Outcomes Research in Review

Betamethasone Before All Late Preterm Deliveries?


Study Overview

**Objective.** To determine whether the administration of betamethasone to women who are likely to deliver in the late preterm period would decrease respiratory and other neonatal complications.

**Design.** Randomized controlled trial.

**Setting and participants.** Participants were women with a singleton pregnancy at 34 weeks 0 days to 36 weeks 5 days of gestation and a high probability of delivery in the late preterm period (which extends to 36 weeks 6 days) within the 17 university-based clinical centers participating in the Maternal Fetal Medicine Units Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). Eligible women were randomly assigned in a 1:1 ratio to a course of 2 intramuscular injections of either 12 mg betamethasone or matching placebo administered 24 hours apart. After administration of the study medications, the women were treated clinically according to local practice, including discharge to home if delivery did not occur.

**Main outcome measures.** The primary outcome was a composite endpoint consisting of need for respiratory support, stillbirth, or neonatal death within 72 hours after delivery. Need for respiratory support was defined as one or more of the following: the use of continuous positive airway pressure (CPAP) or high-flow nasal cannula for at least 2 consecutive hours, supplemental oxygen with a fraction of inspired oxygen of at least 0.30 for at least 4 continuous hours, extracorporeal membrane oxygenation (ECMO), or mechanical ventilation. Secondary outcomes included 2 composite outcomes: (1) respiratory distress syndrome, transient tachypnea of the newborn, or apnea; and (2) respiratory distress syndrome, intraventricular hemorrhage, or necrotizing enterocolitis.

**Main results.** Among 24,133 women assessed for eligibility, 2831 women underwent randomization with 1429 assigned to the betamethasone group and 1402 to the placebo group. A total of 860 (60.2%) in the betamethasone group and 826 (58.9%) in the placebo group received the prespecified 2 doses of study medication. 1083 of the 1145 women (94.6%) who did not receive a second dose delivered before 24 hours. Two women in each study group were lost to follow-up, with outcome information available for 2827 neonates.

The rate of the primary outcome was lower in the betamethasone group (11.6%) than in the placebo group (14.4%), with a relative risk of 0.80% (95% CI 0.66 to 0.97; \( P = 0.02 \)); the number needed to treat was 35.
women to prevent 1 case of the primary outcome. In regard to secondary outcomes, the rate of the composite outcome of severe respiratory complications was also lower in the betamethasone group than in the placebo group (8.1% vs. 12.1%; relative risk 0.67; CI 0.53 to 0.84; \( P < 0.001 \)). Of note, the betamethasone group had a higher incidence of neonatal hypoglycemia when compared to the placebo group (24.0% vs. 15.0%; relative risk 1.60; 95% CI 1.37 to 1.87; \( P < 0.001 \)).

**Conclusion.** Administration of antenatal betamethasone in women at risk for late preterm delivery significantly decreased the rate of respiratory complications in newborns.

**Commentary**

Use of antenatal glucocorticoids for early preterm delivery has been a widely accepted practice, with strong evidence that glucocorticoids reduce adverse neonatal outcomes when administered to women who are likely to deliver before 34 weeks of gestation [1,2]. In addition, use of glucocorticoids at the time of elective cesarean delivery at term from the results of the Antenatal Steroids for Term Elective Caesarean Section (ASTECS) trial demonstrated reduction in the rate of admission to neonatal intensive care units for respiratory complications in the betamethasone group when comparing to placebo [3]. However, the use of glucocorticoids in the late preterm period to prevent adverse neonatal respiratory outcomes remained inconclusive after 2 smaller randomized trials [4,5].

In the current study, Gyamfi-Bannerman and colleagues addressed the issue of whether the use of glucocorticoids, specifically betamethasone, in the late preterm period may prevent adverse neonatal respiratory outcomes. While only 60.2% of the betamethasone group and 58.9% of the placebo group received the proposed 2 doses of study medication, administration of betamethasone decreased the need for substantial respiratory support during the first 72 hours after birth and other respiratory complications.

There were no clinically significant adverse neonatal effects except that the betamethasone cohort babies had a 60% increased relative risk of neonatal hypoglycemia. There were no reported adverse events related to the hypoglycemia, and infants with hypoglycemia were discharged on average 2 days earlier than those without, which suggests that the condition was self-limiting. The authors suggested monitoring neonatal blood glucose after betamethasone exposure in the late preterm period. It will be important to answer questions about the long-term outcomes of this therapy, both benefits and risks, such as the potential reduction of chronic lung diseases or risk of developmental delay due to hypoglycemia [6].

