ORIGINAL RESEARCH ARTICLE

Effectiveness of combined clindamycin phosphate and medroxyprogesterone acetate tablets in treatment of endometritis

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Abstract

This study explores the therapeutic effects of combining clindamycin phosphate tablets (CPT) with medroxyprogesterone acetate tablets (MAT) in treating endometritis. A total of 80 patients with endometritis, admitted between March 2021 and March 2024, were randomly divided into two groups: the control group (n=40) received CPT alone at a dosage of 0.3g per administration, 3 times daily; the observation group (n=40) received CPT (same dosage as control group) plus MAT at 6mg per administration, 3 times daily. Both groups continued treatment for 14 days. The observation group demonstrated a significantly higher treatment efficacy (92.50% vs. 75.00%) and better menstrual recovery. Clinical symptoms, such as pelvic pain and abnormal vaginal secretions, resolved more quickly in the observation group. Additionally, inflammatory markers IL-4, TNF-α, MMP-2, and MMP-9 decreased significantly post-treatment, while TGF-β1 increased and VCAM-1 decreased, indicating improved endometrial repair. No severe adverse reactions were observed. These findings suggest that the combination of CPT and MAT is more effective than CPT alone in alleviating symptoms, reducing inflammation, and promoting menstrual normalization in patients with endometritis. *(Afr J Reprod Health 2025; 29 [9]: 30-38).*

Keywords: Endometritis; Clindamycin phosphate; Medroxyprogesterone acetate; Effectiveness

Résumé

Cette étude explore les effets thérapeutiques de l'association de comprimés de phosphate de clindamycine (CPT) et de comprimés d'acétate de médroxyprogestérone (MAT) dans le traitement de l'endométrite. Au total, 80 patientes atteintes d'endométrite, admises entre mars 2021 et mars 2024, ont été réparties aléatoirement en deux groupes : le groupe témoin (n = 40) a reçu du CPT seul à la dose de 0,3 g par administration, 3 fois par jour ; le groupe d'observation (n = 40) a reçu du CPT (même dosage que le groupe témoin) plus MAT à la dose de 6 mg par administration, 3 fois par jour. Les deux groupes ont poursuivi le traitement pendant 14 jours. Le groupe d'observation a démontré une efficacité thérapeutique significativement supérieure (92,50 % contre 75,00 %) et une meilleure récupération menstruelle. Les symptômes cliniques, tels que les douleurs pelviennes et les sécrétions vaginales anormales, ont disparu plus rapidement dans le groupe d'observation. De plus, les marqueurs inflammatoires IL-4, TNF-α, MMP-2 et MMP-9 ont diminué significativement après le traitement, tandis que TGF-β1 a augmenté et VCAM-1 a diminué, indiquant une amélioration de la réparation endométriale. Aucun effet indésirable grave n'a été observé. Ces résultats suggèrent que l'association CPT et MAT est plus efficace que la CPT seule pour soulager les symptômes, réduire l'inflammation et favoriser la normalisation menstruelle chez les patientes atteintes d'endométrite. *(Afr J Reprod Health 2025; 29 [9]: 30-38).*

Mots-clés: : Endométrite; Phosphate de clindamycine; Acétate de médroxyprogestérone; Efficacité

Introduction

Endometritis, a common disease of the female reproductive system, can be caused by a variety of factors, including bacterial, viral, fungal and other pathogens, as well as physical, chemical, immune and other stimulating factors[1]. The clinical presentations of endometritis are diverse, with mild cases often presenting no discernible symptoms, while severe cases may exhibit fever, abdominal pain, vaginal bleeding, and other associated manifestations[2]. Furthermore, endometritis can also adversely affect a woman's fertility, resulting in complications such as miscarriage, preterm

delivery, and placental abnormalities[3]. Endometritis can be histopathologically categorized as either acute or chronic [4]. Acute endometritis is commonly caused by bacterial, viral, or fungal infections. Symptoms may include fever, abdominal pain, and increased vaginal discharge. Infection and inflammation can result in damage to the uterine lining, impacting the implantation of the fertilized egg and embryo growth, potentially leading to infertility[5].

