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Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

# Should the Copper IUD Be Offered to Women With Heavy Menstrual Bleeding?

***By Rebecca H. Allen, MD, MPH***

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**Dr. Allen reports she is a Nexplanon trainer for Merck.**

SYNOPSIS: In this secondary analysis of the Contraceptive CHOICE Project, there was no difference in copper intrauterine device continuation rates at one year between 165 women who reported heavy menstrual bleeding at baseline and 753 women who did not.

SOURCE: Hobby JH, Zhao Q, Peipert JF. Effect of baseline menstrual bleeding pattern on copper intrauterine device continuation. *Am J Obstet Gynecol* 2018;219:465.e1-5.

This was a secondary analysis of the Contraceptive CHOICE Project, a prospective cohort study from 2007 to 2013 that included 9,256 girls and women in the St. Louis area. Researchers offered the participants two to three years of free contraception of their choice. Eligible participants were between the ages of 14 and 45 years, sexually active with a male partner, and interested in initiating or changing their contraceptive method. Participants were asked to rate their baseline menstrual bleeding as light (using ≤ 10 pads/tampons per period), moderate (11-20 pads/tampons), moderately heavy (21-30 pads/tampons), heavy (> 30 pads/tampons), or too irregular/variable to say. Method continuation was assessed by phone calls three and six months after initiation and then every six months for the duration of the study. The primary outcome was copper intrauterine device (IUD) discontinuation at 12 months. Only two copper IUD users reported that their menses were too irregular to describe, and they were excluded from the analysis. For analysis, women reporting heavy and moderately heavy bleeding were grouped together as "heavy," and women reporting light and moderate bleeding were grouped together as "not heavy."

A total of 1,102 women chose the copper IUD, and continuation data were available for 918 women at 12 months. Of these 918 women, 165 reported bleeding

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as heavy (n = 24) or moderately heavy (n = 141), and 753 reported bleeding as light (n = 192) or moderate (n = 561). Participants in the heavy/moderately heavy category were more likely to be obese and have a history of sexually transmitted infection than women in the light/moderate category. Otherwise, there was no difference between the two groups in terms of age, race, ethnicity, education, income, gravidity, and parity. At 12 months, continuation rates were similar, with 80.2% in the "heavy" group and 85% in the "not heavy" group ($P = 0.24$). The hazard ratio for early discontinuation in the "heavy group" was 1.21 (95% confidence interval, 0.88-1.66). No other predictors of discontinuation were found.

## ■ COMMENTARY

Most gynecologic providers are familiar with the copper IUD, which has been available in the United States since 1988. The device is approved by the U.S. Food and Drug Administration for 10 years of use, although one study has indicated efficacy up to 12 years.[1] The device is highly effective, with failure rates of less than 1%. Counseling for the copper IUD typically has included the warning that the device may increase menstrual bleeding and cramping. Where did this advice come from? One small study of 18 women measured menstrual blood loss before and after insertion of the copper IUD, as measured by the alkaline hematin method.[2] At three months, menstrual blood loss increased by 55%, from 59 mL to 91 mL on average, and remained stable over the next nine months. Nevertheless, there was no significant change in hemoglobin levels among participants over the course of the study. This has been confirmed in other trials that generally have shown no clinically significant changes in hemoglobin levels among women using the copper IUD, even among women with baseline anemia, despite a 50% increase in menstrual blood loss.[3] This has led the Centers for Disease Control and Prevention (CDC) to recommend not screening for anemia prior to copper IUD insertion[4] and labeling use of the copper IUD as category 2 (benefits outweigh risks) among women with baseline anemia.[5]

