

and direct relationships on the left half. Thus, we identified a pronounced factor of sexual dimorphism in the magnitude, direction, and number of relationships between masticatory pressure indices and constitutional parameters in individuals with a brachycephalic skull shape.

Key words: correlations, masticatory pressure, morphometry, jaws, skull shapes.

ORCID кожного автора та його внесок до статті:

Ivanov R. O.: <https://orcid.org/0000-0002-2593-6505>^{BD}
 Sarafyniuk L. A.: <https://orcid.org/0000-0001-8253-5997>^{EF}
 Popova O. I.: <https://orcid.org/0000-0002-7793-021X>^A
 Babiichuk N. F.: <https://orcid.org/0009-0007-6466-1042>^C
 Hlushak A. A.: <https://orcid.org/0000-0003-0730-5571>^E

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Адреса для кореспонденції

Іванов Ростислав Олегович
 Вінницький національний медичний університет ім. М. І. Пирогова
 Україна, 21018, м. Вінниця, вул. Пирогова 56
 Тел.: +380672250773
 E-mail: s001098@vnm.edu.ua

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¹Kotsabin N. V., ²Boyshuk A. V., ³Kosharniy V. V.

MORPHOLOGICAL CHARACTERISTICS OF THE ENDOMETRIUM IN PATIENTS WITH CHRONIC ENDOMETRITIS

¹Reproductive Health Medical Center “Damiya” (Ivano-Frankivsk, Ukraine)

²I. Horbachevsky Ternopil National Medical University (Ternopil, Ukraine) ³Dnipro State Medical University (Dnipro, Ukraine)

nykolynnataliya@yahoo.com

Chronic endometritis is a persistent inflammatory process of the endometrial mucosa that may have a subtle or asymptomatic clinical course and may be associated with impaired reproductive function. Morphological verification of the disease requires a comprehensive assessment of structural endometrial changes and identification of plasma cells. The aim is to perform a comprehensive histological and immunohistochemical assessment of morphological changes in the endometrium of patients with chronic endometritis and to determine the principal structural characteristics of the chronic inflammatory process. Endometrial biopsy specimens obtained from patients with clinically suspected chronic endometritis during the proliferative phase of the menstrual cycle were examined. Histological examination was performed after hematoxylin and eosin staining. Endometrial architecture, the glandular-to-stromal ratio, stromal cellularity and inflammatory infiltration, spiral artery changes, structural alterations of the glands and stroma, and polypoid formations were evaluated. Immunohistochemical staining with antibodies against CD138 was used to identify plasma cells, which were counted in 10 high-power fields. A spectrum of structural changes was identified, including irregular distribution of glands of different calibers, focal changes in the glandular-to-stromal ratio, uneven stromal cellularity, lymphoplasmacytic infiltration, spindle-shaped transformation of stromal cells, and sclerotic changes in spiral arteries. Areas of incomplete shedding of the functional layer, micropolyps, and polypoid formations were also observed in some specimens. CD138-positive plasma cells were detected in all examined cases, ranging from 6 to 28 cells per 10 high-power fields. Chronic endometritis is characterized by a combination of structural remodeling of the glandular and stromal components, vascular changes, and lymphoplasmacytic infiltration. The use of CD138 immunohistochemistry complements conventional histological examination and improves the objectivity of morphological verification of chronic endometritis.

Key words: chronic endometritis, endometrium, morphology, histology, immunohistochemistry, CD138, plasma cells.

Connection of the publication with planned research work.

The study was carried out within the framework of the scientific research work "Improving the diagnostics and treatment of pregnant women with a burdened somatic anamnesis" of the Department of Obstetrics and Gynecology, Faculty of Postgraduate Education, I. Horbachevsky Ternopil National Medical University (state registration number 0121U100153).

Introduction.

Chronic endometritis (CE) is one of the important factors associated with impaired female reproductive function and has been associated with infertility, repeated implantation failure, recurrent pregnancy loss, and reduced effectiveness of assisted reproductive technologies [1–4]. A characteristic feature of the disease is its oligosymptomatic or asymptomatic course, which considerably complicates timely diagnosis and treatment.

