Antibiotic therapy versus no treatment for chronic endometritis: a case-control study

Ettore Cicinelli, M.D.,[a] Leonardo Resta, M.D.,[b] Vera Loizzi, M.D.,[a] Vincenzo Pinto, M.D.,[a] Carla Santarsiero, M.D.,[a] Rossana Cicinelli, M.D.,[a] Pantaleo Greco, M.D.,[c] and Amerigo Vitagliano, M.D.[d]

[a] Department of Obstetrics and Gynaecology, and [b] Institute of Pathology, Faculty of Medicine, University of Bari, Bari, Italy; [c] Department of Medical, Surgical and Technological Sciences, Section of Obstetrics and Gynecology, Azienda Ospedaliero-Universitaria S. Anna, University of Ferrara, Ferrara, Italy; [d] Department of Women's and Children's Health, University of Padua, Padua, Italy

Objective: To demonstrate the infectious nature of chronic endometritis (CE) in an inductive way by comparing the results of germ-oriented antibiotic therapy vs. no treatment in women with CE.
Design: Retrospective, nonconcurrent case-control study.
Setting: Tertiary hysteroscopic center in a university teaching hospital.
Patient(s): Sixty-four consecutive women with CE who received antibiotic therapy (Group A) compared with a historical group of 64 patients with CE who refused antibiotic therapy (Group B).
Interventions(s): CE was diagnosed through hysteroscopy, histology, and immunohistochemistry for CD138. Patients in both groups were tested for CE twice to evaluate the cure rate after antibiotic therapy (Group A) or no treatment (Group B). For patients with persistent disease, antibiotic therapy was repeated up to 3 times. Antibiotics were chosen based on endometrial culture (with antibiogram).
Main Outcome Measure(s): The primary outcome was to compare the cumulative cure rate of CE (defined as the percentage of patients without CE at the test of cure) between groups.
Result(s): Among Group A, 20 patients (31.25%) experienced CE resolution after 1 antibiotic cycle, an additional 20 patients (31.25%) after 2 antibiotic cycles, and 12 patients (19.35%) after 3 antibiotic cycles. In 12 cases (18.75%), CE was persistent after 3 cycles of antibiotics. The cure rate of CE in Group A after 1 cycle of antibiotics was significantly higher than that of Group B (32.25% vs. 6%). Similarly, the cumulative cure rate was considerably higher in Group A vs. Group B (81.3% vs. 6%). Notably, the number of positive cases decreased significantly with all techniques between the first and second evaluation, whereas at the third evaluation, there was a statistical decrease only with hysteroscopy and $CD138^{+}$ cell count but not with histology. The cumulative number of cases of CE diagnosed at hysteroscopy was significantly higher than histology and immunohistochemistry.
Conclusion(s): Our study demonstrated the superiority of antibiotic therapy compared with no treatment for CE cure. Accordingly, the infectious nature of CE is inferred. (Fertil Steril® 2021;115:1541–8. ©2021 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Chronic endometritis, hysteroscopy, histology, immunohistochemistry for CD138, antibiotic therapy, cure rate

Chronic endometritis (CE) is a subtle pathology characterized by an inflammatory state of the endometrium. Previous studies (1, 2) found that CE was frequently associated with the endometrial overgrowth of different bacteria, including *Escherichia coli*, *Streptococcus* spp., *Staphylococcus* spp., *Chlamydia*, *Mycoplasma*, and *Ureaplasma*. This condition is mainly asyptomatic or associated with nonspecific symptoms, such as chronic pelvic pain, dysfunctional uterine bleeding, dyspareunia, and leukorrhea. For these reasons, CE is frequently overlooked by gynecologists (3–5).

Growing evidence (4–8) suggests that CE may exert a negative impact on spontaneous fertility and reduce the success rates of in vitro fertilization (IVF). Notably, the prevalence of CE was found to be high in different studies, up to 56.8% in infertile women (3, 4, 9) and up to 67.6% in women with repeated implantation failure (RIF) (5, 7, 10), suggesting that

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Correspondence: Amerigo Vitagliano, M.D., Department of Women and Children's Health, Unit of Gynecology and Obstetrics, University of Padua, Via Giustiniani 3, 35128, Padua, Italy (E-mail: amerigovitagliano.md@gmail.com).

