

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

SciVerse ScienceDirect

journal homepage: <http://www.elsevier.com/locate/repbio>

## Short Communication

# Inhibition of endometrial fundocervical wave by phloroglucinol and the outcome of in vitro fertilization

Aizhuang Xu, Yanping Li\*, Lin Zhu, Tian Tian, Jie Hao, Jing Zhao, Qiong Zhang

Centre for Reproductive Medicine, Department of Obstetrics and Gynecology, Xiangya Hospital, Central South University Changsha, Hunan 410008, China

### ARTICLE INFO

#### Article history:

Received 20 September 2012

Accepted 7 January 2013

#### Keywords:

Phloroglucinol

Endometrial peristaltic wave

Transvaginal ultrasound

IVF/ICSI-ET

Pregnancy rate

### ABSTRACT

One hundred thirty-five infertile patients were enrolled to investigate the efficacy of phloroglucinol-induced inhibition of the endometrial fundocervical wave and its effect on in vitro fertilization (IVF). We found that phloroglucinol significantly inhibited ( $P < 0.05$ ) peristaltic fundocervical wave, suggesting a feasible way of application of phloroglucinol to suppress endometrial waves during IVF.

© 2013 Published by Elsevier Urban & Partner Sp. z o.o. on behalf of Society for Biology of Reproduction & the Institute of Animal Reproduction and Food Research of Polish Academy of Sciences in Olsztyn.

## 1. Introduction

The endometrial wavelike activities appear to be implicated in in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) embryo transfer (ET) [1]. The endometrial fundocervical (FC) wave during ET may mechanically change the endometrial contraction patterns and affect endometrial receptivity [1,2]. Thus, the reduction of FC wave during ET may be in favor for endometrial receptivity after IVF. Some studies have reported [3,4] that the use of anticholinergic drugs can inhibit endometrial peristaltic waves thus improve pregnancy rate. However, the adverse effects from these drugs, such as dry mouth and dizziness, are commonly observed in patients. Recently, a new class of drugs, oxytocin antagonists, has been reported to be able to suppress uterine contractions and significantly improve pregnancy outcome after IVF-ET [5–7].

The aim of this study was to inhibit the endometrial FC waves by intravenous infusion of phloroglucinol, an antispasmodic agent, and to examine its impact on pregnancy outcome after IVF/ICSI.

## 2. Materials and methods

All experiments were conducted under a protocol approved by the Institutional Review Board Human Subjects Review Committee of the Central South University (Changsha, China). One hundred thirty-five patients with primary or secondary infertility (fallopian tube or male factors) were enrolled in this study from May 2011 to October 2011 in our center. All of the patients had opted for the treatment of short-acting gonadotropin-releasing hormone agonist (GnRH-A) during controlled

\* Corresponding author.

E-mail address: [lisayanping@sina.com](mailto:lisayanping@sina.com) (Y. Li).

ovarian hyper stimulation (COH). Ovulation was monitored by the vaginal ultrasound. In the morning of the day of hCG treatment, all subjects were tested for the serum concentrations of estradiol (E2), progesterone (P4) and luteinizing hormone (LH). Luteal support was given after ovum pick-up by intramuscular (60 mg/day) and oral (0.2 mg/day) progesterone administrations. The embryos were transferred under abdominal ultrasound-guided procedure on the third day after conventional luteal support.

Patients met following criteria were selected: (1) first time under IVF/ICSI-ET; (2) ages 23–35 years old with a menstrual cycle of 25–35 days; (3) basic amounts of the follicle stimulating hormone (FSH) < 10 mIU/ml, and E2 < 80 pg/ml. The followings are exclusive criteria for this study: (1) myoma of uterus, congenital uterine malformations (including uterus didelphys, mediastinum uterus, unicornuate uterus, etc.), history of intrauterine adhesions, endometriosis, endometrial polyps, hydrosalpinx; (2) P4 > 1.01 ng/ml and endometrial thickness < 8 mm on HCG day; (3) the number of embryos transferred less than two good quality embryos (I or II level); (4) other reasons causing transplantation difficult.

The DC-6 Exper-type color ultrasound transducer with frequency of 5–8 MHz (Mindray, Beijing, China) was used in this study. All the ultrasound measurements were performed by a single observer (A.X.). The examinations were made for all patients in the morning (7–8 am) and afternoon (2–3 pm) on the day before ET, and in the morning (7–8 am) on the day of ET. The examiner probe was slowly put into the vagina, scanning the uterine long axis of the median sagittal plane, and focusing on the endometrial area. The probe was fixed close to the vaginal roof, followed by continuous dynamic testing in the utero membrane for 5 min with synchronized video capture. The same observer (A.X.) and a second observer then used VLC media player to have a fast playback of the video with a factor of 4 from the normal speed to record the types and frequencies of endometrial movements.