Chronic endometritis is a prolonged inflammation that can result from acute endometritis or from an untreated infection[6]. The symptoms of chronic endometritis are less severe than in the acute phase, but may lead to chronic pelvic pain and irregular menstruation. Chronic endometritis may also increase the risk of other infections, such as tubal infections, further impacting female reproductive health[7]. Currently, the impact of endometritis on women's physical and mental well-being has emerged as a significant health concern that demands attention.

At present, the treatment of endometritis primarily involves the use of broad-spectrum antibacterial drugs such as clindamycin phosphate tablets (CPT)[8]. However, patients treated solely with antibacterial medications are susceptible to developing drug resistance, and the efficacy is suboptimal. Additionally, they are prone to relapse after discontinuation of the medication, and long-term side effects are evident[9]. Medroxyprogesterone acetate tablet (MAT) is a synthetic progestin medication that exhibits anti-inflammatory, anti-allergic, and immunomodulatory properties[10]. MAT can exert an anti-estrogenic effect and directly target the endometrium to induce its shedding, thereby enhancing the therapeutic efficacy for endometrial lesions[11]. Clinically, these two medications are commonly utilized for the treatment of endometritis. However, the combined efficacy and safety remain unknown. Therefore, it is crucial to explore novel approaches for the treatment of endometritis in order to enhance the quality of life for patients.

The combination of clindamycin phosphate tablets and medroxyprogesterone acetate tablets in the treatment of endometritis can not only exert dual antibacterial and anti-inflammatory effects, but also reduce the reliance on antibiotics. The aim of this study was to assess the impact of clindamycin phosphate tablets alone and in combination with medroxyprogesterone acetate tablets on endometritis by monitoring changes in menstrual status and inflammatory response among patients receiving either treatment. The findings of this research will establish a scientific foundation for further refining the management of endometritis and offer practical guidance for clinical application.

Methods

Patient population

A total of 80 patients diagnosed with endometritis and admitted to the Obstetrics and Gynecology Department of Deyu Medical Ma'anshan General Hospital between March 2021 and March 2024 were included in the study. The inclusion criteria were as follows: (a) patients who fulfill the diagnostic criteria for endometritis as outlined in the 8th edition of Obstetrics and Gynecology [12]; (b) initial diagnosis with no previous treatment; (c) signed informed consent form. The exclusion criteria were as follows: (a) patients afflicted with endometriosis, endometrial cancer, and other related conditions; (b) history of uterine surgery within the last 3 months; (c) patients with a history of hormone drugs and antibiotics in the past 3 months; (d) patients with malignant tumors, infectious diseases or other serious diseases; (e) patients allergic to the investigational drug; (f) patients with a history of mental illness.

Sample size

Sample size was calculated by comparing two sample mean estimate formula calculation: $n_1=n_2=2\times[(t_\alpha/2+t_\beta) \times \sigma/\delta]^2$, $\alpha = 0.05$ (bilateral), $\beta = 0.2$ (unilateral). The study utilized efficacy as the primary outcome measure for determining sample size, which was initially set at 32 cases based on pre-test data. To account for a potential sample loss rate of 10%-20%, the sample size was adjusted and ultimately fixed at 40 cases per group. According to the random number table method, 80 patients were randomly allocated into control and observation groups, with 40 cases in each group.

Treatment plan

The control group received only CPT, at a dosage of 0.3g per administration, 3 times daily. The observation group received MAT in addition to the treatment given to the control group, at a dosage of 6mg per administration, 3 times a day. The two patient groups continued their medication regimen for 14 days, during which they were advised to maintain regular work and rest schedules, avoid strenuous exercise, follow a light diet, refrain from consuming spicy or greasy foods, and abstain from sexual activity.

Outcome indicators

Clinical effects were observed in the two groups [12]: (a) marked effect: menstruation recovered, clinical symptoms disappeared, blood routine test results were normal (including white blood cell count, neutrophil percentage, hemoglobin, and platelet count within the reference ranges, measured using an automated hematology analyzer with standard laboratory reagents and quality control procedures); B-ultrasound showing disappearance of inflammation, and endometrial thickness increasing significantly; (b) effectiveness: the clinical symptoms improved, the blood routine test results tended to be normal (white blood cell count, neutrophil percentage, and other inflammatory-related indices approaching the reference ranges, detected via the same method as above), the inflammation decreased, and the endometrial thickness increased slightly; (c) ineffective: does not meet the above obvious and effective standards, and even the condition even worsened.

