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Hot Topic

To Be, Or Not To Be: The Calculated Politics of Acupuncture in JAMA

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ABSTRACT Ten acupuncture-related articles were published in *The Journal of the American Medical Association* (JAMA) between 1998 and 2017. Five studies showed positive results in terms of the effectiveness of acupuncture/Chinese medicine (CM); five studies showed negative results. This article summarizes the acupuncture-related clinical trials published over the last 20 years in JAMA, and addresses what seems to be a fundamental ambivalence in Western medical journals regarding the scientific validity of acupuncture/CM. As yet there has been no consensus on the role of acupuncture in healthcare in Western countries. This is hardly surprising, considering the conflicting evidence found in published studies. Skepticism regarding acupuncture/CM is largely grounded in the fact that an accurate model for assessing the true clinical effects of acupuncture has yet to be created. This article discusses some of the pitfalls which result from applying Western-based scientific principles to CM, and suggests that in many cases, "negative" studies have been misinterpreted. The clinical experience of acupuncture practitioners is often in direct conflict with many of the negative conclusions published in journals. We are in need of an accurate model for sham and placebo treatments, and must analyze all published studies for design flaws and faulty conclusions.

KEYWORDS Chinese medicine, acupuncture, Western medical journals, study design

Although over 5000 clinical trials on acupuncture have been published to date, acupuncture-related articles are rarely encountered in *The Journal of the American Medical Association* (JAMA). Over the last 20 years, only 10 clinical trials on acupuncture/Chinese medicine (CM) have appeared in JAMA. The November 11, 1998 issue featured a cluster of 3 articles[1-3] on clinical acupuncture trials, and the recent June 27, 2017 issue contained 2 articles[4,5] detailing acupuncture clinical trials. Between 1998 and 2017, 5 additional clinical acupuncture trials[6-10] were published. In terms of results, the outcomes were a wash: 5 clinical trials showed positive outcomes for acupuncture treatment; 5 showed negative outcomes. Is it an accident that positive and negative results have been so finely balanced in the pages of JAMA, or is this pattern the result of JAMA trying to establish a "fair and balanced" approach to alternative medicine in general and acupuncture therapy in particular? The scientific validity of acupuncture continues to be controversial in the West. In its effort to present acupuncture studies without either endorsing or dismissing acupuncture, JAMA seems to be consciously positioning itself at the mid-point of the controversy. In its role as a medical forum, JAMA has neither the obligation, nor the ability, to adjudicate the East/West discrepancy issues that are in play in regard to scientific assessment of acupuncture/CM. This position essentially leaves JAMA straddling a political fence, neither endorsing nor denying the efficacy of acupuncture, for reasons which may be based less on actual clinical trial results and more on an imperative to avoid charges of gullibility and lack of scientific rigor. This article analyzes the acupuncture-related articles published in JAMA, with the objective of illustrating some pitfalls which

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can result from applying Western-based scientific principles to the paradigms and practices of CM.

Over the past 55 years scientific study on acupuncture and its mechanisms has produced a growing number of research articles, varying in quality. Although methodology has improved, there are still many challenges that arise from trying to impose Western scientific standards on an Eastern medical paradigm. A critical factor for many in the scientific world is the absence of a true placebo for acupuncture. Many types of sham acupuncture have been tried, none of which, when analyzed scientifically, show a true non-treatment placebo effect. Additionally, there are no set acupuncture protocols that are used universally to treat any specific illness, injury or condition. Each patient is assessed from many perspectives. The practitioner then determines the most comprehensive pattern affecting the health and well-being of the patient and applies treatment principles and modalities according to CM theory. A fundamental problem arises when Western scientific research tries to analyze or categorize the application of acupuncture in isolation from these underlying theoretical principles. Many studies try to assess one specific acupuncture protocol used in treating a condition defined within Western medicine, without considering the underlying constitution of the patient being treated and without differentiating the pattern according to CM principles. A related problem is that the same Western diagnosis may arise from many different patterns in the CM theoretical system. In that case, acupoint combinations for a specific Western-defined condition could vary widely, depending on how the condition was diagnosed according to CM principles.

JAMA has not been able to shed much light on the role of acupuncture in healthcare, as the studies that have been published in this widely-distributed, much-esteemed journal show conflicting evidence. The conflict, it seems, arises from the reality that an accurate model for assessing the true clinical effects of acupuncture has yet to be created.

