Protocol: AAAR2610

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Title: Auricular acupuncture as an adjunct for pain management during first trimester abortion: a randomized, double-blinded, placebo controlled trial

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Rationale

The Joint Commission announced new pain assessment standards to ensure all patients the right to appropriate management of their pain (Lanser, 2001). Adequate acute pain management is also essential in the provision of safe, high quality abortion care. Of the estimated 1.06 million abortions performed in the United States in 2011; 91% are 1st trimester abortions (Guttmacher, 2016). Most abortions are performed in the outpatient setting with a paracervical block (O'Connell, 2009) but patients still experience moderate pain (Smith, 1979; Belanger, 1989; Renner 2010). In 2013, a cross-sectional survey of abortion facilities in the US and Canada showed that 77% of providers offer moderate sedation and 40% of providers offer general sedation (White, 2015). Moderate sedation and general anesthesia minimize pain (Renner, 2010) but increased cost, side effects, health risks, and recovery time may be prohibitive, limiting abortion access (O'Connell, 2009). Many abortion facilities require that patients receiving moderate and deep sedation have an escort to accompany them home. Given that in 2008, abortion patients traveled an average of 30 miles one way to an abortion facility (Jones, 2014), having to find an escort places a burden on patients finding someone who is willing to give time away from work, school, and other responsibilities to accompany them to and from their appointment. In regards to patient safety, abortion-related mortality is rare with a mortality rate of 0.7 deaths per 100,000 procedures; the most common cause of death related to a surgical abortion of 13 weeks of gestation or less was anesthesia complications (Zane, 2015). For abortion facilities, the cost of maintaining a facility equipped to provide moderate and deep sedation is expensive due to the need to hire qualified staff to provide anesthesia, a nurse to monitor the patient after receiving anesthesia, and the need for larger office space for a post-anesthesia recovery area. Most abortions are performed in the outpatient setting before 13 weeks' gestation (Pazol, 2014) with a paracervical block as the only analgesic (O'Connell, 2009). Paracervical block is associated with improved pain control during dilation and aspiration however, women still experience moderate to severe pain during abortions even with the use of a paracervical block (Smith 1979, Belanger 1989, Renner 2010, Tangsiriwatthana 2013). Adjuncts to local anesthesia could decrease pain during aspiration procedures. Numerous techniques and procedures have been investigated including pharmacologic and nonpharmacologic adjuncts. Premedication with non-steroidal anti-inflammatories such as ibuprofen and naproxen improved pain control while lorazepam, hydrocodone-acetaminophen, and oral midazolam did not (Allen 2009, Renner 2010, Micks 2012; Bayer, 2015). Hypnosis and relaxation exercises did not change reported procedural pain (Renner 2010). Music in one study lessened the pain during abortion (Shapiro 1975, Renner 2010) but this result was not reproduced in recent randomized trials (Guerrero 2012, Wu 2012). Despite these attempts to lessen anxiety and pain associated with abortion under local anesthesia, the results and