CE is characterized by a combination of structural and cellular changes in the endometrium, including disturbances in glandular architecture, remodeling of the stromal component, vascular changes, and chronic inflammatory infiltration. Identification of plasma cells using the immunohistochemical marker CD138 increases the diagnostic accuracy of CE because plasma cells are considered an important morphological indicator of chronic endometrial inflammation [5–8].

In this context, comprehensive morphological and immunohistochemical assessment of endometrial biopsy specimens is important for confirmation of the diagnosis, characterization of the degree of structural alterations, and subsequent selection of an appropriate therapeutic strategy.

Modern studies have demonstrated considerable variability in the diagnostic criteria used for CE, particularly with regard to the number of CD138-positive plasma cells required for diagnosis [6–10]. Different studies have used different cut-off values, which may substantially influence the reported prevalence of CE and the assessment of its association with reproductive outcomes [7, 8].

Systematic reviews and meta-analyses have demonstrated that CE may be associated with adverse reproductive outcomes, although the strength of this association depends on the diagnostic criteria and the population studied [3, 4]. The number and distribution of plasma cells may also influence the clinical significance of the histological findings [8, 9].

Therefore, the identification of CD138-positive plasma cells should not be considered separately from the overall morphological characteristics of the endometrium. Assessment of glandular architecture, stromal cellularity, lymphoplasmacytic infiltration, vascular changes, and polypoid alterations provides additional information concerning the nature and duration of the inflammatory process [5, 10, 11].

The combination of conventional histological examination and CD138 immunohistochemistry therefore represents an important approach for the comprehensive morphological characterization of CE, particularly in women with reproductive disorders.

The aim of the study.

To perform a comprehensive histological and immunohistochemical assessment of morphological changes in the endometrium of patients with chronic endome-

tritis and to determine the principal structural criteria characterizing the chronic inflammatory process.

Object and research methods.

Morphological examination of endometrial biopsy specimens obtained from patients with clinically suspected chronic endometritis was performed. The material was collected during the proliferative phase of the menstrual cycle and subsequently fixed in 10% neutral buffered formalin. This study was conducted in accordance with the requirements of Good Clinical Practice (ICH E2(R6) GCP) and the Declaration of Helsinki of the World Health Organization. All patients provided informed voluntary consent prior to any procedures.

After standard histological processing, the specimens were embedded in paraffin. Serial sections 4–5 µm thick were prepared and stained with hematoxylin and eosin.

Light microscopy was used to assess endometrial architecture, the glandular-to-stromal ratio, glandular shape and distribution, epithelial characteristics, stromal cellularity, the nature and intensity of inflammatory infiltration, the condition of spiral arteries, spindle-shaped transformation of stromal cells, areas of incomplete shedding of the functional layer, polypoid formations, and other structural changes.

For immunohistochemical verification of chronic endometritis, monoclonal antibodies against CD138 (syndecan-1) were used to identify plasma cells in the endometrial stroma. The assessment was performed by counting CD138-positive cells in 10 high-power fields using light microscopy.

The obtained results were compared with diagnostic criteria for chronic endometritis, according to which the presence of more than one CD138-positive plasma cell per 10 high-power fields was considered morphological evidence of a chronic inflammatory process.

Research results and their discussion.

Histological examination of endometrial biopsy specimens stained with hematoxylin and eosin demonstrated that in most cases the morphological pattern corresponded to the mid-proliferative phase or early secretory transformation. The endometrial architecture was characterized by a polypoid configuration with an irregular distribution of glands of different calibers. Round-shaped glands predominated, accompanied by individual tortuous structures. The glandular-to-stromal ratio was most frequently 1:3 and locally changed to 1:2 in some biopsy specimens, indicating focal tissue remodeling (figure 1).

The epithelium of most glands was represented by a single-layered or pseudostratified columnar epithelium with basally located nuclei. The nuclei were round, with moderate hyperchromasia and moderately pronounced mitotic activity. No atypical mitoses were identified in any case. The nuclear-to-cytoplasmic ratio remained within the physiological range (1:2), subnuclear vacuolization was absent, the apical epithelial border was regular, and the lumina of most glands were empty without signs of secretory activity.