Two Trials: JAMA, June 27, 2017 Issue

One trial validates acupuncture's effectiveness for stress urinary incontinence (SUI),[4] whereas the other study finds little utility in acupuncture for treating infertility with polycystic ovary syndrome (POS).[5]

Trial 1

Liu, et al[4] assessed electroacupuncture on the lumbosacral area for its effectiveness at treating SUI. This multicenter, randomized clinical trial (RCT) in Chinese hospitals divided women with SUI equally into either an acupuncture group or a non-penetrating sham group. Of the 482 women who completed 18 session treatments (over 6 weeks), mean urine leakage was 18.4 g in the acupuncture group, and 19.1 g in the sham group. At week 6, mean urine leakage was reduced by 9.9 g in the treatment group, *vs*. a 2.6 g reduction in leakage in the sham group. Therefore, lumbrosacral electroacupuncture was deemed more effective than non-insertion sham electroacupuncture at reducing urine leakage.

Trial 2

This issue of JAMA also featured a trial by Wu, et al[5] on the induction of ovulation by acupuncture in women with POS. Researchers assessed the relative success of acupuncture with or without clomiphene in increasing the ability of women with POS to have children. One thousand participants from 27 hospitals in China were treated during 2012–2015, including 10 months of pregnancy. In this study, both the drug intervention and the acupuncture treatment were compared with a placebo or sham treatment. Drug intervention *vs*. placebo was double-blinded; acupuncture *vs*. sham was single-blinded. Treatments were provided for up to 4 cycles.

Live births occurred in 29.4% of those receiving deep insertion acupuncture with manual and electrostimulation plus clomiphene; compared with 28.0% in those receiving shallow needling plus clomiphene. A noticeable difference was seen between those who received clomiphene *vs*. medication placebo. Live births were seen in 13.9% of those who received deep insertion acupuncture with manual and electrostimulation plus placebo medication, and 16.8% of those who received shallow needling plus placebo medication. Additionally, no significant interaction was observed between deep insertion electroacupuncture and clomiphene. A significantly higher live-birth rate was associated with women who received clomiphene compared to placebo. No significant difference was observed between those who received clomiphene and deep needle acupuncture with manual and electrostimulation and those who received shallow

needling. In this trial, clomiphene was more successful than both deep electroacupuncture and shallow acupuncture at increasing the live-birth rate among women with POS.

Whereas pharmaceutical placebos are distinct, acupuncture placebos are not as clear-cut. In this trial, the "real acupuncture" treatment group received deep needling with manual stimulation and low-frequency electrostimulation as a treatment; and the "sham" treatment consisted of shallow needling. A case can certainly be made that shallow needling is still acupuncture, and is not the same as not being treated with acupuncture.

Three Trials: JAMA, November 11, 1998 Issue

Trial 1

Cardini, et al[1] studied moxibustion for its effect on fetal activity and reversing fetal position in cases of breech presentation. Women in Chinese outpatient clinics who had experienced a normal pregnancy, but were primigravidas at week 33 with fetuses in breech presentation, received either indirect moxibustion at Zhiyin (UB 67) for 7–14 days, or standard Western medical care without attempting to reverse the position of the fetus for up to 14 days. Those who received the CM intervention reported a mean of approximate 48 movements compared to approximately 35 in the control group. During the second week of the intervention, 75.4% of fetuses in the CM group had reversed their position, compared with 47.7% among controls.

Trial 2

Benssoussan, et al[2] conducted a randomized, double-blinded, placebo-controlled study on the effect of Chinese herbal medicine (CHM) on irritable bowel syndrome (IBS) in 116 patients. Patients received one of three treatments over a period of 16 weeks: individualized Chinese herbal formulas prescribed according to CM diagnosis patterns; a standard Chinese herbal formula commonly prescribed for IBS; or a placebo. Patient ratings and physician examination showed both individualized and standardized CHM were significantly effective at reducing IBS symptoms and were associated with significant global improvements. Patients also noted that IBS symptoms had less negative impact on daily life.

Trial 3

A RCT conducted by Shlay, et al[3] on human immunodeficiency virus (HIV) patients with peripheral neuropathy compared the analgesic effect of acupuncture *vs*. amitriptyline hydrochloride. Participants with HIV-associated lower-extremity peripheral neuropathy were randomized into 3 groups: a modified double-blind 2×2 factorial designed standardized acupuncture regimen, amitriptyline, or both modalities combined and compared to placebo; a modified double-blinded designed standardized acupuncture regimen or control acupuncture and either a double-blinded design of amitriptyline or placebo. All participants showed a reduction in mean pain ratings at 6 and 14 weeks. No significant difference was seen between those who received amitriptyline and those who received standardized acupuncture. At 6 weeks, the amitriptyline groups showed greater pain reduction than placebo; however, pain reduction was similar between standardized acupuncture and control acupuncture. At 14 weeks, those who received standardized acupuncture showed a greater reduction in pain than those who received control acupuncture; while those who received amitriptyline showed a similar reduction in pain to placebo. Researchers concluded that the analgesic effect of acupuncture and amitriptyline were similar compared to placebo.