Menstrual state: (a) menstrual volume was measured using a standardized menstrual bleeding map combined with a validated menstrual volume assessment method. Specifically, patients were instructed to use pre-weighed sanitary pads (each pad weighed to the nearest 0.1g before use) and record the number of pads used per day during menstruation. After use, each soiled pad was reweighed, and the difference between the post-use weight and pre-use weight was calculated to determine the menstrual blood volume (assuming 1g of blood equals 1mL). Additionally, the menstrual bleeding map was used to categorize the degree of pad saturation (e.g., light, moderate, heavy) to adjust for potential estimation errors from pad weight alone; (b) the menstrual volume ≥80 mL, as measured by the above method, was considered hypermenorrhea; (c) irregular bleeding outside the normal menstrual cycle is considered to be irregular vaginal bleeding. Clinical symptoms disappearance time: including pelvic pain, increased leucorrhea, vaginal bleeding, inflammation and other symptoms disappear time. Inflammatory response: detection of interleukin-4 (IL-4), tumor necrosis factor alpha (TNF alpha), matrix metalloproteinase-2 (MMP-2), and matrix metalloproteinase-9 (MMP-9) levels in patients before and after treatment. Adverse drug reactions: the adverse drug reactions of patients were counted.

Statistical analysis

Continuous variables were described in terms of mean ± standard deviation. The differences before and after treatment were assessed using a paired *t* test. The independent *t* test was used to analyze the difference of variables between the two groups. Technical data are described in percentage terms and analyzed using χ^2 tests. All statistical analyses were performed using SPSS 22.0. $P < 0.05$ was considered statistically significant.

Ethical considerations: Ethical approval for this study was obtained from the Ethics Committee of Ma'anshan General Hospital (Approval No. 2018132). All participants provided written informed consent before enrollment. The study adhered to the principles of the Declaration of Helsinki, ensuring patient confidentiality, voluntary participation, and the right to withdraw at any time without affecting their medical care. The ethics committee reviewed and monitored the study protocol, including patient recruitment, treatment safety, and data handling procedures.

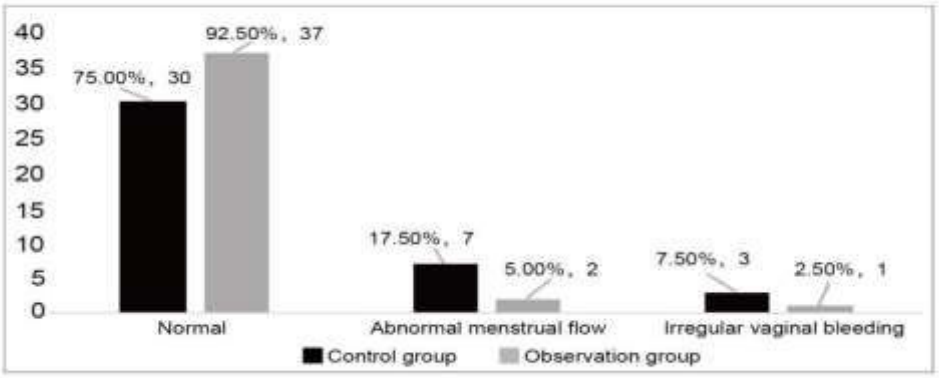
Results

General characteristics of the participants

A total of 80 patients diagnosed with endometritis were enrolled in this study and randomly assigned to either the observation group (n=40) or the control group (n=40). The general demographic and clinical characteristics of the two groups are presented in Table 3.