The stromal component was characterized by uneven cellularity and focal or diffuse lymphoplasmacytic infiltration of varying severity. In some specimens, areas of increased stromal vascularity, spindle-shaped transformation of stromal cells, and areas of incomplete shedding of the functional layer after previous menstrual cycles were observed. In some cases, numerous clus-

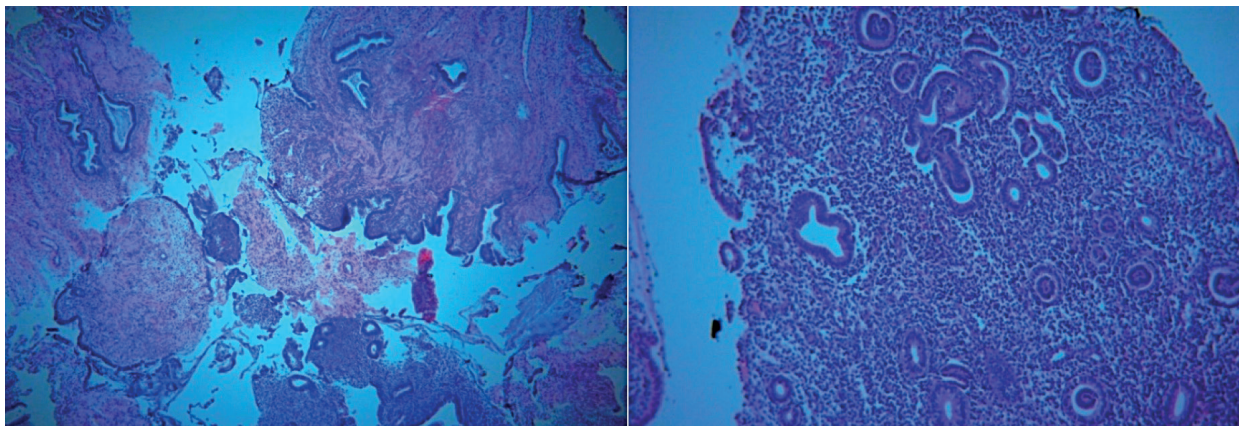


Figure 1 – Irregular distribution of glands of different calibers and focal lymphoplasmacytic infiltration of the stroma. Hematoxylin and eosin staining. Magnification: $\times 100$.

ters of sclerotic spiral arteries were identified, whereas in others they were solitary or completely absent (figure 2).

Additional focal proliferative changes were identified in some patients in the form of hyperplastic-type endometrial polyps, micropolyps, or glandular-fibrous endocervical polyps. These lesions were accompanied by pronounced lymphoplasmacytic infiltration, endocervical glands, erythrocyte extravasation, and individual neutrophilic granulocytes.

Immunohistochemical examination using antibodies against CD138 confirmed the presence of plasma cells in the endometrial stroma in all examined cases. The number of CD138-positive cells ranged from 6 to 28 cells per 10 high-power fields, which substantially exceeded the reference value (up to 1 cell per 10 high-power fields) and corresponded to the diagnostic criteria for chronic endometritis. The highest number of plasma cells was observed in biopsy specimens with the most pronounced lymphoplasmacytic infiltration and structural remodeling of the endometrium (figure 3).

Thus, the combination of histological findings – including irregular distribution of glands, changes in the glandular-to-stromal ratio, focal lymphoplasmacytic infiltration, sclerotic changes in spiral arteries, spindle-shaped transformation of stromal cells, formation of polypoid structures, and increased CD138 expression