Five Trials: JAMA, 1998 to 2017

Trial 1

Shen, et al[6] investigated the effect of acupuncture for chemotherapy-related nausea and vomiting. In this RCT, 104 women with high-risk breast cancer undergoing a highly emetogenic chemotherapy regimen received a 5-day course of either low-frequency electroacupuncture at antiemetic points, shallow needling at control points with placebo electrostimulation, or the chemotherapy regimen without acupuncture. Additionally, patients received three antiemetic medications. Those who received electroacupuncture experienced emesis less frequently than those in the placebo group or the control group during the course of the intervention: 5, 10 and 15 episodes, respectively.

Trial 2

Margolin, et al[7] conducted a single-blinded RCT on auricular acupuncture to determine its effect on cocaine addiction. Six clinics recruited 620 patients, 412 were addicted strictly to cocaine, while 208 on methadone maintenance were being treated for both

opiate and cocaine addiction. Patients received an 8-week course of auricular acupuncture, a needle-insertion control, or a relaxation intervention 5 days per week. According to urine analysis, a similar reduction in cocaine use was observed in all three groups. Researchers found that auricular acupuncture was equally effective to needle insertion control or relaxation control.

Trial 3

An RCT by Linde, et al[8] on migraine headaches was conducted in Germany in 2002–2003. Acupuncture by specialized physicians was compared with sham acupuncture and a wait-list. Patients received 12 sessions over 8 weeks.

According to patient headache diaries, days with moderate to severe headache decreased by a mean of 2.2 days in the acupuncture group, 2.8 days in the sham acupuncture group, and 0.8 days in the wait-list group. No significant difference was seen between the acupuncture and sham acupuncture groups, but significant improvement was seen with acupuncture compared to the wait-list group. Reduction in headache days by at least half was experienced by 51% of those who received acupuncture, and 53% of those who received sham acupuncture. The wait-list group showed a reduction of 15% in headache days. The study concluded that acupuncture and sham acupuncture were equally effective in reducing migraine headaches, and that both were significantly more effective than wait-list. This study indicated that the sham procedure was not a true sham, but actually acupuncture.

Trial 4

A RCT performed by Hinman, et al[9] assessed the potential benefit of laser and needle acupuncture for individuals over 50 with chronic knee pain. Four treatments were assessed: acupuncture, laser acupuncture, sham laser acupuncture, or no acupuncture. Acupuncture and laser acupuncture produced similar improvements in pain and functionality compared with sham laser acupuncture at 12 weeks. Compared with no acupuncture, both acupuncture and laser acupuncture showed some pain reduction at 12 weeks, and increased some functionality compared to control. The study showed that needle and laser acupuncture resulted in modest improvements in pain at 12 weeks, but not at one year, compared with control; and that acupuncture resulted in modest improvement in function compared with control at 12 weeks, but was not significantly different from sham and was not maintained at 1 year. The study concluded that neither laser nor needle acupuncture conferred benefit over sham for pain or function in patients older than 50 years who have moderate or severe chronic knee pain.

Trial 5

The fifth study looked at the lasting effects of acupuncture for the prevention of migraine headache. In a RCT conducted by Zhao, et al,[10] patients received treatment 5 days per week with either acupuncture, sham acupuncture, or were placed on a waiting list. During 2012–2014, 245 patients from Chinese hospitals experiencing migraine headaches 2 to 8 times monthly completed the trial. Significant differences among groups were observed at 16 weeks. The acupuncture group experienced 3.2 fewer migraine attacks, while those who received sham acupuncture experienced 2.1 fewer attacks. Wait-list attacks decreased by 1.4. These results indicated that the effects of acupuncture may be sustained longer than sham acupuncture or wait-list.

Analysis and Summary

The 5 studies cited above which demonstrated positive results validated the clinical experience of millions of CM practitioners. The studies which revealed negative results deserve rigorous analysis for design flaws and faulty conclusions. Space precludes examining all 5 negative studies in detail. Therefore, we will mention problematic aspects of the Hinman study, and then focus on the Wu's study[5] as an example of the need to review negative studies carefully when they contradict the clinical experience of a majority of acupuncture practitioners.

