

CASE REPORT

Acupuncture, endometriosis and *in vitro* fertilization

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Abstract

This report describes the case of a 37-year-old female with moderate endometriosis and infertility. At the time of presentation for treatment, she had undergone 4 months of a 6-month course of gonadotropin-releasing hormone (GnRH) that was to be followed by an *in vitro* fertilization (IVF) cycle. The subject sought treatment for the side effects of the GnRH agonists and to prepare her body for IVF. Acupuncture was used in an attempt to address the menopausal symptoms produced by down-regulation, and improve blood flow to the uterus and ovaries so as to improve the chances of embryo implantation, and reduce the stress and anxiety associated with infertility and IVF treatment. The subject was treated once a week over a 10-week period.

Keywords: acupuncture, endometriosis, *in vitro* fertilization, traditional Chinese medicine.

Introduction

Endometriosis is a common medical condition that is characterized by the growth of ectopic endometrial tissue. The condition occurs when endometrium, which normally lines the inside of the uterus, grows outside or beyond this organ. The misplaced endometrial cells respond to the hormonal stimuli of oestrogen and progesterone during menstruation. The blood, which is unable to leave the body, stagnates at the site of implantation, causing inflammation and scarring.

Gonadotropin-releasing hormone (GnRH) agonists inhibit pituitary hormones, which, in turn, inhibit the production of follicle-stimulating hormone, luteinizing hormone and oestrogen, and therefore, disrupt the menstrual cycle. Starving the endometrium and ectopic plaques of hormonal stimulation can cause the plaques to shrink (Lyttleton 1998).

It is well established that a relationship exists between endometriosis and infertility (Prentice 2001). In some cases, the scarring may completely block the passage of the egg to the uterus, but even women with milder forms of endometriosis can suffer from impaired fertility.

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Clinical reasoning

Chen (1997) demonstrated that acupuncture can normalize the hypothalamic–pituitary–ovarian (HPO) axis through the release of opioids and other peptides in the central and peripheral nervous systems. An imbalance in the pituitary system may prevent a woman from producing the hormones responsible for a normal, ovulating menstrual cycle. The resulting impact on the HPO axis can be a factor in infertility.

Petti *et al.* (1998) showed that acupuncture causes a significant increase in β -endorphin levels during treatment. Because of this impact on β -endorphin levels, which affect GnRH secretion and the menstrual cycle in turn, it is logical to hypothesize that acupuncture may positively influence ovulation and fertility.

Blood flow to the ovaries begins to decline as the female body ages. At the onset of the menopause, the ovarian blood flow is approximately five times less than when a woman is in her reproductive prime (Lewis 2004). There is evidence that acupuncture can improve blood flow to the ovaries. A study by Stener-Victorin *et al.* (2000) examined whether electroacupuncture could increase ovarian blood flow in rats. The strongest ovarian blood flow response occurred when needles were placed in the abdominal muscles, i.e. in the somatic innervations of the uterus and ovaries, or in the abdominal and leg

muscles. The above authors demonstrated that the effect was mediated by the ovarian sympathetic nerves and the supraspinal reflexes.

Stener-Victorin *et al.* (1996) also showed that electroacupuncture can reduce high impedance in the uterine arteries, thus improving uterine blood flow and increasing endometrial receptivity. Successful IVF and embryo transfer requires optimal endometrial receptivity at the time of implantation.

Smeenk *et al.* (2001) examined the influence of anxiety and depression on the outcome of assisted reproductive treatment. These authors suggested that women undergoing IVF treatment are often anxious and depressed because of their infertility and the uncertainties of the treatment with which they have to deal. Anxiety and depression were measured using the State and Trait Anxiety Inventory and the Beck Depression Inventory, respectively. Smeenk *et al.* (2001) found that anxiety in particular can negatively affect treatment outcome and is probably strongest during the implantation phase of the cycle.

In traditional Chinese medicine (TCM), the uterus, heart and kidney form the focus of reproductive activity (Lyttleton 2004). The kidneys are where we store our Essence, i.e. eggs and sperm, the genetic material that we receive from our parents and pass on to our children. The process of ageing depletes Essence (Lewis 2004).