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it may represent a frequent disease among women with reproductive issues (8–12).

The diagnosis of CE is a challenge. Hysteroscopy is a reliable technique for diagnosing CE in expert hands, but its overall accuracy is markedly operator-dependent (2, 13). CE is currently diagnosed based on the histological demonstration of plasma cells within endometrial stromal tissue (1, 4, 7). However, histology also has some diagnostic limits inherent to interobserver variability (3, 6). For all these reasons, immunohistochemical staining with CD138, which allows simple and reliable identification of plasma cells in the endometrial tissue, is gaining much more popularity than histology (14–16).

At present, there is great confusion among physicians about the therapeutic management of women suffering from CE (3). Mostly, CE is treated with antibiotics based on the assumption that it is caused by an underlying infection (7, 9–11). The response of CE to antibiotic therapy has been examined in many cohort studies (4, 6, 8). 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% (8), 99% (17), and 100% (7) in 3 different studies. The positive impact of antibiotic therapy on clinical outcome among subjects with CE also was examined in several cohort studies involving women with recurrent abortions, unexplained infertility, and RIF (7, 17, 18).

Moreover, very recently, the paradigm that CE is due only to bacterial infection of the endometrial mucosa has been questioned (19). A new theory about an impaired inflammatory state of the endometrium relying on a multifaceted pathogenesis (including hormonal, infectious, and autoimmune stimuli) has been formulated. Based on this theory, the entity termed CE should be abandoned (19). However, this theory still lacks scientific demonstration, and its practical applications are uncertain.

In this retrospective, nonconcurrent case-control study, we aimed to demonstrate the infectious nature of CE in an inductive way. Specifically, we evaluated the effectiveness of germ-oriented antibiotic therapy compared with no antibiotic treatment for CE cure.

MATERIALS AND METHODS

Study Design

This was a retrospective, nonconcurrent case-control study, conducted at the Department of Obstetrics and Gynecology, University of Bari. The study was approved by the local ethical committee. All patients gave their written consent for the anonymous use of their clinical data for research purposes, per standard practice at our center.

Participants

We compared women diagnosed with CE who received antibiotic therapy referred to our unit from January 2017 to December 2019 (**Group A**) with a historical group of women referred to our unit from January 2015 to December 2019 (**Group B**) who did not adhere to antibiotic therapy. Patients were selected retrospectively, including all successive cases and the next occurring control, at a 1:1 ratio (n = 64 patients allocated to each group).

We included only women with signs of CE at hysteroscopy whose diagnosis was confirmed by histology and immunohistochemistry for CD138. The diagnosis was based on the demonstration of ≥ 1 plasma cells per 10 high-power fields, according to published criteria (1). All women were referred to the hysteroscopy service due to abnormal uterine bleeding, suspected intrauterine lesions, or infertility, as shown in Table 1.

Exclusion criteria were postmenopausal age, history of endometriosis or adenomyosis, diagnosis of placental remnants, endometrial cancer or atypical hyperplasia, prior diagnosis of CE, previous diagnosis of tuberculosis, autoimmune diseases, hormonal or steroid treatment within 3 months or during the study period, and any antibiotic treatments within 3 months or during the study period (for other reasons).

Data Collection

Clinical data had been collected in our clinical registers by 2 authors (C.S., R.C.). Data included patients' general features (age, body mass index, parity); medical history (health status, pharmacological treatments, history of pelvic inflammatory disease, previous tubal pathologies including tubal obstruction demonstrated by tubal patency tests); the indication for hysteroscopy; and the results of each hysteroscopic, histological, and immunohistochemical examination. In case of missing data, the same author contacted the patients by telephone to complete the information.

Hysteroscopy and Endometrial Sampling

All women underwent diagnostic mini-hysteroscopy in the follicular phase of the menstrual cycle. Mini-hysteroscopy was performed using a lens-based 2.7-mm OD mini-telescope at a 105° angle of visual field, equipped with a 3.5-mm OD single-flow diagnostic sheath (Karl Storz,

TABLE 1

Clinical characteristics of patients included in the study.