**Applications for Clinical Practice**

This multicenter randomized controlled study provides strong evidence for administering antenatal glucocorticoids, such as betamethasone, in women at risk for late preterm delivery. Betamethasone administration significantly decreased the rate of respiratory complications in newborns, with the precaution to monitor for neonatal hypoglycemia.

—Ka Ming Gordon Ngai, MD, MPH

**References**

Acupuncture for Menopausal Vasomotor Symptoms


Study Overview

Objective. To examine the effects of acupuncture on vasomotor symptoms (VMS) and quality of life in perimenopausal and postmenopausal women.

Design. Pragmatic randomized controlled trial.

Setting and participants. Participants were perimenopausal and postmenopausal women aged 45 to 60 years who had 4 or more VMS episodes a day. Women were excluded if they had initiated or changed a dose of any VMS treatment in the 4 weeks prior to the study, initiated or changed the dose of an antidepressant in the prior 3 months, had received acupuncture in the prior 4 weeks, self-reported their health as poor or fair, or had a diagnosis of hemophilia. The study was conducted at the Wake Forest School of Medicine and the Chapel Hill Doctors Healthcare Center in North Carolina with women recruited from the community. Potential participants completed a 2-week hot flash diary to establish that they met the eligibility criteria of 4 or more hot flashes a day.

Intervention. Eligible participants were randomized to either the experimental group, who received up to 20 acupuncture treatments over a 6-month period, or a waitlist control group who received usual care for 6 months followed by the same 6 months of acupuncture treatment received by the experimental group. The researchers decided not to use sham acupuncture in the control group because outside of the experiment women would not receive sham acupuncture and because it has been shown to have an effect on menopausal symptoms in other studies.

Participants could receive up to 20 acupuncture treatments from 1 of the 4 study licensed acupuncturists over a period of 6 months. The acupuncturist assessed the participant and made a traditional Chinese medicine diagnosis to guide treatment at the initial and each subsequent visit. During treatment, acupuncture needles were inserted 0.5 to 3 cm through the skin to achieve a “de Qi” sensation, which is a sensation of heaviness, numbness, soreness, or distention at the insertion site. Acupuncturists were permitted to administer additional acupuncture-related treatments with the exception of the use of Chinese herbal remedies. Additionally, participants were permitted to start other treatments, and 11 women in the acupuncture group and 2 women in the control group started other behavioral treatments during the study.

Main outcome measures. The primary outcome measure was the frequency and severity of hot flashes and night sweats, measured using the Daily Diary of Hot Flashes (DDHF). Secondary measures were the following quality of life indicators: hot flash interference (the degree to which hot flashes interfered with specific daily activities), measured using the Hot Flash-related Daily Interference Scale; sleep quality, measured using the Pittsburgh Sleep Quality Index (PSQI) and the PROMIS Sleep Disturbance short form; menopause related symptoms other than VMS, measured using the Women's Health Questionaire (WHQ); depression, measured using the short form of the Center for Epidemiologic Studies Depression scale (CESD-10); anxiety, measured using the General Anxiety Disorder (GAD-7) and the PROMIS Anxiety short form; perceived stress, measured using the Perceived Stress Scale (PSS); and health-related quality of life (HRQOL), measured using a global visual analog scale (VAS) and the Physical and Mental Health Component scores of the Medical Outcomes Study short form health survey (SF-36).

Main results. The final sample size was 209 women, with 170 randomized to the acupuncture group and 39 to the control group. There were no significant differences between the groups at baseline. The retention rate was 89% at 6 months and 84% at 12 months. At 6 months there was a 36.7% decrease VMS frequency in the acupuncture group compared to a 6.0% increase in the
control group ($P < 0.001$). At 12 months the decrease in VMS frequency was 29.5% in the acupuncture group. The control group began acupuncture at 6 months and by 12 months the frequency of VMS in this group was 31.0% less than at baseline ($P < 0.001$). Overall, the maximal effect was achieved at week 7 with a median of 8 acupuncture treatments. Sensitivity analysis indicated that there were no differences in effect in those who started other behavioral treatments during this period. There were also significant improvements in scores on the hot flash interference scale ($P < 0.001$), fewer sleep problems on the sleep measures, and fewer symptoms on the WHQ for women in the acupuncture group and these effects were maintained at 12 months. In addition, similar results were found in the control group after they initiated acupuncture at 6 months.

