

**RCT (Randomized Clinical Trial) of  
Antibiotic Therapy in Chronic Endometritis**

**NCT 02648698**

**Date: May 30, 2020**

## study protocol

### Background

Chronic endometritis (CE) is a condition characterized by the presence of plasma cell in the endometrial stroma. CE may be associated with abnormal uterine bleeding, intrauterine pathology such as polyp or fibroid, as well as a variety of reproductive failure including infertility, recurrent implantation failure and recurrent pregnancy loss. In women with reproductive failure, the reported prevalence of CE maybe as high as 41%.

CE is often treated with antibiotics on the assumption that it is caused by an underlying infection. The response of CE to antibiotic therapy has been examined in a number of cohort studies. The cure rate, as determined by reduction of plasma cell density in a repeat endometrial biopsy specimen following antibiotic therapy was found to be 75.4%, 99% and 100%.

The impact of antibiotic therapy on clinical outcome among subjects with CE had also been examined in several cohort studies. Cicinelli et al conducted a retrospective study which showed that after antibiotic therapy, the pregnancy rate (PR) and live birth rate (LBR) in women who become CE negative was higher than those who remained CE positive after antibiotic treatment (65.2% versus 33.0% ; 60.8% versus 13.3%, respectively) . In another study involving women with recurrent implantation failure (RIF) study, Kitaya et al. reported that the LBR in the first embryo transform (ET) cycle and cumulative three ET cycles in the cured CE group following antibiotic treatment (32.8% and 38.8%, respectively) was significantly higher than those of the non-CE group (22.1% and 27.9%, respectively). McQueen et al observed that the cumulative LBR was 88% (21/24) for the treated CE group versus 74% (180/244) for the group without CE. In the CE group, the LBR for those before treatment was 7% (7/98) versus 56% (28/50) after treatment.

Despite the apparently encouraging clinical data from the above observational, cohort studies suggesting that antibiotic treatment was effective in curing CE and

improving the reproductive outcome, the impact of antibiotic therapy has not yet been formally examined in any randomized control trial.

### **Objective**

To compare the cure rate of chronic endometritis between subjects who did and did not receive antibiotic treatment.