Kidney yin and yang can be thought of as the hormonal underpinnings of the reproductive system. Kidney yin, with its cooling properties, correlates to oestrogen and follicle-stimulating hormone. Kidney yang, with its warming and holding properties, correlates to progesterone and testosterone (Rosenthal & Anderson 2007).

The emphasis of the TCM paradigm in infertility treatment is to influence how well the eggs are nourished and stimulated to grow, the process of egg release and their movement down the fallopian tube, and the thickness and quality of the endometrium. In TCM, the heart governs the emotions, which explains why stress can have such an impact on fertility. The heart encompasses the mind, as well as the activity of the hypothalamus and pituitary, which control the whole cycle.

Case report

Presentation

The present subject had been trying to become pregnant for 2 years before her endometriosis was diagnosed by laparoscopy.

On subjective examination, the subject described the side effects of the fertility drugs that she had been prescribed. She had experienced insomnia, night sweats and depression. Treating women with endometriosis with GnRH agonists for 3–6 months before an *in vitro* fertilization (IVF) cycle has been shown to increase the odds of clinical pregnancy fourfold (Sallam *et al.* 2006). Because the side effects of the GnRH agonists were quite severe, the subject had been put on low-dose oestrogen, which had lessened her symptoms, but had not resolved them. Since her body was not producing any oestrogen, she was not ovulating or menstruating; she was in temporary menopause and was experiencing its associated symptoms.

The subject's symptoms of endometriosis, which had temporarily resolved at the time of treatment, were dysmenorrhoea with clotting, non-cyclic pelvic pain, pain during urination at the time of menstruation, backache, menstrual irregularity and an inability to conceive naturally over a 2-year period. The discovery of her endometriosis and infertility had shocked her. She described how her inability to conceive had led to feelings of anxiety and depression. The subject was also aware that, statistically, the chances of conception decrease markedly between 35 and 40 years of age, even with IVF treatment (Jansen 2003), and this added to her feelings of anxiety.

Her job was demanding, involving travelling and long working hours. She often found it difficult to relax, and appeared tired and stressed. The subject did not consume much alcohol, but drank many cups of coffee each day. She often dined out or ate ready-made meals. She was of average weight, but did little exercise. At the time of her treatment, the subject said that it was not possible to change her level of work commitment. She felt that she could not sacrifice her career at this point because she did not know if her desire to become a mother would be realized and her job was important to her. Her husband's sperm count and motility were normal, and he was fit and healthy.

Treatment and management plan

The acupuncture treatment was carried out weekly over 2.5 months for a total of 10 sessions and was intended to:

- (1) increase blood flow to the uterus and ovaries, clear stagnated blood and qi, and nourish the kidney system;
- (2) reduce anxiety and depression; and
- (3) provide lifestyle advice.

Table 1. Acupuncture point rationale: (IVF) *in vitro* fertilization; (ST) Stomach; (SP) Spleen; (LV) Liver; (LI) Large Intestine; (KI) Kidney; (BL) Bladder; (GV) Governor Vessel; (PC) Pericardium; and (LU) Lung

Treatment session	Acupuncture points	Rationale
<i>Reduction of menopausal symptoms</i>		
Session 1	ST6, SP6, LV3, LI4, Yingtang	Move qi, clear heat
Session 2	As session 1, plus SP10, Zigong	Move qi, clear heat, move blood
Sessions 3–5	KI3, KI7, Ren 3, Ren 4, Ren 6, ST30, BL23, plus points used in treatments 1 and 2	Nourish kidney system
<i>Preparation of body/l uterus for IVF prior to oocyte retrieval</i>		
Sessions 6–8	ST36, SP6, LV3, KI3, GV20, Zigong, PC6	Improve blood flow to pelvis, reduce stress, support movement of blood in pelvis
Sessions 9–10	Points as above, plus LU7, K16, SP4	Open Ren and Chong vessels

The subject was given a Depression Anxiety Stress Scale (DASS) questionnaire to complete on her first visit and this was used as an outcome measure. The present author's acupuncture point rationale is shown in Table 1. Sterile, disposable stainless-steel needles were used in the selected points (25 × 22 mm).