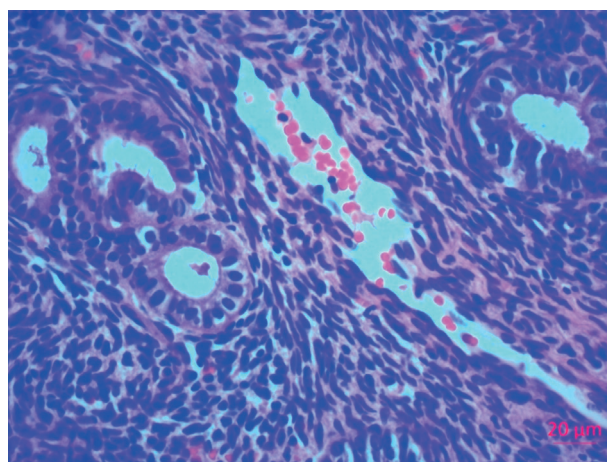


Figure 2 – Cellular composition of the endometrial stroma. Focal lymphoplasmacytic infiltration. Hematoxylin and eosin staining. Magnification: $\times 1000$.

– confirmed the presence of a chronic inflammatory process in the endometrium (figure 4).

The morphological findings obtained in our study are consistent with the current concept of chronic endometritis as a persistent inflammatory process accompanied by plasma-cell infiltration and structural remodeling of the glandular and stromal components of the endometrium [5, 6, 10].

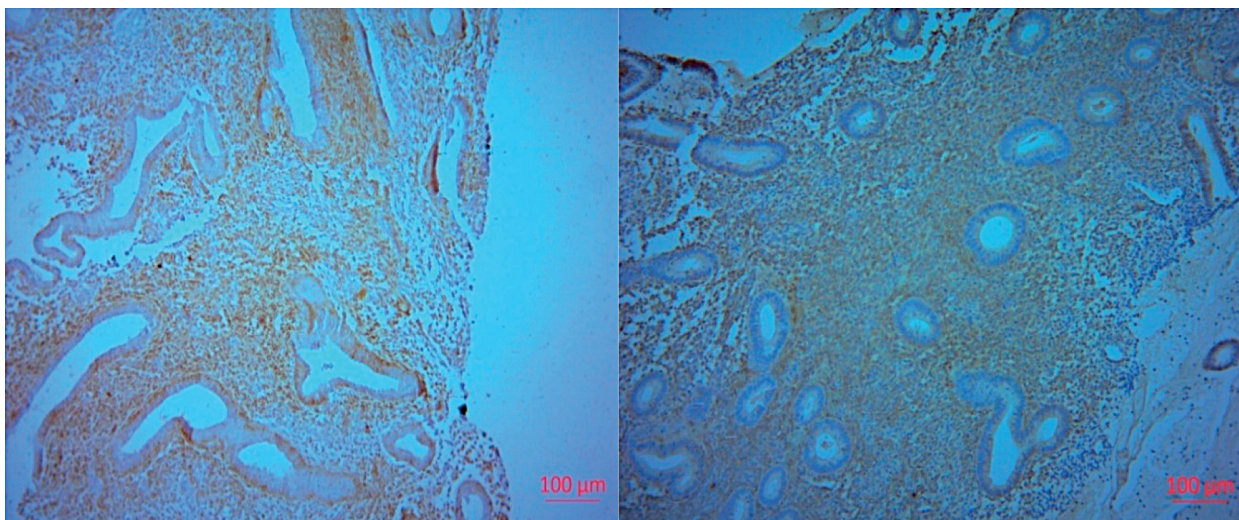


Figure 3 – CD138-positive plasma cells in the endometrial stroma. Immunohistochemical examination, Magnification: $\times 400$.