Rather than assessing the amount of bleeding while using the copper IUD, the goal of this study was to assess whether women with heavy menstrual bleeding at baseline were more likely to discontinue their copper IUD by 12 months. Interestingly, the study did not show that women with heavy or moderately heavy menstrual bleeding were more likely to request the copper IUD be removed. Some might argue that this is a more clinically relevant outcome. This finding also brings into play the subjective nature of our patients' menstrual bleeding assessments. This may be interpreted as a weakness or strength of the study. As a weakness, the investigators did not quantify the baseline menstrual bleeding pattern objectively. However, as a strength, the study is practical, as providers do not perform objective measurements of menstrual blood loss in the office. Clinicians rely on patients' subjective reports of whether they are bothered by the amount of bleeding they are having. In the Hobby et al study, women reporting heavy or moderately heavy menstrual bleeding were just as happy to continue the copper IUD as women reporting light or moderate menstrual bleeding. The authors speculated that these women may be more tolerant of heavy menstrual bleeding in general. Study limitations include the retrospective measure of menstrual blood loss (recalling pad/tampon use) and the fact that there were only 24 women in the original heavy menstrual bleeding group. This may reflect that women with heavy menstrual bleeding self-selected out of the copper IUD group in the first place.

Despite these limitations, this study reminds us that, as providers, we must try to prevent our biases from entering the exam room and counsel all women honestly about the copper IUD. We should not assume automatically that women with heavy menstrual bleeding would not be interested in the copper IUD or that all women would prefer the levonorgestrel IUD. Experts speculate that the increase in menstrual blood loss seen with the copper IUD is caused by higher levels of prostaglandins in the endometrium.[6] In general, women can be counseled that unscheduled spotting or heavy menstrual bleeding, especially during the first three to six months of use, may occur with the copper IUD. Nevertheless, for most women, these side effects will decrease over time and are manageable. Although prophylactic ibuprofen has not been shown to decrease copper IUD removals, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) can be helpful for a current bleeding episode with the copper IUD.[6] The CDC Selected Practice Recommendations for Contraceptive Use recommends five to seven days of NSAIDs for women complaining of heavy bleeding while using the copper IUD.[4] In sum, the copper IUD is safe, reversible, hormone-free, and highly effective, making it an attractive contraceptive option for women. ■

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## ABSTRACT & COMMENTARY

# Hormone Therapy and Mortality: No Overall Effect?

***By Jeffrey T. Jensen, MD, MPH***

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SYNOPSIS: An evaluation of outcomes of users and nonusers of postmenopausal hormonal therapy followed longitudinally in the Danish database showed no overall difference in mortality.

SOURCE: Holm M, Olsen A, Au Yeung SL, et al. Pattern of mortality after menopausal hormone therapy: Long-term follow up in a population-based cohort. *BJOG* 2018; Aug. 14. doi: 10.1111/1471-0528.15433. [Epub ahead of print].

The use of postmenopausal hormone therapy (HT) remains controversial, despite increasing evidence supporting at least short-term benefits for women experiencing menopausal symptoms and intriguing suggestions of other long-term benefits for healthy menopausal women. The Women's Health Initiative (WHI) randomized studies were stopped prematurely because of a suggestion of an overall increased risk of morbidity and mortality. However, most recently, a new analysis of long-term outcomes of women enrolled in WHI has found no evidence of a differential effect on mortality after up to 18 years of follow-up.[1] Although informative, data from the WHI relate to the use of conjugated estrogens with and without medroxyprogesterone acetate, and are not generalizable to other treatment regimens. To provide more context, Holm et al used a population-based cohort to study the association between HT and mortality. The Diet, Cancer and Health Cohort is a large, Danish, population-based study. The cohort, established between 1993 and 1997, includes 29,875 women (aged 50 to 64 years and without a previous cancer diagnosis) who responded to an invitation to participate in a longitudinal study. This corresponds to 7% of the Danish female population in the age range.

A strength of this database was the collection of baseline data that included two self-administered questionnaires, anthropometric measurements, and blood samples obtained at a clinic visit. The questionnaires asked women about use of HT (never, previous, and current use), route of administration (oral, systemic non-oral, and local), and brand names used. Based on this information, investigators categorized women as users of estrogen alone, combination therapy (estrogen and progestogen), and sequential or continuous regimens.