efficacy of these methods is variable and inconsistent. Thus, pain and anxiety management during first trimester abortions remains unresolved. Pain experienced during abortion results from a complex interaction of physical innervation pathways, psychological and social factors (Allen 2013, Renner 2010). Physical pain from cervical dilation and aspiration is due to innervation of the uterine cervix and lower uterine segment through parasympathetic fibers and the uterine fundus through sympathetic fibers (Allen, 2013). Pain during abortion is also influenced by additional factors such as age, self-reported pre-procedure depression and anxiety as well as social and moral concerns about abortion (Belanger, 1989). Adequate pain management during suction aspiration would require interventions that influence physical pain as well as mental and emotional states. Therefore, the complexity of women's experience with pain during abortion makes it challenging to study. Acupuncture affects perception of painful stimuli and anxiety. Peripheral stimulation of acupoints mobilizes central neuropeptides involved in the pathway of anxiety and stress. Also activates opioid receptors, decreases COX-2 activity, and decreases inflammation; thereby inducing analgesia. Ancient Chinese medicine has defined 361 acupuncture points located throughout the body and each point is assigned a number and carries the name of the area of the body it is associated with (Schlaeger, 2017). Acupuncture might complement local anesthesia by providing additional and complementary analgesic and anxiolytic effects. A Cochrane Review evaluating acupuncture an analgesic for obstetrical pain included 13 trials with data reporting on 1986 women; 9 of the 13 trials are randomized controlled trials (RCT) (Smith, 2011) Of the nine trials, a RCT conducted in Denmark with 607 healthy women in labor compared the use of acupuncture, transcutaneous electric nerve stimulation (TENS), and traditional analgesics as pain relief during labor using a 10-point pain VAS. The primary outcome was the need for pharmacological and invasive methods during labor. The mean pain score at randomization was 6.8, no significant differences were found in pain scores among the three groups at any point during labor. However, the use of pharmacological and invasive methods was significantly lower in the acupuncture group (acupuncture vs traditional, $p < 0.001$; acupuncture vs TENS, $p = 0.031$) (Borup, 2009).In a 2014 meta-analysis, RCTs assessed the preoperative anxiolytic efficacy of acupuncture therapy in outpatient, inpatient, emergency and nonemergency settings; 14 publications (N = 1,034) compared groups receiving preoperative acupuncture treatment with control groups receiving a placebo for anxiety (Bae, 2014). Of the 14 publications, five studies used auricular acupuncture and of these 5, they used STAI-S and/or VAS to evaluate anxiety. Battle Field Acupuncture (BFA) was not among the methods of acupuncture tested and most of the studies reviewed in this meta-analysis were of poor quality. Studies that used the State-Trait Anxiety Inventory-State (STAI-S) showed reductions in preoperative anxiety relative to sham acupuncture (Bae, 2014). Also, studies that used visual analogue scales (VAS) showed differences in preoperative anxiety between groups (Bae, 2014). The demonstrated benefits of acupuncture on obstetrical and gynecological related pain and anxiety suggest examining the role of acupuncture in improvement of pain and anxiety during abortion. In auricular acupuncture, a technique of acupuncture, needles are placed in designated acupoints on the external ear in order to alleviate health conditions, in particular pain, in other parts of the body (Oleson, 1998). Some points correspond to specific internal organs to induce analgesic effects, while other auricular acupoints decrease anxiety, modulate pain perception, and nausea. (Michalek-Sauberer 2012, Lin 2014). In a meta-analysis of 13 auricular acupuncture RCTs assessing the efficacy of auricular therapy for pain management by including a sham therapy control group (N = 806); 7 of the 13 studies found a difference in pain greater than 15 points (100 mm VAS); favoring the intervention. However, several of the studies within this meta-analysis are of poor methodically quality (Yeh, 2014). Also, of the 13 studies, 4 involved gynecological procedures

(Yeh, 2014). The gynecological studies used 2-7 auricular acupoints: bladder 36, cardia, central rim, cushion, endocrine, governor vessel 20, helix, internal genitals, kidney, liver, lumbar-sacrum vertebra, occipital, shenmen, stomach, and uterus (Yeh, 2014).Battlefield acupuncture (BFA) is an auricular acupuncture technique developed in 2001 by Air Force Colonel Richard Niemtzow, M.D, that delivers attenuation of pain in minutes using 5 auricular acupuncture points: cingulate gyrus, thalamus, Omega 2, Point Zero, and Shen Men (DVCIPM, 2016; Olesen, 1998). BFA is used in the military because it is fast, easy, safe, and effective (Leggit, 2014). Needle placement takes approximately three minutes and does not require a licensed acupuncturist. The Uniformed Services University of the Health Sciences (USUHS), a United States military medial school teaches BFA in two 2-hour sessions (Leggit, 2014). A 2016 case series describes 4 cases in which emergency physicians with 1 hour of BFA training performed BFA to treat patients with acute pain when opioid analgesia was not an acceptable option. During the case series, the patients initially reported a pain score of 5 - 8 on a 10-point Numeric Pain Rating Scale, which after 1 hour of BFA, repeat pain score was 0 – 4 (Tsai, 2016). For this study, we will use a modified BFA protocol. Instead of using the acupoint Omega 2 for extremity pain, we will use the cervix point on the left ear and uterus point on right ear.

