A Pilot Study Evaluating the Combination of Acupuncture with Sildenafil on Endometrial Thickness

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Introduction

Endometrial thickness has been shown to be an important prognostic factor of successful embryo implantation. If the endometrial thickness is less than 9 mm there is a significant reduction in live birth rates. Though there is conflicting data, preliminary evidence suggests that the administration of vaginal Sildenafil can markedly improve endometrial thickness and result in increased live IVF births. Our clinical observations are consistent with this. However, other clinics report inconsistent results. Therefore, we hypothesized that the difference in response between clinics may involve other factors. When we looked into this, we found that many of our patients were simultaneously receiving acupuncture treatments.

Studies on acupuncture have demonstrated positive effects on implantation rates, ongoing pregnancy rates and the number of live births. Acupuncture has also been shown, via measurements of pulsatility index, to significantly increase blood flow to the uterus. Decreases in pulsatility index have been shown to significantly improve pregnancy rates. Researchers have also found that acupuncture has direct effects on the endometrium. Some of these include increases in progesterone receptor concentration, a reduction in COX-2, and an increase in the activity of nitric oxide synthase. Therefore, the purpose of our investigation was to evaluate the effects of combining acupuncture and Sildenafil suppositories on endometrial lining.

Materials and methods

Subjects were initially five females, ages 35 - 45, with prior IVF or IUI failures. However, one subject was later disqualified due to the discovery of an undisclosed prior lining of 9 mm. All subjects had a Day 3 FSH < 9 mlU/ml and normal uterine cavity by fluid ultrasound or hysteroscopy. Patients were excluded if they had known allergies to any fertility medications, a history of estrogen dependent neoplasms, abnormal uterine cavity, history of DES exposure or Asherman's syndrome.

Following IRB approval, consent, routine tests, FSH and estradiol levels were obtained for each patient and either a fluid ultrasound or HSG was performed less than 6 months prior to initiation of treatment. Protocols were designed for each patient using the fertility clinic's standard techniques for evaluating the necessary dosage of gonadotropins. Patients received a Lupron long protocol using 300 to 450 units of gonadotropin depending on age, prior IVF history and day 3 FSH value.

Each patient was given 25 mg Sildenafil suppositories on CD9 and a series of five acupuncture treatments provided by two acupuncturists who are certified by the National Certification Commission for Acupuncture and Oriental Medicine and the State of California. Thirtyfour gauge 1.5 inch and 38 gauge 1 inch needles (Millenia, China) were

used depending on the location of the acupoints. The 34 gauge needles were used on points located on the trunk of the body and the 38 gauge needles used on the extremities. A far infrared lamp (TDP, China) was utilized for 20 minutes on the lower abdomen, approximately 12-18 inches from the skin's surface. The base protocol included the following acupoints:

Conception Vessel 4 Spleen 6
Conception Vessel 6 Spleen 10
Large Intestine 10 Stomach 36
Kidney 3

Microcurrent stimulation (Electrostimulator 8c.Pro, Pantheon Research, CA) was applied using standard leads in biphasic mode using 10 Hz from (L) Kidney 3 to Conception Vessel 4 and from (R) Kidney 3 to Conception Vessel 6. Needle-moxa was then applied to Conception Vessel 4 and Conception Vessel 6 in the form of Japanese kyutoshin.

In accordance with Japanese meridian therapy, acupoint modifications were then made if any of the following areas were uncomfortable to the patient upon 2 kg palpation.

Location of palpation response	Protocol Addition
(L) Stomach 27-28	(L) Liver 4
(R) Stomach 27-28	(R) Spleen 9
Kidney 16	Ipsilateral Kidney 6
Kidney 2	Insilateral Kidney 10

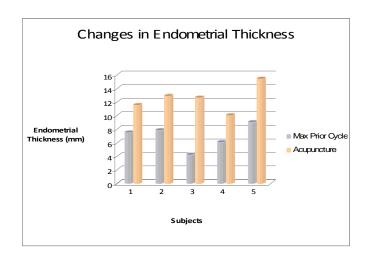
 $Treatments \ were \ administered \ according \ to \ the \ following \ schedule:$

Week	# of Tx	Treatment Timing
1	2	> 2 day space between tx
2	3	< 1 day space between tx

Uterine lining was measured during patients' routine monitoring via fluid ultrasounds which were provided starting from cycle day 3 and repeated throughout stimulation phase.

Results

All four subjects achieved endometrial lining thickness of greater than or equal to 10 mm following the administration of the combination of acupuncture and Sildenafil: including one patient whose lining did not exceed 5 mm in a previous cycle. Another patient, who had not responded to Sildenafil alone in a prior IVF cycle, responded to the combination of Sildenafil and acupuncture. We also noted that endometrial thickness in most patients continued to increase post-hCG administration.



	Lining Max Prior Cycle (mm)	Lining S+Acu (mm)
Patient 1	7.5	11.5
Patient 2	7.8	12.9
Patient 3	4.2	12.6
Patient 4	6.1	10
Patient 5*	9	15.4

Conclusions

This pilot study is consistent with previous reports that acupuncture improves uterine lining measurements over previous cycles.

This preliminary data supports the potential for a synergistic action between acupuncture and Sildenafil. We hypothesize these effects may be due to acupuncture's ability to upregulate nitric oxide synthase. However, we cannot rule out other mechanisms of action since acupuncture has also been shown to affect many other parameters.

The results of this preliminary data may also suggest a role for a similar combination in treating erectile dysfunction. Further testing and data is necessary to verify these results.

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For further information

Please contact <u>wendy@herbalroom.com</u>. More information on this and other acupuncture studies that relate to reproductive medicine can be found at <u>www.herbalroom.com</u>. For an online, PDF-version of this poster presentation, this can be obtained at <u>www.herbalroom.com/PCRS07.pdf</u>.