	Group A (n = 64)	Group B (n = 64)
Age, years ± SD	34.5±8.0	35.3±7.0
Parity, n ± SD	1.2±0.5	1.4±0.2
History of tubal pathology, n (%)		
Hydrosalpinx	2 (3.12)	3 (4.69)
Ectopic pregnancy	1 (1.56)	2 (3.12)
Abnormal tubal patency test*	3 (4.69)	4 (5.62)
Indication for hysteroscopy, n (%)		
Dyfunctional uterine bleeding	36 (56.25)	32 (50)
Ecographic suspicion of polyp	8 (12.5)	12 (18.75)
Infertility	8 (12.5)	10 (15.62)
Submucous myoma	8 (12.5)	6 (9.37)
Suspected mullerian abnormality	4 (6.25)	4 (6.25)

Note: Data are expressed as mean ± SD or absolute numbers and percentages.
Group A, women who received antibiotic therapy; Group B, women who refused antibiotic therapy.
* Sonosalpingography, hysterosalpingography, or laparoscopic chromopertubation (data available only for 16 of 18 women with infertility).

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Tuttlingen, Germany). For minimizing the risk of iatrogenic contamination of the endometrial cavity, all examinations were performed after placing a vaginal speculum and cleaning the external uterine ostium with a gauze soaked in iodine solution.

Saline was employed to distend the uterine cavity at a pressure generated by a simple drop from a bag suspended 1 m above the patient. A 300-W light source with a xenon bulb and a high-definition digital camera (Karl Storz, Tuttlingen, Germany) were used.

The exploration of the uterine cavity consisted of a panoramic view of the cavity followed by a thorough evaluation of the endometrial mucosa as previously described. Diagnosis of CE was based on criteria previously published (13). All hysteroscopies were performed by one author (E.C.).

In the follicular phase of the subsequent cycle, an endometrial biopsy using a 3-mm Novak's curette connected to a 20-mL syringe was performed for cultural and histological purposes to search for infectious agents such as common bacteria, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Mycoplasma* species, *Ureaplasma urealyticum*, and yeast. For minimizing the risk of contaminating endometrial cultures in the vagina, after placing a vaginal speculum and cleaning the external uterine ostium with a gauze soaked in an iodine solution, the Novak's cannula was inserted under visual control into the uterine cavity, taking care to avoid any contact with the vaginal walls. Endometrial samples were diluted in 2 mL of saline and divided into 2 aliquots: one for infectious agent investigations and the other placed in formalin for histological examination.

Endometrial Culture

Specimens for *N. gonorrhoeae* were immediately placed in Stuart's transport medium and transported to the laboratory. Specimens for *Chlamydia*, *Mycoplasma*, and *Ureaplasma* were placed into a transport medium specific for polymerase chain reaction. In the laboratory, vaginal and endometrial specimens were gram stained; then, the swabs and endometrial specimens were plated onto appropriate agar medium: 5% sheep blood Columbia agar base, chocolate agar, mannitol salt agar, or MacConkey agar (Bio Merieux, Rome, Italy) and the presence of microorganisms was evaluated. The plates were incubated for 48 hours in air or 5% carbon dioxide. The identification of bacteria was made using published criteria (Dade International Inc., Milan, Italy). Genital mycoplasmas were quantitatively detected by immunoassay (Mycoplasma-IST; Biomerieux, Rome, Italy). For isolation of yeast, specimens were plated into Saboraud chloramphenicol agar, and identification was made by using commercial kits (API-C System; Biomerieux, Rome, Italy). To detect *C. trachomatis*, *N. gonorrhoeae*, *U. urealyticum*, *U. parvum*, and *Mycoplasma hominis*, all of which are noncultivable strains recoverable from the genital tract, a multiplex RT method (AnyplexTM II STI-7 Detection [V1.1]; Seegene, Seoul, Republic of Korea) was used according to the manufacturer's instructions.

Histology and Immunohistochemistry

The second aliquots of samples were sent for histological and immunohistochemical analyses. Endometrial samples were fixed in neutral formalin and later embedded in paraffin. Five microsections were stained with hematoxylin-eosin. The histological examinations were performed by a single operator (L.R.) who was unaware of hysteroscopic findings. Histological diagnosis of CE was based on criteria described in the literature (16, 17, 20). Attention was paid to the following features: superficial stromal edema, increased stromal density, pleomorphic stromal inflammatory infiltrate dominated by lymphocytes, and plasma cells.

