Antibiotic treatment for chronic endometritis shows more efficacy in success rates of assisted reproductive technology than endometrial scratch in women with repeated implantation failure.

D. Kadogami¹, Y. Nakaoka¹, Y. Morimoto²
¹IVF Namba Clinic, ²HORAC Grand Front Osaka Clinic

Study question(25)： Is the efficacy of antibiotic treatment for chronic endometritis (CE) not due to antibacterial effect but the impact of endometrial scratch?

Summary answer(25)： Antibiotic treatment for CE significantly improves the clinical outcomes in IVF over endometrial scratch alone.

What is known already(100)： CE is defined as a local inflammatory disease and is diagnosed by the presence of plasma cells in the endometrial stroma. Some studies show that CE negatively impacts reproductive outcomes by endometrial receptivity and its prevalence is high in women with repeated implantation failure (RIF). Furthermore, it is also unknown that antibiotic treatment significantly improves the reproductive outcome in women with CE. Alternatively, some authors report that the endometrial scratch has a positive effect on reproductive outcome. So, whether improvement of reproductive outcomes of women diagnosed as CE is due to antibiotic therapy or scratch remains controversial.

Study design, size, duration(75)： Retrospective study in our clinic, between January 2017 to August 2018.

Endometrial biopsy was performed in 156 women with RIF. CE was diagnosed with the presence of plural CD138 positive cells within the stromal in HPF. Women diagnosed as CE(Group1) had a 14-day oral antibiotic administration. The histopathologic cure of CE was evaluated in the second/third-look biopsy obtained during the following menstrual cycle. After confirming the absence of CE, they had further embryo transfers (ET). Women without CE(Group2) had further ET promptly. Subsequent two cryopreserved-thawed ET cycles were follow-up.

Participants/materials, setting, methods(75)： Biopsy was performed from 2-site in Uterus. CE was diagnosed with the presence of plural CD138 positive cells within the stromal in HPF. Women diagnosed as CE(Group1) had a 14-day oral antibiotic administration. After confirming the absence of CE, they had further embryo transfers (ET). Women without CE(Group2) had further ET promptly. Implantation rate (IR), pregnancy rate (PR), miscarriage rate (MR) and mean endometrial thickness on the day of ET (MET) were compared.

Participants/materials, setting, methods(75)： Endometrial biopsy was performed from 2 sites in Uterus. Biopsy samples were immunostained with a monoclonal antibody agent CD138, a specific marker for plasmacytes. CE was diagnosed with the presence of plural CD138 positive cells within the stromal areas in high power field. Women diagnosed as CE(Group1) had a 14-day consecutive administration of oral antibiotic agents. After confirming the absence of CE, they had further embryo transfers (ET). Women without CE(Group2) had further ET promptly. Implantation rate (IR), pregnancy rate (PR), miscarriage rate (MR) and mean endometrial thickness on the day of ET
were compared between the two groups.

Main results(200) : The prevalence of immunohistochemically confirmed CE was 38.5%(60/156). All of them underwent oral doxycycline(200mg/day) and metronidazole(1000mg/day) administration. In the second-look biopsy, the cure rate of CE was 71.7% (43/60). Seventeen women who did not confirm absence of CE were further treated with a combination of oral ciprofloxacin(800mg/day) and metronidazole(1000mg/day). The overall cure rate following two-step oral antibiotic treatment strategy was 98.3% (59/60). At IVF attempt after treatment, in both groups, reproductive outcome in cumulative two ET cycles was improved. Especially, a significantly higher IR and PR was reported in women from Group 1 compared with women from Group 2 (62.0 versus 35.8%, OR 2.60, 95%Cl 1.44-4.20; 48.4 versus 29.3%, OR 2.22, 95%Cl 1.52-3.80). Moreover, in MR, Group1 was significantly lower than Group2 (39.5 versus 54.5%, OR 0.51, 95%CI 0.30-0.85). MET was similar between the Group1 and Group2 (10.89±1.79mm versus 10.87±1.82mm p=0.97). No side effects due to antibiotics were observe.

Limitations(50) : Possible biases related to retrospective studies and to preferential referral of patients with CE, and limited number of cases. Moreover, embryo quality which potentially affect the reproductive outcome is not considered.

Wider implications of the findings(50) : Antibiotic therapy for endometriosis has an positive effect for IVF success rate that exceeds endometrial scratch. This result is encouraging in women with RIF. Studies which consider embryo factor are required. And the association with endometriosis and uterine microbiota is very interesting.

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Trial registration number : Not applicable