ISSN 2706-6819 Vol.5, Issue 1: 58-61, DOI: 10.25236/IJFM.2023.050110

Study of vaginal microecological imbalance and endometrial receptivity change in the treatment of female infertility

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Abstract: *Objective—To understand the relationship between vaginal microecology and endometrial receptivity, and to explore the clinical effect of adjusting vaginal microecology and improving endometrial receptivity in the treatment of female infertility. Study Design—A total of 60 patients with vaginal microecological disorders and poor endometrial receptivity were selected and randomly divided into two groups. The drug treatment group (n = 30) was treated with lactobacillus preparation for 3 months, and the control group (n = 30) was not treated. Three months later, vaginal microecology and endometrial receptivity were detected again by ultrasound. Results—In the drug treatment group, there were significant differences in pH, density, diversity, vaginal flora, cleanliness, PI, endometrial thickness and endometrial type before and after treatment (P < 0.05).The predominance of Lactobacillus in the vagina can be restored by using Lactobacillus preparations. The application of vaginal Lactobacillus preparation is beneficial to improve endometrial receptivity.*

Keywords: *Lactobacillus; Vaginal microecology; Endometrial receptivity; Infertility*

The number of infertility is increasing year by year, accounting for about 10%, which seriously affects population optimization, and has complex pathogenesis and diverse causes. Among them, endometrial receptivity plays a key role in the successful colonization of embryos, and has an obvious effect on improving the clinical pregnancy rate and live birth rate [1]. Many factors affect endometrial receptivity. Abnormal inflammation and immune response caused by microbial imbalance and pathogenic microbial infection in the female reproductive tract may affect endometrial receptivity, interfere with embryo implantation and development, and then affect the success rate of pregnancy, which plays an important role in the occurrence and development of infertility [2-3]. Based on the vaginal microecological evaluation system, this paper explores the changes of endometrial receptivity in female infertility patients with vaginal microecological disorder.

1. Objects and Method

1.1 Object of study

Sixty female infertility patients (without organic and endocrine diseases) who visited the outpatient clinic from December 2021 to December 2022 were selected. The patients were divided into two groups: drug treatment group (n = 30, aged (29.1±2.25) years) and control group (n = 30, aged (28.67±2.12) years). There was no significant difference in age between the two groups. 30 patients in the drug treatment group were treated with Lactobacillus preparation, 1 capsule every night, inserted into the vagina, and discontinued during menstruation.This study has passed the ethical review of our hospital, and all subjects signed the informed consent.

1.2 Methods

1.2.1 Evaluation of endometrial receptivity by vaginal secretion extraction and ultrasound

The method of collecting vaginal secretion was as follows: in the lithotomy position of the bladder, the speculum was lubricates and placed into the vagina, the cervix was exposed, and the samples were taken from the upper 1/3 of the vaginal lateral wall and the vaginal posterior fornices with 2 cotton swabs. One was spread evenly on a clean slide, allowed to dry and fixed, and subjected to Gram's stain

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for morphological examination, while the other was placed in a test tube for functional analysis. Endometrial receptivity was detected by ultrasound, mainly using transvaginal color Doppler ultrasound on the 20th to 22nd day of the menstrual cycle to evaluate endometrial receptivity.

1.2.2 Observation and Follow-up

(1) Observation indicators: evaluation system of vaginal microecology, mainly including five aspects of vaginal flora density, diversity, dominant bacteria, body inflammatory response and causative bacteria morphology, combined with vaginal pH, H_2O_2, leukocyte esterase and other functional indicators. Endometrial receptivity was assessed by endometrial thickness, endometrial type and uterine artery pulsatility index (PI). (2) Follow-up time: 3 months after enrollment, if the menstrual period was every month, the patients were followed up at the end of menstruation. (3) During the follow-up period, antibiotics were not used, sexual life and vaginal irrigation were avoided during medication and before review, and contraceptive tools were required if there was sexual life at other times.

1.3 Diagnostic Criteria

Vaginal microecology detection Based on the vaginal microecological evaluation system, the microbiota of the collected vaginal secretions was analyzed. When the density of vaginal flora was II-III, the diversity was II-III, the dominant bacteria was Lactobacillus, the cleanliness was I degree, the Lactobacillus function was normal (H_2O_2 positive), and vaginal pH <4.5, the vaginal microecology was defined as normal. Dysbiosis can be diagnosed when any of the parameters of density, diversity, dominant bacteria, inflammation, pH and Lactobacillus function are abnormal.

Assessment of endometrial receptivity Endometrial receptivity was assessed by ultrasound, including endometrial thickness 7-10mm, type A endometrium, uterine artery pulsatility index (PI) <2 is most suitable for embryo implantation, which is used as an evaluation method of endometrial receptivity.

1.4 Statistical methods

All the data were processed by SPSS 19.0 software, the count data were described as percentage or component ratio, the difference between groups was compared by Chi-square test, the measurement data conforming to normal distribution was described as "mean ± standard deviation", the difference between groups was analyzed by paired sample t test and independent sample t test, and $P < 0.05$ was considered statistically significant.

2. Results

By paired sample t test, the pH, PI and endometrial thickness of the control group and the drug treatment group before and after treatment were statistically analyzed. The results showed that there was no significant difference in pH, PI and endometrial thickness before and after treatment in the control group ($P > 0.05$). There were significant differences in pH, PI and endometrial thickness before and after treatment in the drug treatment group ($P < 0.05$), and the specific results are shown in Table 1 and Table 2.