Table 1: Comparison of baseline characteristics between the two groups

Characteristic	Control group (n = 40)	Observation group (n = 40)	P value
Age (years), mean ± SD	29.8	30.2	0.483
Disease duration (weeks), mean ± SD	16.9	16.8	0.749
BMI (kg/m²), mean ± SD	23.0	23.0	0.981



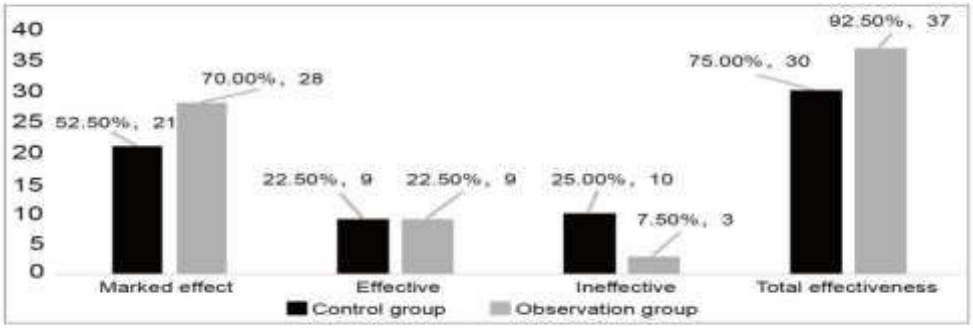


Table 2: Comparison of clinical symptom disappearance time between two groups

Symptom type	Observation group (n=40)	Control group (n=40)	*t* value	*P* value
Pelvic area pain	5.5±1.1	6.5±1.3	4.0	<0.001
Increased vaginal discharge	10.8±2.1	12.1±2.3	2.8	0.007
Vaginal bleeding	4.9±1.09	6.4±1.5	5.4	<0.001
Inflammation	6.2±1.1	8.4±1.5	7.6	<0.001

Table 3: Comparison of inflammatory response between the two groups before and after treatment

Inflammatory index	Observation group (n=40) Before treatment	After treatment	Control group (n=40) Before treatment	After treatment
IL-4 (μg/L)	12.0±1.8	7.1±1.0*Δ	11.7±1.6	8.3±1.1*
TNF-α (pg/mL)	54.4±9.5	34.9±5.2*Δ	53.6±8.2	40.48±6.7*
MMP-2 (μg/L)	0.8±0.2	0.3±0.1*Δ	0.8±0.1	0.5±0.1*
MMP-9 (μg/L)	0.5±0.1	0.3±0.1*Δ	0.5±0.1	0.4±0.1*
TGF-β1 (μmol/L)	18.9±2.8	27.3±4.0*Δ	19.3±2.8	24.3±3.4*
VCAM-1 (μg/mL)	104.5±22.1	64.1±7.5*Δ	106.8±21.3	73.1±9.3*

There were no statistically significant differences in age, disease duration, or BMI between the observation group and the control group (all P > 0.05), indicating that the two groups were comparable at baseline (P>0.05). table 1

Comparison of curative effect and menstrual status between the two groups

There were no significant differences in the rates of marked effect, effective rate, and ineffective rate between the observation group and the control group. The total effectiveness rate was 92.50% in the observation group and 75.00% in the control group (Figure 1). The total effectiveness rate of observation group was significantly higher than that of control group (χ^2=4.501, $P < 0.05$) (Figure 1). 92.50% of patients in the observation group had normal menstruation after treatment, while 75.00% of patients in the control group had normal menstruation (Figure 2). The proportion of menses returning to normal after treatment in observation group was significantly higher than that in control group (χ^2=4.501, $P < 0.05$).

Comparison of symptom resolution time and inflammatory response

The absence time of pelvic pain in the observation group (5.47±1.08 days) was significantly shorter than that in the control group (6.52±1.26 days) ($P < 0.05$). The disappearance days of vaginal secretions in the observation group was 10.79 days, which was significantly shorter than 12.14 days in the control group ($P < 0.05$) (Table 2). The disappearance days of vaginal bleeding in the observation group was 4.86 days, while in the control group it was 6.43 days, with a statistically significant difference ($P < 0.05$) (Table 2). In addition, the disappearance time of inflammation in the observation group was shorter than that in the control group ($P < 0.05$) (Table 2). After the treatment, the levels of IL-4, TNF-α, MMP-2 and MMP-9 in both groups decreased compared to pre-treatment levels (Table 3). Furthermore, the observation group exhibited significantly lower levels than the control group ($P < 0.05$) (Table 3). After treatment, TGF-β1 levels in both groups were higher than before treatment, while VCAM-1 levels were lower than before treatment. After treatment, TGF-β1 level in observation group was higher than that in control group, and VCAM-1 level was lower than that in control group, the difference was statistically significant ($P < 0.05$) (Table 3). No serious adverse reactions occurred in both groups during the treatment period.