Hinman's paper on knee pain was immediately disputed by clinical acupuncturists, whose experience supports the effectiveness of acupuncture in knee pain patients of all ages. In a previous paper,[11] I summarized and demonstrated that Hinman's trial contained at least 4 flaws: flawed research design; questionable acupuncture protocols; violation of research ethics; and misinterpretations of research results.

The ovulation induction trial by Wu, et al[5]

demonstrated a live-birth rate of 29.4% in the active acupuncture plus clomiphene group, 28.0% in the control acupuncture plus clomiphene group, 13.9% in the active acupuncture plus placebo group, and 16.8% in the control acupuncture plus placebo group. A significant difference exists between clomiphene and placebo, and an insignificant difference between active and control acupuncture. Therefore, Wu concluded that acupuncture as an infertility treatment in women with POS was invalidated. This conclusion, too, was disputed by acupuncturists.

In a study published in *New England Journal of Medicine* by Legro, et al[12] compared the ability of clomiphene *vs*. metformin to induce ovulation for women with infertility secondary to POS, the live-birth rate was 22.5% in the clomiphene plus placebo group, 7.2% in the metformin plus placebo group, and 26.8% in the clomiphene and metformin combination group. Another study by Legro, et al[13] compared letrozole *vs*. clomiphene for infertility due to POS, found live-birth rates of 27.5% and 19.1% in the letrozole and clomiphene groups, respectively. The 22.5% live birth rate for the clomiphene group in the first Legro study,[12] and the 19.1% live birth rate for clomiphene group in the second Legro study[13] are much lower than the 29.4% rate found in the Wu' s study on the effect of acupuncture and clomiphene combination. For women with POS, the live birth rate is assumed to be 5% without any interventions. In Wu's study, 13.9% and 16.8% rates in the acupuncture and sham acupuncture groups are almost 3 times higher than live-birth results with no intervention. When live-birth rates occurring with the use of acupuncture are compared with the live-birth rates with no intervention, and when the live-birth rate for acupuncture plus clomiphene is compared with the live-birth rate for clomiphene alone, the conclusions to be drawn about the effectiveness of acupuncture intervention are markedly contradictory to the conclusion reported by Wu.[5] This failure to recognize the improved success rate actually resulting from acupuncture intervention is even more remarkable, considering that Dr. Legro was one of the contributors to the Wu's study.[5]

A factor in the Wu's study which definitely needs to be taken into account is the issue of what constitutes "sham" acupuncture. The sham acupuncture was a style called "soft acupuncture,"[14] which is widely practiced in the United States, but not commonly practiced or understood in China. "Soft acupuncture" involves shallow needling at the subcutaneous level. Traditionally-practiced Chinese "hard acupuncture" emphasizes obtaining a strong sensation with deeper needling. Contrary to what many Chinese practitioners believe, "soft acupuncture" does produce a measurable physiological response in patients. Its mechanism is thought to be mediated through mast cells.[15] "Real" sham acupuncture does not induce any downstream physiological effects. The difficulty of devising a form of sham acupuncture which does not stimulate subcutaneous receptors, but which still persuades a patient that he is receiving acupuncture is a significant problem in the design of valid acupuncture studies.

Are the success rates cited in the Legro[10,12] and Wu[5] studies comparable? It is often contended that different cultural expectations between Chinese patients and Western patients will influence the results of acupuncture studies. However, ethnicity or race could not affect the ovulation rate cycle with clomiphene, which is comparable across groups. The above analysis indicates that in absolute terms acupuncture is effective for ovulation in comparison with no acupuncture treatment.

It is not the responsibility of JAMA or other medical journals to resolve the inconsistencies inherent in the effort to apply the metrics of Western medicine to the empirically-based practices of CM. However, medical journals need to have rigorous standards for article selection. It is more important to evaluate the scientific soundness of an article and reject articles which have significant design flaws than it is to maintain an artificial balance between "positive" and "negative" trial results. We are certainly not advocating the suppression of negative-outcome studies, all studies must be evaluated on their own terms. But when negative results appear which are counterintuitive and counter-experiential to the acupuncture practitioners who have successfully treated these conditions over several thousand years, at least they warrant a close analysis and evaluation of the study's design and conclusions. Too often, negative trial results are accepted at a superficial level and passed along as the definitive answer, especially when they appear in well-regarded journals.

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