The present author aimed to achieve *de qi*, (i.e. a sensation of soreness, numbness or distension) around the chosen points during the initial insertion. The needles were inserted for 15 min during the first treatment session and were rotated after 10 min to maintain *de qi*. The insertion time was gradually increased at subsequent sessions until a maximum of 40 min was achieved.

A heat pad was put on the subject's lower back around Urinary Bladder 23 (the Back Shu point of the kidney) to promote the flow of blood/qi to the meridian, and she was encouraged to do this at home on a daily basis. She was also taught how to perform femoral artery massage (Lewis 2004) on a daily basis to encourage the flow of blood into the abdomen.

The needles were used bilaterally, which meant that up to 20 were used for stimulation. The gradual increase in the time that the needles were left *in situ* and the number used meant that no serious side effects were experienced.

The main side effect was drowsiness post-treatment and on the following day. The subject had been warned that this might be a possibility, and therefore, arranged for a friend to collect her after the treatment sessions.

Dietary and lifestyle advice was introduced over the course of treatment. For example, she was advised to reduce her caffeine intake since it stimulates the sympathetic nervous system and could have been contributing to her poor sleeping pattern and feelings of anxiety. The aim was

to make the subject think about nurturing her body, mind and spirit before her IVF treatment in order to optimize her chances. Up to this point, her lifestyle had left little time for considerations of this kind, and she had not realized that it might be hindering her chances of conception. The physical effects of stress on the body were explained to the subject as well as how it could affect reproductive health. She was advised to take up a form of exercise such as yoga (to relax and energize). It was also suggested that she should try to focus some of her energies on herself and her well-being, rather than her career.

Physiological reasoning for acupuncture selection

Chen (1997) demonstrated that acupuncture can normalize the HPO axis by releasing opioids and other peptides in the central and peripheral nervous systems. An imbalance in the pituitary system may prevent a woman from producing the hormones responsible for a normal, ovulating menstrual cycle. The resulting impact on the HPO axis can be a factor in infertility. In addition to the central modulation of the hypothalamic–pituitary axis, acupuncture can be used to alter sympathetic outflow (Bradnam 2007). With its central sympatho-inhibitory effect, acupuncture may contribute to reduced uterine artery impedance, and therefore, increase blood flow to the uterus. Many strong traditional Chinese acupuncture points are located in the extremities. Bekkering & van Bussel (1998) stated that these points have a significant sympathetic innervation, and therefore, may be more useful in manipulating sympathetic responses.

Stress increases the activity of the hypothalamic–pituitary–adrenal axis and decreases reproductive functions (Stener-

Victorin *et al.* 2002). If the adrenal glands are overworked, blood flow is diverted from the uterus and ovaries. Adrenaline also inhibits the utilization of progesterone, one of the key reproductive hormones (Lewis 2004). Corticotrophin-releasing factor, adrenocorticotrophic hormone, β -endorphin and adrenal corticosteroids all play important roles in modulating the effects of stress on reproductive functions (Rivier & Rivest 1991). Acupuncture appears to reduce stress by increasing β -endorphin levels in the brain and through its sympatho-inhibitory effects (Chang *et al.* 2002). Points that are known to have a calming effect on the sympathetic nervous system include Liver (LV) 3 and LV4 (the 'four gates') and Pericardium 6.

Acupuncture was shown by Petti *et al.* (1998) to cause a significant increase in β -endorphin levels during treatment, an effect that lasts for up to 24 h. The β -endorphin is derived from its precursor protein, proopiometelanocortin, which is present in abundant amounts in the neuronal cells of the arcuate nucleus of the hypothalamus, pituitary and medulla, as well as in peripheral tissues, including the intestines and ovaries. The influence of endogenous opioid peptides on gonadotropin secretion and the menstrual cycle is believed to be mediated by their action on GnRH (Chang *et al.* 2002). The hypothalamic β -endorphin centre and the GnRH pulse generator are both situated within the arcuate nucleus. Because acupuncture treatment impacts on β -endorphin levels, which affect GnRH secretion and the menstrual cycle in turn, it is logical to hypothesize that acupuncture may influence ovulation and fertility.