Discussion

Endometritis is a common condition among women of childbearing age, with pathogenic bacteria such as streptococcus, staphylococcus, and Escherichia coli being the primary culprits[1-2]. Initially, patients may exhibit no overt clinical symptoms or signs. however, as the disease progresses, they may experience pelvic pain, menstrual irregularities, fever, and other manifestations[5]. Without timely and effective treatment during the acute stage, chronic endometritis may develop, potentially leading to infertility and significantly impacting patients' quality of life[13-14]. At present, the treatment of endometritis was aimed at eliminating

pathogenic microorganisms in reproductive tract, relieving clinical symptoms and improving endometrial inflammation[15]. The main treatment was anti-inflammatory, and the treatment drugs were antibiotics. However, inflammation is a complex process, and simply eliminating infected pathogenic microorganisms with antibiotics cannot completely eliminate the inflammatory response and subsequent damage in patients, resulting in poor effect[16]. CPT can be hydrolyzed to clindamycin in the body after oral administration, which can play a broad spectrum antibacterial effect, inhibit the infection of pathogenic microorganisms in the endometrial, and achieve the purpose of treatment[17].

But antibiotics alone are less effective. Pathological changes such as inflammation and uterine thinning in patients with endometritis were related to the decrease of estrogen and progesterone in the body[18]. Therefore, the use of estrogen and progesterone therapy has become a new direction to improve the clinical efficacy of endometritis. The medroxyprogesterone acetate is a synthetic progestin that promotes endometrial secretion, proliferation, and thickening[19]. It accelerates the shedding of infected endometrial tissue, reduces endometrial permeability, inhibits inflammation spread, and achieves anti-inflammatory therapeutic effects[20]. The aim of this study was to compare the effectiveness of CPT as a standalone treatment and in combination with MAT for the management of endometritis.

The results of this study demonstrated that the combined medication in the observation group led to higher clinical treatment efficiency and a greater proportion of menses returning to normal compared to the control group receiving single medication. This suggests that combining clindamycin phosphate tablets with medroxyprogesterone acetate tablets in the treatment of endometritis could further enhance efficacy beyond antibiotics alone, thereby aiding patients in achieving normal menstruation. Medroxyprogesterone acetate, as a progestin, can suppress the secretion of pituitary gonadotropins and facilitate the transition of the endometrium from the proliferative phase to the secretory phase, thereby inducing a state of low estrogen in patients and delaying abnormal menstruation[21]. Concurrent administration with antibiotics effectively clears the uterine cavity during this period, which is more conducive to restoring normal menstruation[22]. In this study, the disappearance time of clinical symptoms in the observation group was also shorter than that in the control group, suggesting that the combination of CPT and MAT was more conducive to the disappearance of symptoms in patients with endometritis. This may be attributed to the ability of clindamycin phosphate tablets to eradicate pathogenic microorganisms, while medroxyprogesterone acetate tablets can facilitate endometrial renewal and repair[23]. Both mechanisms contributed to improving the inflammatory state of the endometrium infected by pathogenic microorganisms in distinct ways.

The occurrence and progression of endometritis are intricately linked to inflammation, which is a multifaceted process encompassing alterations in the levels of numerous factors[24]. IL-4 and TNF-α were commonly used inflammatory indicators in clinical diagnosis, and their high levels indicated that the body was in a state of inflammation[25-26]. MMP-2 and MMP-9 were matrix metalloproteinases, which were involved in the inflammatory response and tissue repair process of the body, especially in the degeneration and proliferation of uterine epithelial cells and uterine remodeling process. The increase of the levels of MMP-2 and MMP-9 will increase endometrial permeability and affect endometrial repair, thus aggravating inflammation[27]. In this study, the levels of IL-4, TNF-α, MMP-2 and MMP-9 in the observation group were significantly superior to those in the control group, suggesting that the combination of CPT and MAT was more effective in ameliorating the inflammatory state of patients with endometritis. This may be attributed to the potential of MAT to facilitate endometrial repair, decrease endometrial permeability, and alleviate inflammatory conditions, thereby enhancing the anti-inflammatory effects of antibiotics. TGF-β1 was a growth factor that regulates various physiological processes including cell growth, differentiation, migration, and apoptosis. It exerted local immunosuppressive effects, mediated the synthesis and secretion of pro-inflammatory factors, and served as an indicator of endometrial inflammatory damage [28]. VCAM-1 was a member