Conclusion. Overall, acupuncture resulted in significant and sustained improvements in VMS and quality of life measures.

Commentary

More than half of women will experience frequent VMS beginning with the menopause transition [1] and lasting an average of 7.4 years [2]. The effect of VMS on women’s quality of life is considerable, including anxiety, stress, decreased energy, sleep disruption and interference with leisure, social, and work activities [3,4]. Estrogen therapy remains the most effective therapy for VMS; however, its use is contraindicated in many women and duration of use is limited [5]. Therefore, safe and effective alternate therapies are needed.

Acupuncture is a traditional Chinese medicine therapy that has gained popularity in recent years for therapeutic management of many conditions, including pain, nausea related to pregnancy or chemotherapy, anxiety, headache, and addiction. Evidence regarding effectiveness has been equivocal, with studies of its effectiveness in some conditions, such as nausea and dental pain, showing strong positive results while evidence for its use in other conditions is lacking or inconsistent [6]. There have been consistent positive findings in prior research of the use of acupuncture to reduce the severity and frequency of VMS, however, according to the authors of this study, little is known about the long-term effects or the effect on quality of life. Additionally, most studies use sham acupuncture in the control group, which would not be offered to women outside a study protocol and has been shown to have a physiological effect of its own. Therefore, the authors conducted a pragmatic randomized control trial; designing the intervention so that it more closely reflected what happens in a real world clinical setting, to examine the overall effects and effect on quality of life measures.

The results of this study were a significant positive effect of acupuncture on the frequency and severity of VMS in the acupuncture group that was sustained over 12 months and improvements on all quality of life measures. There was also a significant effect in the control group when they received the intervention after the initial 6-month period. As the authors note, it is unclear if improvements in the quality of life indicators were a direct effect of the acupuncture or secondary to the relief of the vasomotor symptoms. Its use in women who experience other menopause-related symptoms, such as mood disorders or sleep disruption, in the absence of VMS needs further study.

The authors compare their results with that of research on the use of selective serotonin reuptake inhibitors (SSRIs) for VMS, one of the more efficacious alternatives to hormone therapy. As they note, though the reduction was somewhat less than that found with SSRIs (for example 35% for acupuncture vs. 47% with escitalopram), the risk of adverse effects is much lower with acupuncture. The only reported adverse effects in this study were 2 women who reported pain during treatment and 1 who reported numbness while SSRIs are known to have significant adverse effects. In addition, the results in this study were sustained longer, until the final follow-up at 6 months, while women who used escitalopram relapsed three weeks after discontinuing the medication.

The use of a pragmatic design allows for more confidence that the findings will translate to the real world setting. The number and timing of acupuncture treatments were determined by each woman with the acupuncturist as would happen in the clinical setting. In addition, the initiation of other therapies during the treatment stage was allowed, with 11 women in the acupuncture group and 2 women in the treatment group starting other behavioral interventions during that time. Though this approach has a small chance of introducing confounding variables, sensitivity analysis indicated it did not. As such, this design results in a study that is an accurate reflection of the experience of women receiving acupuncture in the clinical setting and thus good external validity.
OUTCOMES RESEARCH IN REVIEW

There were 2 limitations of note. Though retention was excellent, 89% and 84% for the acupuncture and control group respectively, it is unknown if the women who dropped out did so due to lack of improvement, in which case the actual reduction in VMS would have been less than reported. Additionally, the use of self-report (diaries) of VMS can be unreliable and biased.

Applications for Clinical Practice

The results of this study indicate that acupuncture offers women a safe and effective therapy for VMS. The optimal dose appears to be 8 treatments. Clinicians should consider it as a first-line treatment for women with moderate to severe VMS who have contraindications to hormone therapy and before prescribing SSRI therapy, which carries the potential for significant adverse effects.

—Karen Roush, PhD, RN

References


Group Visits for Discussing Advance Care Planning


Study Overview

Objective. To describe the feasibility of a primary care–based group visit model focused on advance care planning.

Design. Qualitative study.

Setting and participants. Participants were patients attending the Senior Clinic, a patient-centered medical home at the University of Colorado Hospital in Aurora, CO. Patients had to be aged 65, English speakers, and receiving primary care at the Clinic. Participants could be referred by their primary care clinician, a partner or friend, or self-refer in response to flyers.Clinicians were not asked to prioritize patients with poor health status or known end-of-life needs.