Table 1: Comparison of pH, PI and endometrial thickness between control group.

	t value	df	P value
Before and after treatment pH	-1.151	29	0.259
Before and after treatment endometial thickness	0.56	29	0.579
Before and after treatment PI	0.205	29	0.839

Table 2: Comparison of pH, PI and endometrial thickness between drug group.

	t value	df	P value
Before and after treatment pH	4.522	29	0.000
Before and after treatment endometial thickness	-2.549	29	0.016
Before and after treatment PI	1.881	29	0.070

The chi-square test was used to analyze the density, diversity, vaginal flora, cleanliness and endometrial types in the control group and the drug treatment group before and after treatment. The

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results showed that there was no significant difference in density, diversity, vaginal flora, cleanliness and endometrial types in the control group before and after treatment (P > 0.05). In the drug treatment group, there were significant differences in density, diversity, vaginal flora, cleanliness and endometrial types before and after treatment (P < 0.05), and the specific results are shown in Table 3 and Table 4.

Table 3: Comparison before and after treatment between control group.

control group		normal	abnormal	Chi-square	P value
the density of vaginal flora	before	25	5	0.130	0.718
	after	26	4		
diversity	before	24	6	1.180	0.278
	after	27	3		
vaginal flora	before	25	5	0.000	1.000
	after	25	5		
cleanliness	before	19	11	0.070	0.787
	after	20	10		
Endometrial type	before	5	25	0.110	0.739
	after	6	24		

Table 4: Comparison before and after treatment between drug group.

drug group		normal	abnormal	Chi-square	P value
the density of vaginal flora	before	24	6	4.04	0.044
	after	29	1		
diversity	before	23	7	5.19	0.023
	after	29	1		
vaginal flora	before	21	9	5.45	0.020
	after	28	2		
cleanliness	before	20	10	6.67	0.010
	after	28	2		
Endometrial type	before	6	24	4.80	0.029
	after	14	16		

3. Conclusions

The female reproductive tract microbiome is a complex and dynamic microecosystem [4]. The reproductive tract microbiota forms a homeostatic and reciprocal relationship with the human host and plays an important role in vaginal health and disease. Changes in internal and/or external factors lead to the destruction of the balanced ecosystem, which is called reproductive tract microecological dysbiosis [5]. A healthy vaginal microbiota is mainly dominated by Lactobacillus, which can coordinate the growth of other bacteria, maintain the acidic environment and cleanliness of the vagina, inhibit the growth of pathogenic microorganisms, and play an important role in maintaining the vaginal microecological balance and the defense of the reproductive tract [6].

Some studies [7] have found microbial communities different from the vagina in the cervical canal, uterine cavity, fallopian tube and peritoneal fluid of women by 16S rRNA sequencing. The results reflect the continuum of microbiota along the female reproductive tract. Studies have shown that infertile women have more mycoplasma in the vagina and Gardnerella in the cervix [8]. Endometrial microecology is a part of the microecology of the female reproductive tract [9]. Abnormal endometrial microecology is associated with negative effects on reproductive function and is considered as a new cause of implantation failure and pregnancy loss [10]. No studies have been reported on the reduction of endometrial receptivity caused by infections caused by vaginal microbial dysbiosis or subclinical infections by lactic acid bacteria preparations to reduce the proportion of infertility patients. In the control group, there was no significant difference in pH, density, diversity, vaginal flora, cleanliness, endometrial thickness, PI, and endometrial types before and after treatment (P>0.05). Vaginal microecological disorders were not improved by vaginal self-purification without drugs. In the drug treatment group, there were significant differences in pH, density, diversity, vaginal flora, cleanliness, endometrial thickness, PI, and endometrial types before and after treatment (P < 0.05). The application of Lactobacillus preparation can restore the dominant position of Lactobacillus in the vagina, maintain its acidic environment, and regulate vaginal pH and cleanliness to the normal direction. It has therapeutic significance for vaginal microecological abnormalities and vaginal inflammation. Endometrial receptivity was improved in patients treated with vaginal lactobacillus preparations.

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However, since endometrial receptivity is one of the factors in the evaluation of female reproductive capacity, and there were no pregnancy cases in this study, it is impossible to conclude whether adjusting vaginal microecology is beneficial to improving female reproductive capacity.

Eliminate the growth of abnormal bacteria in the vagina and maintain the ecological balance. The application of vaginal Lactobacillus preparation can quickly restore the dominant position of Lactobacillus in the vagina, and regulate the conditions of vaginal microenvironment to maintain health from the perspective of microecology, which plays an important role in infertility patients with vaginal microecological abnormalities. It has exceeded the existing concept of diagnosis and treatment of vaginal infectious diseases, and has changed the main treatment method of killing microorganisms into a new treatment mode of sterilization, repair and restoration of vaginal microecological balance environment. The treatment basis of "treating bacteria with bacteria, treating diseases with bacteria" has promoted the transformation from the bactericidal era of biomedicomedica to the pro-bacterial era of ecological medicine.

Acknowledgement

Fund Project:Medical and Health Science and Technology Program of Zhuji City, Zhejiang Province [Project No. 2021YW030]

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