To assess outcomes, the investigators linked cohort members to the Danish Causes of Death registry using their unique national personal identification numbers. In the analysis, the investigators considered alcohol intake, smoking, physical activity, and body mass index as possible confounders based on a priori hypotheses of associations with the outcome. They calculated associations between HT and mortality using Cox's proportional hazards models.

At baseline, 54.4% of the women had never used hormones, 15.5% were previous users, and 30.0% were current users. Among those women using hormones at baseline, 30% used estrogen only, 21% used continuous combined, and 32% used combined sequential. The type of HT was not defined in 17% of women. Most of the participants reported use of oral HT.

During a median follow-up interval of 17.6 years, 4,098 participants died. Of these, 2,155 died from cancer, 671 died from cardiovascular disease, and 1,084 died from other causes. The cause of death was not determined in 188 cases. After adjustment for relevant lifestyle risk factors, hormone use did not affect all-cause mortality, regardless of type or route.

Looking more closely at specific causes of death, the investigators found no differences in cancer-specific mortality or mortality from other causes between women on HT and never users. They further subdivided death due to specific causes of cancer and specific causes of

cardiovascular diseases. They found colorectal cancer mortality markedly lower among both current (hazard ratio [HR], 0.64; 95% confidence interval [CI], 0.46-0.89) and previous users (HR, 0.67; 95% CI, 0.46-0.99) compared with never users. They found the opposite association with breast cancer mortality; current users had significantly higher mortality compared with never users (HR, 1.34; 95% CI, 1.05-1.72). The risk was highest and statistically significant only for combined continuous HT (HR, 1.56; 95% CI, 1.05-2.31) and not statistically significant (HR, 1.37; 95% CI, 0.95-1.98) for women reporting use of estrogen only.

[The take-home message for clinicians counseling women on the risks and benefits of hormone therapy is positive. … This allows us to focus on counseling women on important quality-of-life issues, such as reduction in hot flashes, protection against fracture risk, and improved sexual function.]

Although no overall associations were observed between HT and cardiovascular disease, an interesting increase was seen in the risk of ischemic heart disease associated with use of local estrogen only (relative risk, 2.74; 95% CI, 1.38-5.44). Aside from this, the authors found no other associations between current or past HT use, or type of HT and risk of death.

## ■ COMMENTARY

This paper adds to our understanding of the long-term risks of postmenopausal hormone therapy. The paper offers few surprises with respect to cancer. A reduction in the risk of colon cancer death and a slight increase in breast cancer mortality were seen with users of combined HT, findings also reported in the WHI.[2] The lack of effect of HT on overall cancer mortality is highly reassuring. Even more reassuring is the lack of an association between systemic HT and *death* from ischemic heart disease or stroke. Interestingly, the only cardiovascular association with a moderate effect size (HR > 2), death from ischemic heart disease, occurred in users of local (e.g., vaginal) estrogen, a route of administration not associated with systemic risks or benefits. This effect may be explained by the very low numbers of women who reported use of local therapy only. Adverse prescription bias also may have influenced this outcome if clinicians were less likely to prescribe systemic HT for women with underlying cardiovascular disease risk. However, it is important to note that these results reflect HT use initiated prior to the publication of WHI, a time in which clinicians generally agreed that use of HT was cardioprotective.

Similar to many of the database studies reported by this group, the paper has both strengths and weaknesses. A major strength was the establishment of a cohort that included accurate collection of baseline data on body mass index (BMI) and hormone use. Unfortunately, we do not know much about continuation of use or how many women discontinued or initiated HT after the baseline assessment. We also rely on self-report to categorize the type of HT, which is surprising given the availability of accurate pharmacy records linked to unique national identity numbers. This group has used these pharmacy records to track exposure to hormonal contraception, so I am surprised at the lack of attempt to better follow HT exposure in this cohort. A major limitation of the other Danish registries studies is the lack of ability to adjust for baseline confounders, such as BMI, a notable strength of this study. In a companion paper using the same cohort, the same author group reported that a healthy lifestyle (e.g., regular exercise, nonsmoking) contributes to benefits seen with HT.[3]