of the immunoglobulin superfamily that mediated the adhesion between white blood cells, lymphocytes and vascular endothelial cells. Overexpression of VCAM-1 can aggravate vascular endothelial injury and was also associated with local pathological injury of endometritis [29]. In this study, the observation group showed a higher level of TGF-β1 and a lower level of VCAM-1 compared to the control group after treatment, indicating that the combination of MAT was more effective in alleviating endometrial pathological injury. This may be attributed to the ability of MAT to promote endometrial repair, improve uterine circulation, and reduce inflammation. Furthermore, no serious adverse drug reactions were observed during the treatment of patients in this study, suggesting that the drug combination was safe

Study strengths and limitations

The main strengths of this study include the prospective, randomized, parallel-group design; the use of validated outcome measures (PBAC-chart for menstrual volume, automated CBC analyser, and quantitative ELISA for inflammatory markers); and the homogeneous patient population (newly diagnosed, treatment-naïve endometritis). These elements reduce selection and information bias and enhance internal validity.

Despite these strengths, the study has certain limitations. First, the sample size was relatively small (80 patients in total), which may limit the generalizability of the findings to a broader population. Second, the follow-up period was absent, so long-term outcomes such as recurrence rate and long-term endometrial repair status could not be evaluated. Third, the mechanism underlying the synergistic effect of CPT and MAT was not explored at the molecular level (e.g., specific signaling pathways), which warrants further in vitro or in vivo studies. Fourth, the study only included patients from a single center (Ma'anshan General Hospital), potentially introducing selection bias and reducing the external validity of the results.

Our findings suggest that adding MAT to standard antibiotic therapy is both more effective and safe for treating endometritis in routine clinical practice. National or institutional guidelines could consider recommending a short (14-day) course of combined CPT + MAT as first-line therapy, especially in settings where chronic endometritis and its sequelae (infertility, recurrent pregnancy loss) are prevalent. Policy makers should weigh the modest incremental drug cost against the potential savings from reduced follow-up visits, fewer repeat treatments, and improved reproductive outcomes. Larger, multi-centre trials with longer follow-up and cost-effectiveness analyses are warranted before formal policy adoption

Competing interests

The authors declare no competing interests

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Author contributions

A. L. Zhang,Z. X. Fanconceived and designed the study. A. L. Zhang,Z. X. F was responsible for data collection and analysis. L. Guo,Q. P. Zhang contributed to the interpretation of the results and manuscript drafting. Z. X. Fan revised the manuscript critically for important intellectual content. All authors read and approved the final version of the manuscript.

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References

1.Singh N and Sethi A. Endometritis - Diagnosis,Treatment and its impact on fertility - A Scoping Review. *JBRA Assist Reprod*. 2022;26(3):538-546. Published 2022 Aug 4. doi:10.5935/1518-0557.20220015

2. Margulies SL, Flores V, Parkash V and Pal L. Chronic endometritis: A prevalent yet poorly understood entity. *Int J Gynaecol Obstet*. 2022;158(1):194-200. doi:10.1002/ijgo.13962

3. Kimura F, Takebayashi A, Ishida M, Nakamura A, Kitazawa J, Morimune A, Hirata K, Takahashi A, Tsuji S, Takashima A, Amano T, Tsuji S, Ono T, Kaku S,

Kasahara K, Moritani S, Kushima R and Murakami T. Review: Chronic endometritis and its effect on reproduction. *J Obstet Gynaecol Res.* 2019 May;45(5):951-960. doi: 10.1111/jog.13937.

