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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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METABOLOMIC MARKERS OF ENDOMETRIOSIS: PROSPECTS

Bakhtiyarov Kamil Rafaelevich[1], Ivantsova Margarita Vladimirovna[2], Kukes Ilya Vladimirovich[3], Ignatko Irina Vladimirovna[4], Glagovsky Pavel Borisovich[5].

[1]Professor of the Department of Obstetrics, Gynecology and Perinatology, N.V. Sklifosovsky Institute of Clinical Medicine (ICM), I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University), chief obstetrician-gynecologist LLC «Set Semeinyh Medicinskih Centrov». 8-2 Trubetskaya str., Moscow, Russia.

[2]Obstetrician-gynecologist, doctor of ultrasound diagnostics, postgraduate student of the Department of Obstetrics, Gynecology and Perinatology, N.V. Sklifosovsky Institute of Clinical Medicine (ICM), I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University). 8-2 Trubetskaya str., Moscow, Russia.

[3]Clinical pharmacologist, immunologist, head of the scientific and clinical department of ANO "International Association of Clinical Pharmacologists and Pharmacists". 11-10, Yauzskaya str., Moscow, Russia.

[4]Doctor of Medical Sciences, Professor, Corresponding Member of the Russian Academy of Sciences, Head of the Department of Obstetrics, Gynecology and Perinatology, N.V. Sklifosovsky Institute of Clinical Medicine (ICM), I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University). 8-2 Trubetskaya str., Moscow, Russia.

[5]Doctor of clinical laboratory diagnostics, general director of Chromsystems Lab LLC. 20-2 Nauchny dr., Moscow, Russia.

Abstract.

Objective: Endometriosis is a widespread pathology among women of reproductive age. The pathophysiological mechanisms of the disease aren't enough understood yet. In addition, the "gold" standard of diagnosis is still laparoscopy. Worldwide, patients may experience a delay in the diagnosis of endometriosis by approximately 6 to 12 years.
Aim of the study: To conduct a systematic analysis of the data presented in modern literature on the metabolomic diagnosis of endometriosis in general and endometrioid cystadenomas in particular.

Materials and methods: The review includes data from world studies over the past 7 years regarding metabolomic screening for endometriosis.

Results: Metabolomic changes characteristic of endometriosis, noted in the metabolism of amino acids, organic acids, lipids, purines, are presented. The described disorders reflect the processes of oxidative stress, mitochondrial dysfunction, endothelial dysfunction, and active angiogenesis.

Conclusion: The identified metabolomic changes may improve and speed up the process of diagnosing endometriosis in general and endometrioid cystadenomas in particular in a non-invasive way. Certain detailed violations of metabolic processes can become a promising point of application for the correction of symptoms and the treatment of this pathology.

Key words. Endometriosis, endometrioid cystadenomas, metabolomics, metabolome, markers, amino acids, organic acids, lipids, purines, oxidative stress, mitochondrial dysfunction, endothelial dysfunction.

Introduction.

Endometriosis is a pathological process in which the presence of tissue similar to the endometrium outside the uterine cavity is determined by morphological and functional properties. The disease is characterized by a nonspecific clinical picture; debilitating pelvic pain, dysmenorrhea, dyspareuria, and infertility are often noted [1-3]. This pathology is widespread among women of reproductive age (up to 15%) [4]. In addition, endometriosis occurs in 35% of women with infertility, as well as in 78% of women suffering from chronic pelvic pain [5-7]. Endometriotic cystadenomas are a common cause of markedly reduced quality of life in women. The disease is characterized by a chronic course and progresses significantly over time in about 50% of patients. In addition, approximately 50% of women with endometriosis experience recurrent symptoms over a 5-year period, regardless of treatment approach [8-11].

The main method of diagnosing this disease is still laparoscopy. Currently, no imaging modality is accurate enough to replace surgery [12]. Ultrasound examination of the pelvic organs is routinely used. Magnetic resonance imaging is usually used before surgery [5]. According to various studies around the world, patients may experience a delay in the diagnosis of endometriosis from about 6 to 12 years, which greatly complicates adequate treatment, reduces the quality of life of women and imposes a significant financial burden on patients and the healthcare system [5,8]. The discovery of new biomarkers useful for the early diagnosis of endometrioid cystadenomas is of great importance.