Sections (5 μm) were cut and incubated with mouse anti-human monoclonal CD138 antibody. The clone of anti-CD138 monoclonal antibody used in our study was MI15 Cell Marque (Biocare Medical, Concord, California). $CD138^+$ plasma cells were identified in the stroma. At least 50 high-power fields were examined per specimen. The biopsies were graded as "negative" for CE if there was <1 plasma cell identified per 10 high-power fields and "positive" when there was ≥ 1 plasma cell identified per 10 high-power fields, according to published criteria. All endometrial biopsy specimens were examined by a single consultant histopathologist.

Antibiotic Therapy

Antibiotic treatment was based on antibiogram results and performed as previously published (4, 18). In most cases positive for gram-negative bacteria, ciprofloxacin 500 mg twice a day for 10 days was prescribed as the first-line therapy. In the case of gram-positive bacteria, amoxicillin and clavulanate 1 g twice a day for 8 days was prescribed. *Mycoplasma* and *U. urealyticum* were treated with josamycin 1 g twice a day for 12 days; in case of persistence, minocycline 100 mg twice a day for 12 days was employed.

In women with negative cultures, a treatment based on ceftriaxone 250 mg intramuscular injection in a single dose plus doxycycline 100 mg orally twice a day for 14 days with metronidazole 500 mg orally twice a day for 14 days was administered, according to Centers for Disease Control guidelines.

Ascertainment of CE Cure

In the follicular phase of the menstrual cycle following antibiotic treatment, all women in Group A underwent a repeat endometrial biopsy for endometrial culture, histology, and CD138 immunohistochemical examination. In case of negativization of cultures, histology, and $CD138^+$ count, a hysteroscopy was performed to confirm the resolution of CE. In case of CE persistence at histology, immunohistochemistry, or hysteroscopy, the protocol was repeated (until triple negativization) up to 3 times. In Group B, all patients underwent a repeat diagnostic protocol for CE (hysteroscopy plus endometrial biopsy in the follicular phase of the subsequent menstrual cycle) after a waiting period of 2 complete menstrual cycles.

Statistical Analysis

Analyses were performed using Epi Info 6.04 (Centers for Disease Control and Prevention, Atlanta, Georgia). Continuous variables were reported as means with standard deviation (SD), whereas qualitative variables were presented as absolute frequencies and percentages. Comparisons between categorical variables were tested using contingency tables and the chi-square test or Fisher's test when necessary. Comparisons between normally distributed continuous variables were made by using Student's *t* test. A value of $P<.05$ was considered statistically significant.

Study Endpoints

The primary endpoint consisted of comparing the pooled rate of CE resolution in Group A (defined as the total percentage of patients without CE at hysteroscopy, histology, and immunohistochemistry after 3 antibiotic cycles) vs. Group B. The secondary endpoint was to compare the rate of CE resolution between groups after the first antibiotic cycle. The tertiary endpoint was to compare hysteroscopic, histological, and immunohistochemical findings after antibiotic therapy.

RESULTS

The demographic characteristics of the study population are displayed in Table 1. The age, body mass index, and parity were not significantly different between groups. Eight patients (n = 3 in Group A; n = 5 in Group B) had a history of pelvic inflammatory disease. Among these women, 5 had undergone laparoscopic unilateral or bilateral salpingectomy due to hydrosalpinx. In the infertile subpopulation (n = 18 women), 7 patients had tubal obstruction diagnosed by sonosalpingography, hysterosalpingography, or laparoscopic chromopertubation.

In Group A (receiving antibiotics), CE was cured in 20 cases (32.25%) after 1 antibiotic cycle, in 40 cases (62.5%) after 2 cycles, and in 52 cases (81.25%) after 3 cycles. In 12 cases (18.75%), CE was persistent after 3 antibiotic cycles.

The pooled rate of CE resolution was considerably higher in Group A than Group B (81.25% vs. 6.25%; $P<.0001$). Notably, a statistical difference between groups was already present after 1 antibiotic cycle (32.25% vs. 6.25%; $P=.02$).