The take-home message for clinicians counseling women on the risks and benefits of HT is positive. We all will die someday, but we want to avoid premature mortality. This study supports a lack of association between HT and overall mortality. While I personally believe that HT may have additional benefit, this study shows that at a minimum, women using HT should experience no overall risk. This allows us to focus on counseling about important quality-of-life issues such as reduction in hot flashes,[4] protection against fracture risk,[5] and improved sexual function.[6] ■

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ABSTRACT & COMMENTARY

# Initial Management of Patients With Medication-Overuse Headache

*By Louise M. Klebanoff, MD*

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**Dr. Klebanoff reports no financial relationships relevant to this field of study.**

SYNOPSIS: As part of a randomized treatment trial for medication-overuse headache, a simple protocol that provided early advice on stopping excessive medications was effective in one-third of patients, even before any prophylactic medications were started.

SOURCE: Corbelli I, Sarchielli P, Eusebi P, et al; SAMOHA Study Group. Early management of patients with medication-overuse headache: Results from a multicenter clinical study. *Eur J Neurol* 2018;25:1027-1033.

Medication-overuse headache (MOH) is a chronic headache disorder resulting from frequent intake of pain medication, including analgesics, nonsteroidal anti-inflammatory drugs, triptans, opioids, and ergotamine. The estimated prevalence of MOH in the Western world is 1-2%, with a peak incidence of 5% in women 40-50 years of age. Patients with MOH have lower scores on quality-of-life assessment scales when compared to patients with chronic headaches without MOH, episodic headache, and healthy controls. Despite the frequency of the condition and the high burden of disability it causes, there is no established consensus on the standard of care. Withdrawal of the abused medication is advised, but recommendations regarding the methods of detoxification and administration of prophylactic medications are inconsistent. In addition, the prognosis remains poor, with approximately 30% of patients relapsing within one year of withdrawal of medication.

Patients with MOH can be divided into two subtypes, simple (Type I) and complex (Type II). Type II patients have significantly more comorbidities, including psychopathology (mood, anxiety, or substance addiction disorders), a long duration of MOH (> 1 year), a history of relapse following withdrawal, and daily use of multiple doses of symptomatic medication.

Corbelli et al reported on patients enrolled in the multicenter, placebo-controlled Sodium vAlproate in the Treatment of Medication Overuse HeadAche (SAMOHA) study. At the initial visit, patients were given simple advice regarding MOH; they were advised to stop the abused medication. After initial assessment, each patient completed a four-week observation period followed by a six-day inpatient detoxification phase during which the abused drugs were discontinued and then a 12-week, double-blind treatment period in which they were treated with valproate 800 mg/day or placebo. After the four-week observational period, patients were reassessed to see if they still met International Headache Society revised criteria for MOH, at which point they were randomized to the treatment arm of the study. The researchers screened 130 patients at the nine participating centers. Most patients (80%) were women; the mean age was 42 years; and the headaches were chronic for an average of 4.6 years, with an average of 24 days of headache per month. The most commonly abused medications were acetaminophen, acetylsalicylic acid, or other nonsteroidal anti-inflammatory drugs.

After the initial observation period, 88 (67.7%) patients still met inclusion criteria and continued the study; 34 patients no longer met inclusion criteria. The patients whose headaches improved so that they no longer met inclusion criteria were significantly younger and had a significantly shorter history of chronicity when compared to those who continued to meet inclusion criteria. Since a significant proportion of patients with MOH improved after receiving simple advice, it is important to counsel patients regarding MOH early in their clinical care. In addition, when conducting studies regarding the management of MOH, it is important to have a period of observation following simple advice to ensure that the patients studied have persistent MOH.