Outcome measurements and results

In the present case, the outcome measurements were the results of the DASS questionnaire, which showed that the subject had moderate stress and anxiety levels, and mild depression when she first completed it. On repeating the measure 2.5 months later, her stress and anxiety levels were shown to be mild, and her depression remained mild. Subjective improvements included an increase in her energy, an improved sleep pattern, a decrease in night sweats and an increase in her sense of well-being. She was trying to make the recommended lifestyle changes, but was finding this difficult.

The subject's first IVF cycle was unsuccessful. She continued with the lifestyle changes and acupuncture treatment, and eventually conceived during her third cycle of IVF.

Discussion

The use of acupuncture in reproductive medicine has not been thoroughly investigated to date, and there are few systematic reviews of complementary or alternative approaches to the treatment of infertility. Although there is a growing evidence base supporting the use of acupuncture during the IVF process to improve pregnancy rates and live births (Manheimer *et al.* 2008), its role in the treatment of female infertility (e.g. endometriosis) has yet to be established.

The treatment of infertility using TCM predates Western medicine by centuries. Rosenthal & Anderson (2007) stated that integrating medical disease diagnoses, blood tests and the stages of the IVF process into modern practice can help to further define TCM diagnosis and treatment, and improve clinical outcomes. To date, there has been limited research examining any relationship between TCM and Western medical diagnoses. However, a study by Coyle & Smith (2005) found evidence of an association between a Western diagnosis of endometriosis, and a TCM diagnosis of blood and qi stagnation. In TCM, qi is said to lead the blood, and when either becomes stagnant, there can be painful periods, clotting of the blood, premenstrual tension and abnormal menstrual bleeding, which are all symptoms of endometriosis (Lyttleton 2004).

Although the cause of endometriosis is poorly understood in Western medicine, it has been hypothesized that a dysfunction in the ovaries or hormonal issues producing luteal phase defects causes the problems that leading to the condition. Approximately 27% of women with mild endometriosis also have ovulatory dysfunction or luteal phase defect. It is also possible that endometrial implants secrete prostaglandins, which can cause muscle spasms in the reproductive organs and hinder their proper functioning (Lewis 2004).

It is not possible to draw definitive conclusions from a single case study. It is difficult to say what role, if any, acupuncture played in the present subject's eventual successful conception. Statistically, the chance of a successful implantation and live birth increase with repeated IVF treatments.

The subject had a positive expectation that acupuncture could work for her. Using sham acupuncture, real acupuncture and skin prick, Pariente *et al.* (2005) demonstrated that expectation and belief in treatment have a physiological effect on the brain that appears to

mediate a potentially powerful non-specific clinical response to acupuncture. This could have contributed to a placebo effect.

The present study could have been improved by the use of additional subjects, and by incorporating TCM tongue and pulse diagnosis into the assessment. An experienced TCM practitioner will gain valuable clinical information from looking at a patient's complexion, eyes, body tone and shape (Lewis 2004). These observations can form the basis of a diagnosis and treatment progression, but were not carried out in the present case because of a lack of training.

The present author attempted to integrate the TCM approach to diagnosis and treatment with the available scientific evidence. Both paradigms offer a reasonable explanation for the health improvements – and the eventual positive pregnancy result – shown by the subject. In TCM, there is an association between blood and the mind, or shen. Blood houses and nourishes the mind, and when blood is deficient or stagnant, mental health and well-being can be impaired. Reduced stagnation of the blood could account for the present subject's increased feelings of well-being. She also reported having more energy. This could be the result of a reduction of stress levels, but could also be a consequence of the treatment effect of moving blood and qi, and reduced caffeine consumption. From a scientific point of view, the normalizing of the HPO axis and the central sympatho-inhibitory effects on stress and blood flow could have contributed to the positive outcome.

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