The number of CE diagnoses showed some inconsistency between hysteroscopy, histology, and immunohistochemistry (Table 2). Notably, the number of CE diagnoses decreased significantly with all techniques after the first and second antibiotic cycles, whereas after the third antibiotic cycle, we found a statistical reduction in CE prevalence at hysteroscopy and immunohistochemistry, but not at histology (Table 3, Fig. 1, and Supplemental Table S1, available online). When considering all the evaluations (i.e., after the first, second, and third antibiotic cycles), the number of positive cases was significantly higher at hysteroscopy compared with both histology and immunohistochemistry (with the exception of month 2). In particular, after the third antibiotic cycle, the number of patients with a diagnosis of CE at hysteroscopy was 3.1 times higher than at $CD138^+$ cell count.

There was no adverse reaction to the antibiotic treatment. No complications resulted from hysteroscopy and biopsies, including significant bleeding, infection, or fluid absorption during the study.

TABLE 2

Specific etiological agents found during endometrial investigations in women with evidence of CE by hysteroscopy, histology, and $CD138^+$ cell count.

	Group A (n = 64)	Group B (n = 64)
Escherichia coli	20	18
Streptococci	14	17
Staphylococci	2	0
Enterococcus faecalis	20	13
Klbsiella pneumoniae	0	2
Chlamydia	0	0
Ureaplasma	16	20
Yeast	2	0
Total bacteria	74	70

Note: Group A, women treated with antibiotics; Group B, control group of women not taking antibiotic therapy.

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DISCUSSION

Our study provides novel, relevant information for physicians about the clinical management of CE, which historically has been considered an enigmatic condition due to nonspecific symptomathology, nonstandardized diagnostic approach, and uncertain treatment effects (3–6). In recent times, different scientists have focused their efforts on trying to clarify the CE "gray zone," with heterogenous results (13, 21). All previous studies on CE therapy suffered from the lack of an untreated control group; thus, the evidence basis of CE treatment with antibiotics was still missing. To our knowledge, this is the first study providing evidence on CE therapy through a direct comparison between patients treated by antibiotics and untreated controls.

In the present experience, antibiotic treatment yielded an overall cure rate of CE of 81.25% compared with 6.25% of spontaneous resolution in the control group. Moreover, the results of this study demonstrate that even accepting the possibility of noninfectious forms of CE (19), the infectious origin is largely the most prevalent in our population, and this justifie a preliminary approach based on antibiotics.

These promising results warrant some considerations. In our study, we adopted germ-oriented antibiotic therapy in each single case (i.e., treatment was individualized based on endometrial culture and antibiogram results). Therefore, our results in terms of CE cure are not directly comparable with those from the majority of other studies applying empiric antibiotic treatments (including various combinations of doxycycline, metronidazole, ofloxacin, ciprofloxacin, amoxicillin with clavulanate, and ceftriaxone) (11, 15–17, 20–22). As CE can be associated with different subtypes of germs (i.e., 40.6% gram-negative and 53.1% gram-positive bacteria in

TABLE 3

Results of hysteroscopy, histology, and immunohistochemistry after the first, second, and third antibiotic treatment cycles among patients who received antibiotic therapy (Group A).

	1 Round of Antibiotics			2 Rounds of Antibiotics			3 Rounds of Antibiotics		
	HYS	HIS	IHC	HYS	HIS	IHC	HYS	HIS	IHC
Positive	44	22	34	24	8	16	12	4	4
Negative	20	42	30	40	56	48	52	60	60

Note: Data are expressed as absolute numbers.
HIS = histology; HYS = hysteroscopy; IHC = immunohistochemistry.