4. Margulies SL, Dhingra I, Flores V, Hecht JL, Fadare O, Pal L and Parkash V. The Diagnostic Criteria for Chronic Endometritis: A Survey of Pathologists. *Int J Gynecol Pathol*. 2021 Nov 1;40(6):556-562. doi: 10.1097/PGP.0000000000000737.
5. Haggerty CL, Ness RB, Amortegui A, Hendrix SL, Hillier SL, Holley RL, Peipert J, Randall H, Sondheimer SJ, Soper DE, Sweet RL and Trucco G. Endometritis does not predict reproductive morbidity after pelvic inflammatory disease. *Am J Obstet Gynecol.* 2003 Jan;188(1):141-8. doi: 10.1067/mob.2003.87.
6. Margulies SL, Dhingra I, Flores V, Hecht JL, Fadare O, Pal L and Parkash V. The Diagnostic Criteria for Chronic Endometritis: A Survey of Pathologists. *Int J Gynecol Pathol*. 2021 Nov 1;40(6):556-562. doi: 10.1097/PGP.0000000000000737.
7. Tsonis O, Gkrozou F, Dimitriou E, Barmpalia Z, Tsonis K, Vatopoulou A and Paschopoulos M. Hysteroscopic features suggestive of chronic endometritis: a systematic review. *Hum Fertil (Camb).* 2023 Dec;26(6):1530-1543. doi: 10.1080/14647273.2023.2265155.
8. Alrowaily N, D'Souza R, Dong S, Chowdhury S, Ryu M and Ronzoni S. Determining the optimal antibiotic regimen for chorioamnionitis: A systematic review and meta-analysis. *Acta Obstet Gynecol Scand.* 2021;100(5):818-831. doi:10.1111/aogs.14044
9. Mackeen AD, Packard RE, Ota E and Speer L. Antibiotic regimens for postpartum endometritis. *Cochrane Database Syst Rev.* 2015;2015(2):CD001067. Published 2015 Feb 2. doi:10.1002/14651858.CD001067.pub3
10. Munro MG, Mainor N, Basu R, Brisinger M and Barreda L. Oral medroxyprogesterone acetate and combination oral contraceptives for acute uterine bleeding: a randomized controlled trial. *Obstet Gynecol.* 2006;108(4):924-929. doi:10.1097/01.AOG.0000238343.62063.22
11. Tsai YC, Tseng JT, Wang CY, Su MT, Huang JY and Kuo PL. Medroxyprogesterone acetate drives M2 macrophage differentiation toward a phenotype of decidual macrophage. *Mol Cell Endocrinol.* 2017;452:74-83. doi:10.1016/j.mce.2017.05.015
12. Xie Xing and Gou Wenli. Obstetrics and Gynecology, 8th edition [M]. *Beijing: People's Medical Publishing House*, 2013:256.
13. Klimaszyk K, Svarre Nielsen H, Wender-Ozegowska E and Kedzia M. Chronic endometritis - is it time to clarify diagnostic criteria?. *Ginekol Pol.* 2023;94(2):152-157. doi:10.5603/GP.a2022.0147
14. Petrina MAB, Cosentino LA, Wiesenfeld HC, Darville T and Hillier SL. Susceptibility of endometrial isolates recovered from women with clinical pelvic inflammatory disease or histological endometritis to antimicrobial agents. *Anaerobe.* 2019;56:61-65. doi:10.1016/j.anaerobe.2019.02.005
15. Barański W, Baryczka A, Zduńczyk S, Tobolski D and Janowski T. Prevalence of subclinical endometritis in dairy cows that recovered after treatment of clinical endometritis with cephapirin and PGF2α. *Theriogenology.* 2022;192:166-171. doi:10.1016/j.theriogenology.2022.08.031
16. Odendaal J, Black N, Bouliotis G, Guck J, Underwood M, Fisher J and Quenby S. Preconceptual administration of doxycycline in women with recurrent miscarriage and chronic endometritis: protocol for the Chronic Endometritis and Recurrent Miscarriage (CERM) trial, a multicentre, double-blind, placebo-controlled, adaptive randomised trial with an embedded translational substudy. *BMJ Open.* 2023 Dec 1;13(12):e081470. doi: 10.1136/bmjopen-2023-081470. PMID: 38040426;
17. Feng Yanyan, Zhang Lei and Zhu Yunshan. Evaluation of the efficacy of cefuroxime axetil and clindamycin phosphate vaginal cream in the treatment of simple aerobic bacterial vaginitis [J]. *Chinese Journal of Practical Gynecology and Obstetrics*, 2018, 34(09): 1055-1057.
18. Qu D, Yang M, Tong L, Yu X, Jing Q, Yang Y and Zhou H. Combination of Dydrogesterone and Antibiotic Versus Antibiotic Alone for Chronic Endometritis: a Randomized Controlled Trial Study. *Reprod Sci.* 2021 Nov;28(11):3073-3080. doi: 10.1007/s43032-021-00583-6.
19. Han SJ, Kim H, Ku SY, Suh CS. Comparison of resumption of ovulation after cessation of oral contraceptives and medroxyprogesterone acetate in women with polycystic ovary syndrome. *Gynecol Endocrinol.* 2024;40(1):2309349. doi:10.1080/09513590.2024.2309349
20. Murakami H, Hayashi M, Terada S and Ohmichi M. Medroxyprogesterone acetate-resistant endometrial cancer cells are susceptible to ferroptosis inducers. *Life Sci.* 2023;325:121753. doi:10.1016/j.lfs.2023.121753
21. Tasker C, Pizutelli V, Lo Y, Ramratnam B, Roche NE and Chang TL. Depot medroxyprogesterone acetate administration increases cervical CCR5+CD4+ T cells and induces immunosuppressive milieu at the cervicovaginal mucosa. *AIDS.* 2020;34(5):729-735. doi:10.1097/QAD.0000000000002475
22. Yuk JS, Song JY, Lee JH, Park WI, Ahn HS and Kim HJ. Levonorgestrel-Releasing Intrauterine Systems Versus Oral Cyclic Medroxyprogesterone Acetate in Endometrial Hyperplasia Therapy: A Meta-Analysis. *Ann Surg Oncol.* 2017;24(5):1322-1329. doi:10.1245/s10434-016-5699-9
23. De Fijter CW, Verbrugh HA, Heezius HC, van der Meulen J, Oe PL, Donker AJ and Verhoef J. Effect of clindamycin on the intracellular bactericidal capacity of human peritoneal macrophages. *J Antimicrob Chemother.* 1990 Oct;26(4):525-32. doi: 10.1093/jac/26.4.525.