Intervention. Groups of patients met for 2 sessions (1 month apart), each 2 hours in length, facilitated by a geriatrician and a social worker. About 1 hour was spent on discussion of advance care planning concepts, including sharing experiences and considering values. Other time in the session was for introductions/rapport building, individual goal setting, and optional completion or directives and/or individual clinical visits. Facilitators were supported by a Facilitator’s Communication Guide and used educational materials and handouts with the group.

Main outcome measures. Researchers used the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework to evaluate the project.

Main results. Patients were referred by 10 out of 11 clinicians. Of 80 patients approached, 32 participated in 5 group visit cohorts (40% participation rate) and 27 participated in both sessions (84% retention rate). Mean age was 79 years; 59% of participants were female and 72% white. Most evaluated the group visit as better than usual clinic visits for discussing advance care planning. Patients reported increases in detailed advance care
planning conversations after participating (19% to 41%, \( P = 0.02 \)). Patients were willing to share personal values and challenges related to advance care planning and they initiated discussions about a broad range of relevant topics.

**Conclusion.** A group visit to facilitate discussions about advance care planning and increase patient engagement is feasible. This model warrants further evaluation for effectiveness in improving advance care planning outcomes for patients, clinicians, and the system.

**Commentary**

An understanding of patients’ care goals is an essential element of high-quality care, allowing clinicians to align the care provided with what is most important to the patient [1]. Existing evidence does not support the commonly held belief that communication about end-of-life issues increases patient distress [1]. Early discussions about goals of care are associated with better quality of life, reduced use of nonbeneficial medical care near death, enhanced goal-consistent care, positive family outcomes, and reduced costs; however, significant barriers to having advance care planning discussions exist [2], including communication issues and lack of appropriate counseling by clinicians in primary care. Clinicians cite limited time and lack of clinic-based support as factors that impede discussions with patients about advance care planning.

New models are being developed in order to facilitate the process. Group medical visits have been recognized as a useful and effective strategy for approaching patients [1]. The current study describes what the authors say is the first advance care planning group visit, which they named the “Conversation Group Medical Visit” (CGMV). Its aim is to engage patients in a discussion of key advance care planning concepts and support patient-initiated advance care planning actions, such as choosing surrogate decision makers, deciding on preferences during serious illness, discussing preferences with decision makers and health care providers, and documenting advance directives in the electronic health record [3].

As part of the group medical visits, participants receive an agenda, a personal copy of their EHR highlighting current advance care planning documentation, if any, and a blank medical durable power of attorney form. Facilitators use educational materials including videos from the PREPARE website (prepareforyourcare.org) that demonstrate a family’s conversation, advance directives, and various degrees of flexibility in the decision-making role. A Conversation Starter Kit is also used, which prompts individuals to think about their values and guides conversations about preferences.

Researchers used the RE-AIM framework [4] to evaluate the implementation of this group medical visit model. This framework looks at Reach (if older adults would participate in the medical group visits), Effectiveness (related to participant's engagement in the conversations), the Adoption of the model by health providers (clinician referral patterns), Implementation (related to the attendance of patients at both clinical and group visits and aspects of planning discussed), and Maintenance (not assessed in this study).

There was a 40% participation rate. Reasons given for declining to participate were having participated in past advance care planning conversation or having an existing advance directive (30%), lack of interest (13%), illness (3.3%), lack of transportation (3.3%), and other/unknown (50%). Regarding effectiveness, the majority of patients rated the group visit as better than usual clinic visits for talking about advance care planning. Participants reported that they received useful information and felt comfortable talking about advance care planning in the group. In addition, participants reported finding it helpful to talk with others about advance care planning (92%). Participants also reported an overall increase (19% to 41%) in advance care planning conversations with family members after participating in the group visit (\( P = 0.02 \)). Participants said these conversations included enough details that they felt confident that their family members knew their wishes. Thus, enrollment in a CGMV led to improvements in conversation not only between patient and health care provider but also between family members.

Several themes were identified during discussions. Patients shared personal values and challenges related to advance care planning. Also, the facilitated discussions introduced key advance care planning concepts and encouraged patients to share related experiences, questions, successes, and challenges in regards to these topics. An interesting finding was that patients in groups of 4 or 5 seemed less engaged in the discussion than those in groups of 7 to 9 patients.

**Applications for Clinical Practice**

This novel strategy to facilitate discussions about advance care planning showed promising results and appears fea-
sible, but further study is needed to evaluate the model. It may prove useful as a new model of advance care planning in primary care. Further longitudinal research is encouraged.

—Paloma Cesar de Sales, BS, RN, MS

References