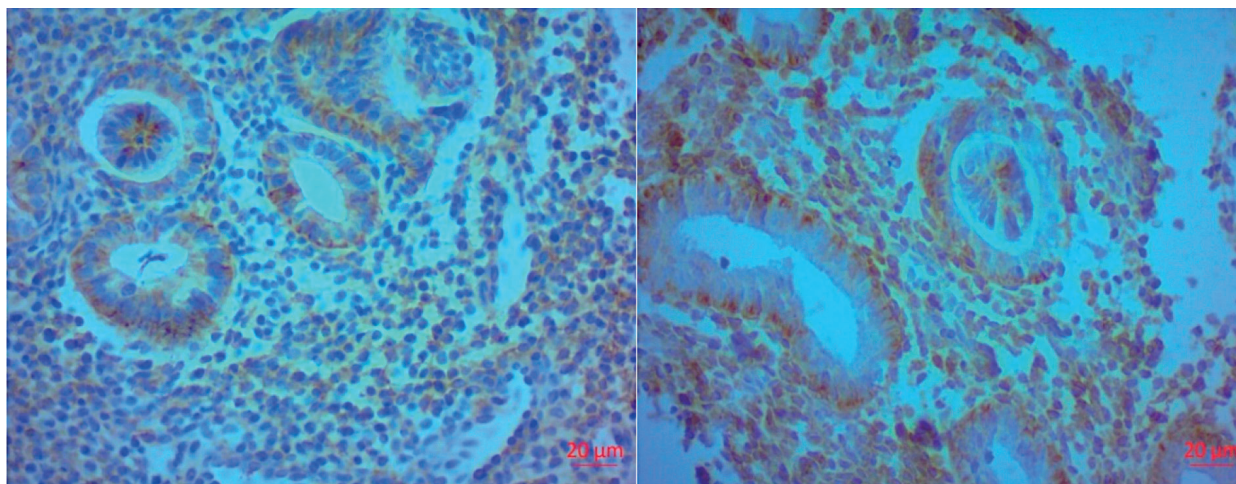


Figure 4 – Pronounced CD138 expression in a patient with severe chronic endometritis. Immunohistochemical examination. Magnification: $\times 1000$.

An important finding of our study was the detection of CD138-positive plasma cells in all examined biopsy specimens. Their number ranged from 6 to 28 cells per 10 high-power fields. These values exceed the low threshold levels used in some contemporary studies for morphological verification of chronic endometritis. At the same time, published data demonstrate that there is no single universally accepted cut-off value for the number of CD138-positive plasma cells, which remains one of the main causes of heterogeneity in the diagnostic criteria for chronic endometritis [7, 8, 12].

Santoro et al., in a systematic review and meta-analysis, demonstrated that studies have used thresholds ranging from 1 to 50 plasma cells per 10 high-power fields, while a statistically significant association with recurrent pregnancy loss was observed at a threshold of ≥ 5 cells per 10 high-power fields [8]. Therefore, the range of 6–28 CD138-positive cells per 10 high-power fields observed in our study corresponds to levels of plasma-cell infiltration that are considered clinically relevant in a number of contemporary studies.

Our findings are also consistent with the results of Bulut et al., who demonstrated an adverse effect of chronic endometritis on reproductive outcomes when a threshold of ≥ 5 CD138-positive plasma cells was used [9]. At the same time, systematic reviews indicate that the clinical significance of chronic endometritis may depend on the severity of plasma-cell infiltration [4, 8, 13].

The present findings confirm the need to assess CD138-positive plasma cells not in isolation but within the context of the overall morphological pattern. The combination of lymphoplasmacytic infiltration with glandular irregularity, stromal remodeling, spiral artery changes, and polypoid structures constitutes a morphological complex characteristic of a persistent inflammatory process.

It should be emphasized that individual morphological features of chronic endometritis are not absolutely specific. Therefore, the use of CD138 immunohistochemistry provides a more objective means of identifying plasma cells and complements the results of conventional histological examination [6, 10, 14].

Taken together, the findings indicate that comprehensive histological and immunohistochemical assessment is an appropriate approach for the morphological

characterization of chronic endometritis, particularly in patients with reproductive disorders.

Conclusions.

1. The morphological pattern of the endometrium in patients with chronic endometritis is characterized by a complex of structural changes, including disturbances of glandular architecture, alterations in the glandular-to-stromal ratio, focal or diffuse lymphoplasmacytic infiltration, stromal remodeling, and sclerotic changes in spiral arteries.

2. Additional morphological manifestations of chronic endometritis include spindle-shaped transformation of stromal cells, areas of incomplete shedding of the functional layer, formation of micropolyps, and polypoid lesions, indicating a prolonged course of the chronic inflammatory process.