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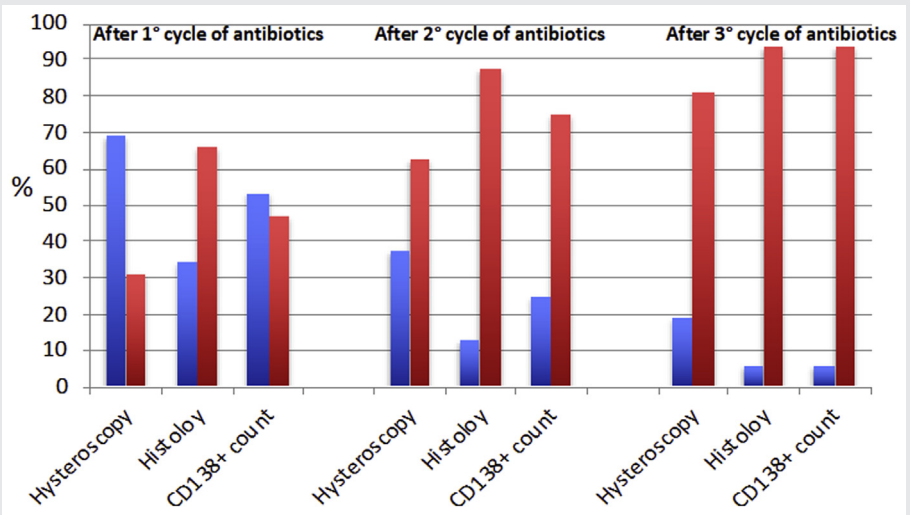
our study), we may suppose that empiric therapy is more likely to fail compared with germ-oriented therapy. However, previous cohort studies surprisingly found CE cure rates with empiric therapy that were similar to ours. For instance, Johnston-MacAnanny et al. (11) administered oral doxycycline (200 mg/day for 14 days) to a cohort of patients with CE and a history of RIF, resulting in a cure rate of 70% (n = 7 of 10 patients). Additional treatment with a combination of ciprofloxacin and metronidazole (500 mg of each per day for 14 days) effectively eliminated CE in the remaining 3 patients. Using the same antibiotic regimen for CE, Yang and coworkers (22) prospectively investigated the effectiveness of antibiotic therapy in a large cohort of women with a history of RIF. Oral doxycycline alone (200 mg/day for 14 days) provided an almost immediate cure of CE in their study, with success rates of 92.3% (n = 108/117 patients). The cumulative cure rate of CE reached 99.1% (n = 116/117 women) following second-line treatment with metronidazole (500 mg/day for 14 days) and ciprofloxacin (400 mg/day for 14 days). In another study, McQueen et al. (10) treated a cohort of women with CE and recurrent pregnancy loss with ofloxacin (800 mg/day for 14 days) and metronidazole (1,000 mg/day for 14 days). The therapy was effective in curing CE in 73% (19/26) of patients. The remaining 9 patients with CE persistence received doxycycline alone, doxycycline and metronidazole, or metronidazole and ciprofloxacin.

Besides a study design involving the presence of controls, our study also differs from others in the methods for ascertaining CE resolution. Indeed, we considered the patients as cured of CE when hysteroscopy, histology, and immunohistochemistry all were negative, whereas other studies mainly relied on the results of histological or immunohistochemical examination alone (11, 15–17, 20–22). Although we may speculate that our diagnostic approach could have higher accuracy compared with others, we also must acknowledge that the use of 3 diagnostic tests may lead to a higher rate of false-positive results. However, we point out that potential bias inherent to false-positive results pertained to the entire

FIGURE 1



Women from Group A (receiving antibiotic therapy) diagnosed with CE at hysteroscopy, histology, and immunohistochemistry for CD138 during 3 courses of antibiotic treatment. Red bars represent cured cases, whereas blue bars represent cases with persistent CE. Data are presented as percentages.

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study population and therefore was unlikely to affect comparisons between groups.

Moreover, to minimize the bias due to interobserver variability in the diagnoses of CE, in our study, all hysteroscopies were performed by a single physician, and histological and immunohistochemical analyses were completed by a single pathologist. Regarding this point, we also must acknowledge that both the hysteroscopist and pathologist involved in the study were unblinded to CE treatment. Although studies investigating the effectiveness of a certain therapy for a specific disease should ideally use blinded outcome assessment to avoid bias in estimated treatment effects, this method was not applicable to our study due to its retrospective design. Accordingly, a certain bias in the assessment of CE cure cannot be excluded. Arguably, this bias could mainly pertain to hysteroscopy because the hysteroscopic diagnosis of CE was influenced by subjective interpretation (2, 13), whereas the histopathological count of endometrial plasma cells was shown to have good objectivity and reliability (23). All these disparities between our study and others should be thoroughly considered do not allow for making easy comparisons between data.