Classification system for endometrial peristaltic waves described by van Gestel et al. [8] were used in this study: CF: the wave from cervix to fundus; FC: the wave from fundus to cervix; N: no movement – intimal quiescent state observed for 5 min without obvious movement; R: irregular wave or random wave – a smaller range of motion, no obvious directionality and rhythm; OP: opposite wave – the endometrium of the fundus and the cervix has begun to shrink at the same time, the direction pointing to the uterine cavity, showing a centripetal movement.

Patients were divided into three groups according to the results of the peristaltic waves recorded. Fifty-six patients showed a FC wave in both morning and afternoon of the day before ET, and on the day of ET. They were randomly divided into a phloroglucinol-treatment FC (PT-FC) group ( $n = 27$ ) and a FC group ( $n = 29$ ) by using 'random sampling' function implemented in R – a commonly used statistical software. The patients without FC wave recorded were set as the control group ( $n = 42$ ). The remaining thirty-seven patients showed a FC wave either in the morning or afternoon of the day before ET, or a FC wave in both morning and afternoon of the day before ET but without a FC wave on the day of ET. These patients were not suitable to be assigned to any of the groups thus were excluded from this study. The treatments were

given after the patients signed the consent form. The patients in the PT-FC group received one time intravenous infusion of phloroglucinol (80 mg in 500 ml 5% glucose saline) (Wushi Pharmaceutical Co., Hubei, China) in the afternoon of the day prior to ET. The same dose of phloroglucinol was infused twice a day for the next five days. Patients from FC and control groups received only saline. The same reduction level of uterine contraction caused by hydration was expected in all groups.

The changes of endometrial waves on the day of ET were classified into following groups: (1) FC wave disappearance: no negative wave was found; (2) FC wave reduction: the frequency of FC waves reduced; (3) FC wave increase: the frequency of FC waves increased; (4) no change: the frequency of FC waves remained unchanged. Clinical pregnancy refers to positive urinary hCG on the days 12–14 and gestational sac found by the transvaginal ultrasound examination on the day 28 post ET. Miscarriage refers to natural termination of pregnancy before completed 12th week of gestation. Ectopic pregnancy refers to development of the implanted fertilized egg locating outside the uterine cavity.

SPSS 13.0 statistical software (SPSS Inc., Chicago, IL) was used for analysis. Analysis of Variance (ANOVA) was used to compare the age, basic serum concentrations of FSH, LH and E2, serum concentrations of E2, LH and P4 on hCG treatment day as well as endometrial thickness.  $\chi^2$  test was used to compare the frequency of waves on the day of ET; The Monte Carlo based  $\chi^2$  test or Fisher's exact test was used to investigate insemination since the expected frequencies for >20% cells of contingency table were less than 5.  $\chi^2$  test was used to compare the disappearance rate of FC wave, the clinical pregnancy rate, the miscarriage rate and ectopic pregnancy rate between the PT-FC group and FC group on the day of ET. Fisher's exact test was also carried out to compare the reduction rate of FC wave. The Kruskal–Wallis rank test was utilized to compare the frequency of various waves.

### 3. Results and discussion

Among the 135 patients, 42 patients did not show the presence of FC wave, 56 patients (41%) showed the presence of FC wave. Age of patients, basic serum concentrations of FSH, LH and E2, endometrial thickness and serum concentrations of E2, LH and P4 on the day of hCG treatment did not differ ( $P > 0.05$ ) among the three examined groups (Supplementary Table 1). Serum concentrations of E2 and P4 on the day before ET showed no statistical difference ( $P > 0.05$ ) among the groups (Supplementary Table 2).

Phloroglucinol is a type of non-atropine class of antispasmodic medicine. It belongs to a class B drug used during pregnancy. Both animal data [9] and clinical epidemiologic study [10] have shown that phloroglucinol is not teratogenic during pregnancy. In the PT-FC group, application of phloroglucinol reduced the FC waves in all treated subjects on the day of ET, and 20 patients (74%) showed a complete disappearance of FC wave. In the FC group, 10 patients showed disappearance of FC wave, 6 patients showed reduction of FC wave, 9 patients showed increase of FC wave, and 4 patients showed no change of FC wave on the day of ET.

Download English Version:

<https://daneshyari.com/en/article/2062653>

Download Persian Version:

<https://daneshyari.com/article/2062653>

[Daneshyari.com](https://daneshyari.com)