3. Immunohistochemical examination using the CD138 marker confirms the presence of plasma cells in the endometrial stroma and represents a highly informative method for morphological verification of chronic endometritis. The detected number of CD138-positive cells (6–28 per 10 high-power fields) substantially exceeds the reference values and corresponds to currently used diagnostic criteria for the disease.

4. The combined use of histological and immunohistochemical methods provides high diagnostic informativeness in the assessment of the endometrium, makes it possible to objectively confirm chronic endometritis, and may be used to guide subsequent therapeutic management in patients with reproductive disorders.

Prospects for further research.

Further research should focus on the comprehensive correlation of morphological and immunohistochemical characteristics of the endometrium with microbiological findings, the condition of the vaginal and cervical microbiota, clinical characteristics of patients, and outcomes of assisted reproductive technology programs. Particular attention should be paid to the relationship between the number of CD138-positive plasma cells, the severity of structural remodeling of the endometrium, and the effectiveness of treatment for chronic endometritis.

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МОРФОЛОГІЧНА ХАРАКТЕРИСТИКА ЕНДОМЕТРІЯ У ПАЦІЄНТОК ІЗ ХРОНІЧНИМ ЕНДОМЕТРИТОМ

Коцабин Н. В., Бойчук А. В., Кошарний В. В.

Резюме. Хронічний ендометрит є тривалим запальним процесом ендометрія, який часто має малосимптомний перебіг та може бути пов'язаний із порушеннями репродуктивної функції. Морфологічна верифікація захворювання має важливе значення, оскільки гістологічне дослідження дозволяє оцінити структурну перебудову ендометрія, а CD138-імуногістохімія – виявити плазматичні клітини.

Мета дослідження – провести комплексну гістологічну та імуногістохімічну оцінку морфологічних змін ендометрія у пацієнток із хронічним ендометритом.

Досліджено біоптати ендометрія, отримані у проліферативну фазу менструального циклу. Гістологічне дослідження проводили з фарбуванням гематоксиліном та еозином. Оцінювали архітектуру ендометрія, форму і розташування залоз, співвідношення залозистого та стромального компонентів, клітинність строми, характер запальної інфільтрації, стан спіральних артерій та структурні зміни стромальних клітин. Для виявлення плазматичних клітин застосовували імуногістохімічне дослідження з антитілами до CD138 та проводили їх кількісний підрахунок у 10 полях зору.

Гістологічно виявлено комплексну перебудову ендометрія: нерівномірне розташування залоз різного калібру, зміни співвідношення залозистого і стромального компонентів, нерівномірну клітинність строми та вогнищеву або дифузну лімфоцитарну інфільтрацію. У частині біоптатів визначали веретенподібну трансформацію стромальних клітин, неповне відторгнення функціонального шару, склеротичні зміни спіральних артерій, мікрополіпи та поліподібні утворення. CD138-позитивні плазматичні клітини виявлено у всіх досліджених випадках; їх кількість становила 6–28 клітин на 10 полів зору.

Отримані результати свідчать, що хронічний ендометрит супроводжується не лише плазмоцитарною інфільтрацією, а й комплексною перебудовою залозистого, стромального та судинного компонентів ендометрія. Поєднання гістології та CD138-імуногістохімії підвищує об'єктивність морфологічної верифікації захворювання.

Ключові слова: хронічний ендометрит, ендометрій, морфологія, гістологія, імуногістохімія, CD138, плазматичні клітини.

MORPHOLOGICAL CHARACTERISTICS OF THE ENDOMETRIUM IN PATIENTS WITH CHRONIC ENDOMETRITIS

Kotsabin N. V., Boychuk A. V., Kosharniy V. V.

Abstract. Chronic endometritis is a prolonged inflammatory process of the endometrium that often follows an asymptomatic or paucisymptomatic course and may be associated with reproductive dysfunction. Morphological verification of the disease is crucial, as histological examination allows for the assessment of endometrial structural remodeling, while CD138 immunohistochemistry enables the detection of plasma cells.

The aim of the study was to conduct a comprehensive histological and immunohistochemical assessment of endometrial morphological changes in patients with chronic endometritis.