## ■ COMMENTARY

The study, part of the SAMOHA study, suggests that simple advice given at an early clinical assessment can be helpful in the management of MOH, especially in the younger patient population with fewer years of chronic headache. In addition, when conducting research on this patient population, an observation period is needed to exclude patients who rapidly improve following simple advice. The patients with persistent MOH who failed to improve following simple advice have more psychological comorbidities and a longer duration of chronic headache and remain more challenging to treat. The management of this patient population, including recommendations regarding type of detoxification and institution of prophylactic medications, needs further study. Perhaps the results of the completed SAMOHA study will provide additional treatment recommendations. ■

ABSTRACT & COMMENTARY

# Acupuncture as Adjunct Therapy for Infertility in Polycystic Ovary Syndrome

*By Robert S. Lindgren, MD, and Nancy J. Selfridge, MD*

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**Dr. Lindgren and Dr. Selfridge report no financial relationships relevant to this field of study.**

SYNOPSIS: Acupuncture as an adjunctive therapy for treating infertility in Chinese women with polycystic ovary syndrome receiving clomiphene citrate or placebo offered no benefit over sham acupuncture.

SOURCE: Wu XK, Stener-Victorin E, Kuang HY, et al. Effect of acupuncture and clomiphene in Chinese women with polycystic ovary syndrome. *JAMA* 2017;317:2502-2514.

Polycystic ovary syndrome (PCOS) is a common endocrine disorder that causes infertility in women of reproductive age.[1] It is characterized by ovulatory dysfunction, excess androgen production and associated manifestations, and polycystic ovaries. The etiology remains unknown. Prevalence estimates vary and range from 2.2% to as high as 26%, depending on which diagnostic inclusion criteria are used.[1]

Although clomiphene citrate is a first-line treatment for anovulation and infertility related to PCOS,[2] investigations of alternative methods to treat infertility in women with PCOS have been ongoing. A Cochrane Review found insufficient evidence to support the use of acupuncture for the treatment of ovulation disorders in women with PCOS, despite some individual trials that demonstrated acupuncture as effective for ovulation induction.[3] For example, investigators in one study concluded that higher ovulation frequency occurred in women with PCOS receiving repeated acupuncture treatments.[4] Studies showing benefit have had methodologic flaws or have been underpowered, preventing sufficient statistically significant evidence to change clinical management. Wu et al devised an adequately powered trial to investigate the effects of acupuncture as an adjunct therapy with clomiphene on live birth rates in Chinese women with PCOS and infertility.

The PCOS Acupuncture and Clomiphene Trial (PCOSAct) was a randomized, placebo-controlled, multicenter trial that included patients at 21 sites in the National Clinical Trial Base of Chinese Medicine in Gynecology from Mainland China. This $2 \times 2$ factorial trial was designed to examine the effects of active or sham acupuncture in combination with clomiphene or placebo to determine the effects on live births in Chinese women diagnosed with PCOS. Lacking strong preliminary data on live birth after acupuncture, 10% was chosen as the minimal clinically detectable difference likely to change clinical practice.

The investigators calculated that 1,000 women would need to be enrolled in the study based on the following assumptions: a 25% live birth rate with both active interventions; a 15% live birth rate with one active and one control intervention; a 5% live birth rate with both control interventions; an 80% power at a significance level of $P \leq 0.05$; and a 10% dropout rate. The investigators screened 4,645 women with PCOS and determined 1,000 participants were eligible for inclusion. These participants were randomly assigned and placed in a 1:1:1:1 ratio into four intervention groups: active acupuncture plus clomiphene, sham acupuncture plus clomiphene, active acupuncture plus placebo, and sham acupuncture plus placebo. The assignments were double-blinded to everyone except the acupuncturists, who knew if they were delivering active or sham acupuncture.