It should be noted that the causes and mechanisms of endometriosis are not well understood. The above-described aspects of endometriosis, such as understanding of the pathophysiology, delayed and invasive diagnosis, inconsistent clinical presentation, and unknown etiology, present a challenge to the scientific and medical community. Metabolomics can serve as a tool for their clarification.

Metabolomics & concepts.

A metabolome is a collection of all metabolites that are the end product of metabolism in a cell, tissue, organ, or organism. They and the influence of the environment on them are studied by metabolomics [13]. Metabolomic screening, in turn, is aimed directly at the consideration of pathogenesis and comorbidity by reflecting them in pathological metabolic processes [14,15].

Of interest for early diagnosis, prognosis, and, accordingly, timely effective therapy for endometriosis in general and endometrioid cystadenomas in particular is a non-invasive examination through metabolomic screening. Metabolic analysis is promising in the diagnosis of endometriosis due to the fact that ectopic tissue has specific pathological metabolic pathways [8,14,16].

The central role in endometrioid cystadenomas belongs to local inflammation [1]. In support of this claim, a wide range

of studies have shown that the peritoneal fluid of patients with endometriosis contains high levels of macrophages and immune cells that secrete cytokines, angiogenic factors, and growth factors. Another factor affecting the expression of these cytokines and other cell adhesion molecules is oxidative stress, which is a concomitant component of inflammation associated with endometrioid cystadenomas [1,14,17].

Metabolomics for endometrioid cystadenomas, analysis of world literature.

Pathogenetic pathways are reflected in various groups of metabolic indicators, metabolic panels. Studies demonstrate altered amino acid levels in blood serum, urine, ectopic endometrial tissue, and follicular fluid. Dutta et al. in two studies noted an increase in serum leucine levels in patients with endometriosis, while Jana et al. showed a decrease. It should be noted that Dutta et al. took blood samples from women during the secretory phase of the menstrual cycle, while Jana et al. during the follicular phase. The metabolome is a dynamic system and is subject to environmental influences and genetic changes [18,19,20]. Thus, hormonal dynamics during the phases of the menstrual cycle can affect the amino acid levels of patients with endometriosis. The reason for this may be changes in ectopic tissue throughout the menstrual cycle. Vicente-Munoz et al. found differences in metabolic parameters using urine samples taken in the follicular and luteal phases of the menstrual cycle. However, regardless of the phase of the menstrual cycle, the levels of taurine and lysine differed markedly from the norm [21-24].

Research shows interesting changes in taurine levels. Taurine is associated with high cell proliferation and also acts as an antioxidant. An increase in the content of taurine was noted at high oxidative stress. Because endometriosis is characterized by high concentrations of reactive oxygen species, elevated taurine levels may play a role in reducing high oxidative stress states [14,25].

In a study by Ghazi et al. an elevated level of 2-methoxyestradiol has been described. This compound inhibits angiogenesis and cell proliferation. Elevated levels of 2-methoxyestradiol may also play a protective role, preventing angiogenesis and proliferation of endometrial cells [26].

In addition, Murgia F. et al. found an increase in the concentration of β-hydroxybutyric acid and glutamine, as well as changes in pathways such as nitrogen metabolism, pyrimidine metabolism, glutamine, and glutamate metabolism, and aminoacyl-tRNA biosynthesis. Accumulation of β-hydroxybutyric acid concentration may be an indirect sign of oxidative stress. The most significant glutamine-producing tissue is muscle mass, but glutamine is also released in small amounts by lung and brain cells. Which is considered to be correlated with the modulation of nerve pain, since the compound is an excitatory neurotransmitter. An increase in glutamine levels in certain areas of the brain in women with chronic pelvic pain was identified in the study with endometriosis. Thus, its role in the occurrence or worsening of chronic pelvic pain in patients with endometriosis in general and endometrioid cystadenomas in particular is suggested [1,11].

Tryptophan, as a characteristic metabolite in endometriosis and endometrioid cystadenomas, is characterized by changes in biosynthesis. Murgia F. et al. showed a decrease in tryptophan. The importance of this amino acid is that its catabolism may be involved in the immune tolerance of endometriotic implant cells [1,8].