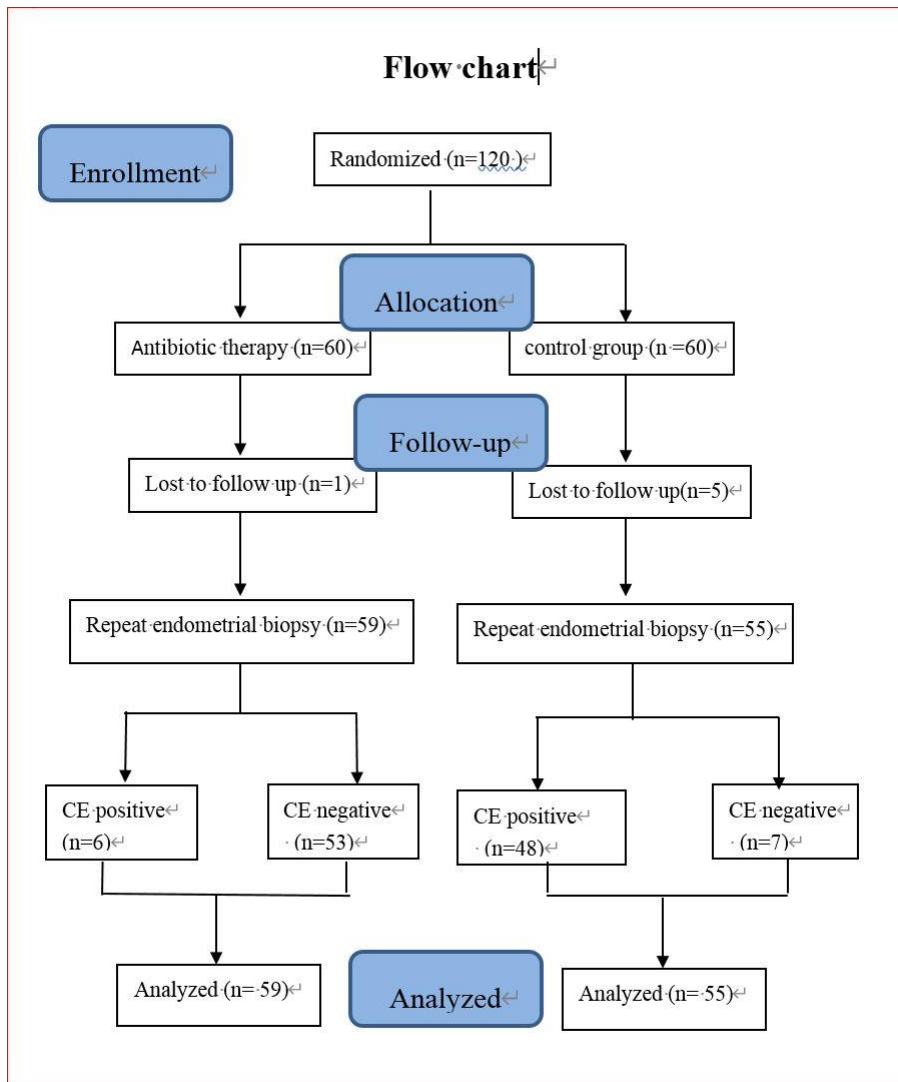
### **Design**

Prospective, Single-blind randomized, controlled trial.

This RCT was conducted in the Hysteroscopic Centre, Fuxing Hospital, Capital Medical University, a national training centre for hysteroscopy in China between 2016 and 2018. During the period of study, women who were referred to the center for hysteroscopy for investigation of reproductive failure including infertility, recurrent miscarriage (RM) or recurrent implantation failure (RIF), as well as abnormal menstruation had endometrial biopsy obtained for histological examination including CD138 immunohistochemical staining as a routine procedure.

The inclusion criteria for patient participation in this study included: (1) CD138 immunohistochemical staining of endometrial specimen showed presence of one or more plasma cells per 10HPF which confirmed chronic endometritis, according to published criteria; (2) women who were pre-menopausal; (3) no evidence of endometrial hyperplasia or malignancy or structural uterine pathology; (4) agreement to have a second endometrial biopsy ~4 weeks after the initial endometrial biopsy; and (5) written informed consent obtained.

The exclusion criteria included: (1) women who received steroid hormone therapy within one month of recruitment; (2) allergy or suspected allergy to the chosen antibiotic therapy; (3) women who developed any concurrent infection and received any antibiotic therapy during the period of study other than the one prescribed according to the study protocol.



A total of 120 subjects were randomized in antibiotic group and control group in a 1:1 ratio using a computer-generated randomization list, 6 subjects did not attend for second hysteroscopy and endometrial biopsy. At the end, 59 subjects in the antibiotic group and 55 subjects in the control group completed the study according to the protocol, these 114 cases were included in the final analysis.

**Methods**

Women randomized to antibiotic group received oral Levofloxacin 500 mg and Tinidazole 1000 mg daily for 14 days. Women randomized to the control group did not receive any treatment. Initially it was planned for women in the control group to take placebo, but the organization was difficult, so it was changed prior to the start of

the study to an open label study. A repeat endometrial biopsy was performed 4-8 weeks after the initial biopsy to determine if CE was still present.

The conversion rate of CE (from positive to negative) in two group were compared.

### **statistical analysis plan**

The comparison of results between the two groups was made with the use of an independent-sample t-test for continuous variables and contingency table analysis for categorical variables. A P value of  $<.05$  was considered to be significant. All statistical tests were two sided. Statistical analysis was performed with the use of SPSS for PC version 21(2016).