Both active and sham acupuncture treatments were administered for 30 minutes twice a week, for a maximum of 32 treatments. Active acupuncture points were located in the abdominal and leg muscles associated with known autonomic innervation of the ovaries and the uterus according to traditional Chinese medicine, as well as in the hands and head. Manual and low-frequency electrical stimulation of the needles was applied in the active acupuncture treatments. In the sham acupuncture protocol, four needles were inserted superficially (less than 5 mm) without manual stimulation, one in each shoulder and upper arm at non-acupuncture points. The four needles were attached to electrodes and the acupuncturist simulated switching on the stimulator, mimicking the active acupuncture protocol, although no electrical stimulation actually was delivered.

For the medication protocol, subjects were given initial oral doses of clomiphene 50 mg or placebo between days 3 and 7 of the menstrual cycle. In patients with irregular menses and without recent menstruation, the researchers induced withdrawal bleeding with medroxyprogesterone acetate (5 mg/d) for 10 days. These patients also took clomiphene or placebo between days 3 and 7 of active

**Table 1: Primary Outcome Data Comparing Clomiphene/Placebo With Acupuncture/Sham Acupuncture – Live Births**

| Number of live births (% live births) | | | | | |
|---|---|---|---|---|---|
| Clomiphene citrate | | | Placebo | | |
| + ACU<br>n = 235 | + sACU<br>n = 236 | Total<br>n = 471 | + ACU<br>n = 223 | + sACU<br>n = 232 | Total<br>n = 455 |
| 69 (29.4%) | 66 (28.0%) | 135 (28.7%) | 31 (13.9%) | 39 (16.8%) | 70 (15.4%) |
| **Absolute differences (95% CI)** | | | | | |
| Effect of acupuncture | | | Effect of clomiphene | | |
| + CC | + PC | Overall | + ACU | + sACU | Overall |
| 1.4<br>(-6.8 to 9.6) | -2.9<br>(-9.5 to 3.7) | -0.6<br>(-5.9 to 4.7) | 15.5<br>(8.1 to 22.8) | 11.2<br>(3.7 to 18.6) | 13.3<br>(8.0 to 18.5) |
| CC: clomiphene citrate; PC: placebo; ACU: active acupuncture; sACU: control (sham) acupuncture | | | | | |
| Source: Wu XK, Stener-Victorin E, Kuang HY, et al. Effect of acupuncture and clomiphene in Chinese women with polycystic ovary syndrome. *JAMA* 2017;317:2502-2514. | | | | | |

bleeding. Doses of oral medication or placebo were increased by one pill in the absence of ovulation or maintained in the presence of ovulation. The maximum dosage did not exceed 150 mg per day or 750 mg per cycle. In the absence of conception, the protocol was repeated for a maximum of four menstrual cycles. Patients were instructed to have regular intercourse every two to three days, and pregnancy and ovulation were ascertained by weekly monitoring of urinary human chorionic gonadotropin and serum progesterone levels. Pregnant patients were followed within the study with ultrasonography every two weeks until fetal heart motion was visible, then referred for routine obstetric care. Birth outcomes for these patients were obtained from their obstetrical records.

The primary outcome was live birth, defined by the authors as 20 weeks' gestation or later. See Table 1 for a summary of results. There were 69 live births (29.4%) in 235 patients receiving active acupuncture plus clomiphene, 66 (28.0%) in 236 patients with sham acupuncture plus clomiphene, 31 (13.9%) in 223 patients with active acupuncture plus placebo, and 39 (16.8%) in 232 patients with sham acupuncture plus placebo. Since no significant effect was noted on live births between clomiphene with and without active acupuncture ($P = 0.39$), the authors examined the main effects of clomiphene and active acupuncture. Clomiphene treatment was associated with significantly higher live birth rates than placebo treatment: 135 of 471 (28.7%) for clomiphene vs. 70 of 455 (15.4%) for placebo, a difference of 13.3% (95% confidence interval [CI], 8.0-18.5%). The live birth rate was not significantly different between the groups treated with active and sham acupuncture: 100 of 458 (21.8%) for active acupuncture vs. 105 of 468 (22.4%) for sham acupuncture, a difference of -0.6% (95% CI, -5.9% to 4.7%). Adverse events also were examined, as were quality-of-life scores using standard instruments such as the SF-36. Bruising at the needle placement sites and incident diarrhea were significantly higher in the active acupuncture groups compared to the sham acupuncture groups.

