplitude, but the pattern of details was different. Multiple areas of the cortex were activated, and the increased ratio of the γ wave was not observed during fainting. During acupuncture needle insertion, only the sensory cortex was activated and the γ waves were increased.

This single case is presented to improve the understanding of fainting during acupuncture as an adverse event and to explore the mechanism of acupuncture treatment, despite the absence of statistics and repeatability. This information

can provide a new viewpoint about the mechanism of acupuncture treatment and the possibility of new techniques based on acupuncture.

A randomised controlled trial examining the effect of acupuncture at the EX-HN3 (Yintang) point on pre-operative anxiety levels in neurosurgical patients.

Wiles MD, Mamdani J, Pullman M, Andrzejowski JC. *Anaesthesia.* 2017;72(3):335–342.

THIS RANDOMIZED CONTROLLED TRIAL was performed in Sheffield, United Kingdom. Preoperative anxiety is an unpleasant state of psychological distress that occurs in up to 87% of patients awaiting neurosurgical procedures. Sedative medication is undesirable in this population due to the need for early postoperative neurological assessment. Acupuncture has previously been shown to reduce preoperative anxiety, but studies involving neurosurgical patients are lacking. This single-center, prospective, randomized controlled trial was designed to determine the effect of acupuncture at the EX-HN3 (Yintang point) on preoperative anxiety levels in neurosurgical patients. The study was prospectively registered before participant recruitment. After measuring baseline anxiety levels, 128 patients were randomly allocated in a 1:1 ratio by a web-based computer program to receive either acupuncture at the EX-HN3 (Yintang) point (acupuncture group) or no intervention (control group). Participants were not blinded, but all analyses were performed by a member of the research team who was unaware of the group allocation. The primary outcome measure was anxiety level after 30 minutes, as measured by the six-item short form of the State-Trait Anxiety Inventory (possible score range 20–80). Sixty-two patients in each group were subsequently analyzed. Median (IQR [range]) anxiety State-Trait Anxiety Inventory score reduced significantly in the acupuncture group (46.7 (36.7–53.3 [23.3–70.0]) to 40.0 (30.0–46.7) [20.0–53.3]), $P < 0.001$, with no change seen in the control group (41.7 (33.3–53.3 [20.0–76.7]) to 43.3 (36.7–50.0 [20.0–76.7]), $P = 0.829$). There were no adverse events in either group. Acupuncture at the EX-HN3 point reduces preoperative anxiety levels in patients awaiting neurosurgery.

The efficacy of acupuncture on menopausal symptoms (ACOM study): protocol for a randomised study.

Lund KS, Brodersen J, Siersma V, Waldorff FB. *Dan Med J.* 2017;64(3). pii:A5344.

FOUR RESEARCHERS FROM DENMARK performed this study. Around 75% of menopausal women experience

hot flushes (HF), which 10–20% of all postmenopausal women find very distressing. The aim of this study was to evaluate the efficacy of acupuncture on moderate-to-severe menopausal symptoms in general and HF in particular. This was an unblinded randomized trial (cross-over) with 1:1 allocation to early (intervention) versus late (control) acupuncture. The women included in the study suffered from moderate-to-severe HF and received a weekly treatment for five consecutive weeks in the following predefined acupuncture points: CV-3, CV-4, LR-8, SP-6, and SP-9. All acupuncturists were medical doctors educated in acupuncture. The primary outcome was a change in HF from baseline to week 6, measured by the HF scale from the Meno Scores Questionnaire (MSQ). Secondary outcomes were changes in other menopausal symptoms, such as day and night sweats and menopausal-specific sleeping problems, also measured by other scales from the MSQ. A total of 68 patients needed to be enrolled to detect a relevant clinical reduction on the

above MSQ scales. Both intention-to-treat and per-protocol analyses were conducted; four or more treatments were considered adequate adherence.

In the ACOM study, the authors explored the potential benefits of acupuncture on moderate-to-severe menopausal symptoms. The cross-over design offers the possibility of examining the legacy effect of acupuncture.

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