Finally, our study surprisingly found higher persistence of CE signs after antibiotic therapy at hysteroscopy compared with histology and immunohistochemistry. This result is of complex interpretation. On the one hand, someone might speculate that hysteroscopy (as performed in expert hands) may provide higher sensitivity compared to other techniques as it uniquely allows a thorough evaluation of endometrial features without limitations inherent to the quality and quantity of tissue sampled (as for histology and immunohistochemistry). On the other hand, we must acknowledge that hysteroscopic examination is biased by subjective interpretation and currently does not represent the diagnostic gold standard for CE (23, 24). Since our study was not originally designed for comparing the diagnostic accuracy of hysteroscopy, histology, and immunohistochemistry, this matter warrants further investigation by purpose-designed studies.

Originality, strict inclusion criteria, and rigorous methodology were the main points of strength of our study. Our findings mainly suffer from the limits of the retrospective character of the study design (including the lack of blinding for the hysteroscopist and pathologist to antibiotic treatment), the relatively small number of patients included ($n = 64$ per group), and the blinded endometrial samplings. Additionally, women in the control group received a single control hysteroscopy plus endometrial biopsy after a waiting period of 2 menstrual cycles, and the probability of CE self-resolution in the long term could not be assessed. All of these factors may potentially limit drawing precise conclusions on the exact cure rate of CE through germ-oriented antibiotic therapy.

In conclusion, germ-oriented antibiotic therapy was significantly superior to no treatment for the cure of CE. Accordingly, future interventional studies on CE therapy involving untreated controls are probably discouraged for ethical reasons. Based on our findings, a predominant infectious nature of CE can be inferred. Future research is needed to evaluate the superiority of germ-oriented antibiotic therapy over empiric antibiotic therapy for CE cure.

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Terapia antibiótica frente a no tratamiento para la endometritis crónica: un estudio de casos y controles.

Objetivo: Demostrar la naturaleza infecciosa de la endometritis crónica (EC) de forma inductiva comparando los resultados de la terapia antibiótica orientada al germen frente a la ausencia de tratamiento en mujeres con EC.

Diseño: Estudio de casos y controles retrospectivo y no concurrente.

Lugar: Centro histeroscópico terciario en un hospital universitario de enseñanza.

Paciente(s): Sesenta y cuatro mujeres consecutivas con CE que recibieron terapia antibiótica (Grupo A) en comparación con un grupo histórico de 64 pacientes con CE que rechazaron la terapia antibiótica (Grupo B).

Intervenciones: La EC se diagnosticó mediante histeroscopia, histología e inmunohistoquímica para CD138. Las pacientes de ambos grupos fueron sometidas a pruebas de EC dos veces para evaluar la tasa de curación tras la terapia con antibióticos (Grupo A) o sin tratamiento (Grupo B). En el caso de los pacientes con enfermedad persistente, la terapia antibiótica se repitió hasta 3 veces. Los antibióticos se eligieron en función del cultivo endometrial (con antibiograma).

Medida(s) de resultado principal(es): El resultado primario fue comparar la tasa de curación acumulada de CE (definida como el porcentaje de pacientes sin EC en la prueba de curación) entre los grupos.

Resultado(s): Entre el grupo A, 20 pacientes (31,25%) experimentaron la resolución de la EC después de 1 ciclo de antibióticos, otros 20 pacientes (31,25%) después de 2 ciclos de antibióticos y 12 pacientes (19,35%) después de 3 ciclos de antibióticos. En 12 casos (18,75%), la EC persistía después de 3 ciclos de antibióticos. La tasa de curación de la EC en el Grupo A tras 1 ciclo de antibióticos fue significativamente mayor que la del Grupo B (32,25% frente al 6%). Del mismo modo, la tasa de curación acumulada fue considerablemente mayor en el Grupo A frente al Grupo B (81,3% frente al 6%). En particular, el número de casos positivos disminuyó significativamente con todas las técnicas entre la primera y la segunda evaluación, mientras que en la tercera evaluación, sólo hubo una disminución estadística con la histeroscopia y el recuento de células CD138 , pero no con la histología. El número acumulado de casos de CE diagnosticados con la histeroscopia fue significativamente mayor que con la histología y la inmunohistoquímica.

Conclusiones: Nuestro estudio demostró la superioridad de la terapia antibiótica en comparación con la ausencia de tratamiento para la curación del EC. En consecuencia, se infiere la naturaleza infecciosa de la EC.