Study Design

The proposed study will be a randomized, double blinded, placebo-controlled trial to evaluate the efficacy of auricular acupuncture as adjunct for pain management during first trimester uterine aspiration. Patient written informed consent to participate in the study, will be collected on an iPad along with the HIPPA authorization form. In-person electronic signature will be captured on the electronic informed consent form. Study personnel obtaining consent will be physically present at time of signature. A paper copy of the signed informed consent form is given to the patient. In acupuncture literature, some argue that differences in outcomes between acupuncture and placebo or sham control groups are attenuated due to stimulation from placebo adhesives (in the case of the planned intervention in this study) and from a placebo effect per se. Therefore, we revised our primary objective to compare the effect of auricular acupuncture on decreasing pain and anxiety to a routine care control group, rather than to a sham-acupuncture control group (which becomes a secondary objective).In order to assess the efficacy, we plan to: Measure effectiveness of auricular acupuncture as an adjunct to ibuprofen and paracervical block for pain control during first trimester uterine aspiration by comparing the mean maximum pain score (measured by 100mm pain VAS immediately following the procedure) between women randomized to receive auricular acupuncture and routine-care controls. Secondarily we plan to: Measure effectiveness of auricular acupuncture as an adjunct to ibuprofen and paracervical block for pain control during uterine aspiration by comparing the mean maximum pain score (measured by 100mm pain VAS) between women randomized to receive auricular acupuncture or placebo adhesives. Also, to assess these differences between women randomized to receive placebo adhesives and routine-care controls to estimate the magnitude of the placebo effect. Measure effectiveness of auricular acupuncture in decreasing anxiety during first trimester uterine aspiration by comparing the mean maximum anxiety score during the procedure (measured by 100m anxiety VAS) between women randomized to auricular acupuncture, placebo adhesives, and routine-care controls at the completion of the procedure, participants will complete a satisfaction survey. The satisfaction survey will compare overall satisfaction at the end of the visit between women receiving auricular acupuncture versus women receiving other treatment within the study. Statistical Procedures: Provide sufficient details so

that the adequacy of the statistical procedures can be evaluated including power calculations to justify the number of participants to be enrolled into the study. Definitions of subject terms such We will randomize participants to either 1 - auricular acupuncture with pyonex needle, 2 - placebo adhesive, or 3 – routine care using a 1:1:1 ratio. The randomization scheme will use randomly permuted blocks with a block size of 6 or 9. An investigator experienced with generating randomization sequences and not directly involved in the study will be responsible for creating the entire randomized schedule; first by defining the sequence of block sizes and second, by defining the assignments within each block. The division research office at CUMC will prepare opaque, sealed envelopes containing cards indicating whether a given patient has been randomized to receive 1 - auricular acupuncture with pyonex needles 2 - placebo adhesives, or 3 – routine care. The allocation will remain concealed from the patient and abortion provider. The medical provider performing acupuncture will open the sealed, opaque envelope immediately prior to the suction aspiration procedure and perform the intervention according to randomization assignment.

Statistical Procedures

We will analyze the maximum mean pain score during the procedure; as measured by VAS-P among women randomized to receive: 1) auricular acupuncture or routine-care, 2) auricular acupuncture or placebo 3) placebo or routine-care care. We will also analyze the maximum mean anxiety score during the procedure; as measured by VAS-A among women randomized to receive: 1) auricular acupuncture or routine-care, 2) auricular acupuncture or placebo 3) placebo or routine care. A satisfaction survey will assess the participants' global satisfaction. We will carry out both an intention-to-treat analysis and a per-protocol analysis. We will use bivariate analysis with the student's t-test to compare means and. We will also use regression to control for baseline pain and anxiety in assessing maximum pain and anxiety. The absolute value and direction of change for each of the measured variables will be the focus of this analysis. Data analysis will take place upon completion of data collection. We will use SPSS or SAS for analysis. Using Guerrero's pain study as reference, we base the power calculations on an expected mean maximum pain score of 60 and SD 24.7 in the control group (Guerrero, 2012). To detect a 15 mm or greater reduction in the pain score with 80% power using a two-sided alpha of 0.05, we estimate enrolling: 43 participants per study group. Waiting to enroll women in the study after all pre-operative procedures and surgical consent are completed will greatly disrupt clinic flow, thus enrollment will take place earlier, which means that we will lose about 20% of participants before the procedure, as noted during the acupuncture pilot study. Therefore, we will enroll an additional 26 participants to account for the estimated 20% that will be released from the study.