Endometrial biopsy samples obtained during the proliferative phase of the menstrual cycle were analyzed. Histological examination was performed using hematoxylin and eosin staining. Parameters evaluated included endometrial architecture, gland shape and distribution, the ratio of glandular to stromal components, stromal cellularity, the nature of inflammatory infiltration, the state of spiral arteries, and structural changes in stromal cells. Immunohistochemical analysis using anti-CD138 antibodies was employed to detect plasma cells, and their numbers were quantified across 10 fields of view.

Histological analysis revealed complex endometrial remodeling: irregular distribution of glands of varying calibers, altered ratios of glandular to stromal components, uneven stromal cellularity, and focal or diffuse lymphoplasmacytic infiltration. In some biopsy samples, spindle-shaped transformation of stromal cells, incomplete shedding of the functional layer, sclerotic changes in spiral arteries, micropolyps, and polypoid formations were observed. CD138-positive plasma cells were detected in all cases examined; their count ranged from 6 to 28 cells per 10 fields of view.

The results indicate that chronic endometritis is accompanied not only by plasmacytic infiltration but also by complex remodeling of the glandular, stromal, and vascular components of the endometrium. Combining histology with CD138 immunohistochemistry enhances the objectivity of the morphological verification of the disease.

Key words: chronic endometritis, endometrium, morphology, histology, immunohistochemistry, CD138, plasma cells.

ORCID and contributionship:

Kotsabin N. V.: <https://orcid.org/0000-0002-8264-6475> ^{ABDEF}

Boychuk A. V.: <https://orcid.org/0000-0002-2191-0383> ^{AEF}

Kosharnyi V. V.: <https://orcid.org/0000-0002-7815-3950> ^{BCDE}

Conflict of interest:

The authors declare no conflict of interest.

Corresponding author

Kotsabin Nataliia Volodymyrivna
Reproductive Health Medical Center "Damiya"
Ukraine, 49000, Ivano-Frankivsk, 112b Fedkovycha str.
Tel.: +380503733757
E-mail: nykolynnataliya@yahoo.com

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article.

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Штепа К. В., Шепітько В. І., Стецук Є. В., Вільхова О. В., Рудь М. В., Борута Н. В.

СТАН ГЕМОМІКРОЦИРКУЛЯТОРНОГО РУСЛА ТА АЦИНАРНО-ПРОТОКОВОГО АПАРАТУ МАЛИХ СЛИННИХ ЗАЛОЗ ТВЕРДОГО ПІДНЕБІННЯ ЗА ДІЇ ТРИПТОРЕЛІНУ ТА КОРЕКЦІЇ КВЕРЦЕТИНОМ У ЩУРІВ

Полтавський державний медичний університет (м. Полтава, Україна)

Katerinashtepa87@gmail.com

Малі слинні залози твердого піднебіння чутливо реагують на системні гормональні зміни, що можуть супроводжуватися порушеннями мікроциркуляції та структурної організації залозистого апарату. Перспективним засобом корекції таких змін є кверцетин, якому притаманні антиоксидантні, мембрано- та ангіопротекторні властивості. Мета дослідження – оцінити стан гемомікроциркуляторного русла та ацинарно-протокового апарату малих слинних залоз твердого піднебіння щурів за умов дії триптореліну та корекції кверцетином. Дослідження проведено на білих щурах, розподілених на контрольну групу, групу хімічної кастрації та групу корекції. Хімічну кастрацію моделювали одноразовим підшкірним введенням триптореліну (0,3 мг/кг), кверцетин вводили перорально по 100 мг/кг тричі на тиждень. Проводили гістологічне та морфометричне дослідження судин мікроциркуляторного русла, ацинусів і вивідних проток. Статистичну значущість оцінювали за критерієм Манна-Уїтні ($p < 0,05$). Тривала дія триптореліну спричиняла хронозалежні зміни: упродовж 6–9 місяців переважала дилатація артерій, капілярів і венул, тоді як на 12-му місяці зменшення діаметрів артерій і капілярів свідчило про виснаження компенсаторних механізмів. В ацинарно-протоковому апараті ранні компенсаторні зміни поступово