These results show that among Chinese women with PCOS, the use of acupuncture with or without clomiphene does not increase live birth rates. These results show that actual and sham acupuncture, with or without clomiphene, had similar, nonsignificant effects on the rates of live births in Chinese women with PCOS. The authors concluded that these findings do not support acupuncture as an infertility treatment for Chinese women with PCOS.

## ■ COMMENTARY

Although it is not uncommon for infertility centers to offer acupuncture to patients, especially those seeking assisted reproduction with in vitro fertilization, evidence of efficacy for increasing live births has not been shown.[5] This is another study that fails to support acupuncture for improving fertility and live birth outcomes in a specific patient population plagued by ovulatory dysfunction and low fertility. On the other hand, this study bolsters existing evidence supporting clomiphene as first-line pharmacologic therapy for improving live birth rates in infertile women with PCOS.[2]

PCOS management strategies include diet, exercise, weight loss when needed, and a variety of medications to manage insulin resistance and other symptoms.[3] When clomiphene fails in patients with PCOS, strategies to improve fertility also include improving insulin resistance, mainly with metformin.[2] This practice suggests that insulin resistance may contribute to infertility in these patients, and it begs whether integrative therapies aimed at reducing insulin resistance might be helpful, including acupuncture. Further, the authors suggested that the

standardized acupuncture intervention in this study, aimed solely at inducing ovulation, would be atypical of traditional acupuncture treatment, which characteristically is individualized to a specific patient rather than a specific medical condition.

The strengths of this study include its design, methodology, and size. There were similar withdrawal rates across all groups and high adherence rates among participants. Since the study only involved Chinese women in China, the results should not be generalized to women of other ethnic groups or geographic locations. The authors concluded that their findings do not support acupuncture as treatment for infertility due to PCOS. However, without a true control group receiving neither treatment or placebo, one could argue that true and sham acupuncture both improved fertility rates, but less so than clomiphene.

Although acupuncture treatment in this study resulted in increased rates of diarrhea and bruising at needle sites, these side effects, though undesirable, occurred relatively infrequently. Further, the authors cited a clear placebo effect from both actual and sham acupuncture in increasing live birth rates compared to a previous study using physical therapy as a control intervention. Acupuncture is a safe intervention, and few options for treating PCOS-related infertility exist. Despite the absence of evidence of efficacy suggested by this study, there are enough lingering questions to suggest that PCOS patients who wish to pursue individualized acupuncture as an adjunct therapy for infertility should be informed, but not discouraged, assuming cost of treatment is not a burden. ■

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## CME/CE QUESTIONS

1. **In the study by Hobby et al, copper intrauterine device (IUD) users were more likely to discontinue their IUD if they had heavy menstrual bleeding at baseline.**
   a. True
   b. False
2. **Results from the Danish study of hormone therapy and mortality demonstrate that compared to never users, users of hormone therapy have which of the following?**
   a. An overall increased risk of cancer death due to an increased risk of breast cancer
   b. An overall increased risk of cancer death due to an increased risk of colon cancer
   c. An overall decreased risk of cancer death due to a decreased risk of breast cancer
   d. No overall risk of death due to cancer, cardiovascular disease, or all causes
3. **Patients with simple medication-overuse headaches should be:**
   a. given medications for headache prophylaxis.
   b. admitted for inpatient detoxification.
   c. continued on analgesics as needed.
   d. educated about medication-overuse headache and advised to stop the abused medication.
4. **In the PCOS Acupuncture and Clomiphene Trial, which of the following was noted as a statistically significantly side effect of active acupuncture compared to sham acupuncture?**
   a. Headache
   b. Diarrhea
   c. Skin discoloration
   d. Myalgia

## [IN FUTURE ISSUES]

A New Treatment for Postpartum Depression

Is Paternal Age Important for Perinatal Outcomes?