24. Woodward EM and Troedsson MH. Inflammatory mechanisms of endometritis. *Equine Vet J.* 2015;47(4):384-389. doi:10.1111/evj.12403
25. Miao Y, Ishfaq M, Liu Y, Wu Z, Wang J, Li R, Qian F, Ding L and Li J. Baicalin attenuates endometritis in a rabbit model induced by infection with Escherichia coli and Staphylococcus aureus via NF-κB and JNK signaling pathways. *Domest Anim Endocrinol.* 2021 Jan;74:106508. doi: 10.1016/j.domaniend.2020.106508.
26. Huang Q, Yang Y, Yuan L, Zhao Y and Qin A. Oil-based contrast for hysterosalpingography-regulated Th1/Th2-type cytokines and alleviated inflammation in rats with LPS-induced chronic endometritis. *J Obstet Gynaecol Res.* 2023;49(1):243-252. doi:10.1111/jog.15451
27. Amaral A, Fernandes C, Rebordão MR, Szóstek-Mioduchowska A, Lukasik K, Gawronska-Kozak B, Telo da Gama L, Skarzynski DJ and Ferreira-Dias G. The In Vitro Inhibitory Effect of Sivelestat on Elastase Induced Collagen and Metallopeptidase Expression in Equine Endometrium. *Animals (Basel).* 2020 May 16;10(5):863. doi: 10.3390/ani10050863.
28. Moreau JM, Velegraki M, Bolyard C, Rosenblum MD and Li Z. Transforming growth factor-β1 in regulatory T cell biology. *Sci Immunol.* 2022;7(69):eabi4613. doi:10.1126/sciimmunol.abi4613
29. Troncoso MF, Ortiz-Quintero J, Garrido-Moreno V, Sanhueza-Olivares F, Guerrero-Moncayo A, Chiong M, Castro PF, García L, Gabrielli L, Corbalán R, Garrido-Olivares L and Lavandero S. VCAM-1 as a predictor biomarker in cardiovascular disease. *Biochim Biophys Acta Mol Basis Dis.* 2021 Sep 1;1867(9):166170. doi: 10.1016/j.bbadis.2021.166170