Altered amino acid levels could potentially explain the pathogenetic aspects of endometriosis and endometrioid cystadenomas. As is known, ectopic tissue cells are characterized by high proliferation, angiogenesis, antiapoptotic, cell invasion, and increased energy demand. All these qualities require a high catabolic state in which amino acids can serve as an important source of energy, since they can be converted into intermediate products of the tricarboxylic acid cycle and support the energy needs of rapidly growing cells of ectopic tissue. Studies have noted an imbalance in the levels of several amino acids when analyzing their metabolic pathways [8,20,27-30,31].

The metabolome in endometriosis is characterized by marked changes in the lipid profile. Phospholipids play an important role in cellular processes such as proliferation, survival, cell transformation, ectopic progression, and differentiation. Studies have noted elevated levels of lysophosphatidylethanolamine, omega-3 arachidonic acid, and phosphatidic acid in plasma, follicular fluid, and peritoneal fluid, while reduced levels of phosphatidylcholine and phosphatidylserine have been observed in ectopic tissue [14,28,31]. In particular, phosphatidic acid is a phospholipid known for its diverse participation in cellular processes, which is one of the main mediators of cellular transformation, survival, and proliferation of endometrioid cells outside the uterine cavity. In addition, phosphatidic acid stimulates oxidative stress leading to the production of reactive oxygen species [14,16,20,29].

Under the influence of cyclooxygenase enzymes, arachidonic acid is transformed into prostaglandins, thromboxanes and leukotrienes. A decrease in the ratio of eicosatetraenoic acid to arachidonic acid directly correlates with disease severity. Also, Li et al. showed that the concentration of arachidonic acid was significantly higher in women with endometriosis than in women in the control group [14].

Malondialdehyde, which is a lipid peroxidase, is also a marker of oxidative stress in endometriosis. Studies have noted higher serum levels of malondialdehyde in patients with endometriosis compared to healthy controls. In addition, women with endometriosis are reported to have higher levels of lipid hydroperoxides, vitamin E, and catalase [8].

Superoxide dismutase is an antioxidant enzyme involved in oxidative stress. A decrease in its activity in the plasma of affected patients was registered, which confirms the theory of a decrease in antioxidant capacity in endometriosis. An increased activity of carbonic anhydrase, as an oxidative stress enzyme, was also noted in women with endometriosis compared with healthy women, along with a cytosolic decrease in the content of glutathione in women with endometriosis [8,17].

Changes in the levels of phosphocholine and phosphatidylcholine, which are considered biomarkers of cell proliferation, have been reported in ectopic tissues, follicular fluid, and peritoneal fluid [14]. It should be noted

that phosphocholine is an intermediate product in the synthesis of phosphatidylcholine, the most common phospholipid. Phosphatidylcholine is a source of production of sphingomyelins and prostaglandins identified in tissues, follicular fluid, and peritoneal fluid in this pathology. They may be involved in the process of denervation and subsequent reinnervation in endometriosis, as well as cell preservation [9,13,25,27,31,32]. It can be argued that altered lipid levels are characteristic of endometrioid lesions and reflect the pathogenetic aspects of the disease. Lipidomics shows significant potential for explaining the mechanisms involved in endometriosis.

In connection with the above-described features of the needs and metabolism of ectopic tissue cells in endometriosis, it is worth considering the metabolic panels of organic acids. Organic acids such as pyruvate, succinate, and citrate are important intermediates in the tricarboxylic acid cycle [19,20,24]. Studies have noted marked increases in their levels in serum and follicular fluid. This may indicate the activation of the tricarboxylic acid cycle for the formation of ATP and, as a result, providing energy for the rapid proliferation of endometrial-like cells. On the other hand, lower glucose levels and higher levels were found in patients with endometrial lesions, indicating a high anaerobic metabolism. The authors note a reduced activity of antioxidant enzymes, in particular, an insufficient level of reduced glutathione, which leads to the synthesis of a by-product, 2-hydroxybutyrate. Elevated levels were found in the blood serum of patients with endometriosis, which correlates with the process of chronic inflammation and tissue damage in endometriosis [10,14,15,24,31,33].

Studies also demonstrate high concentrations of guanosine, hypoxanthine, inosine, and xanthosine in combination with low levels of uric acid in the eutopic endometrium of patients with endometriosis. As well as low expression of purine nucleoside phosphorylase, which protects purines from destruction and negatively affects the processes of embryo implantation [12,19,20,24,26]. What may be relevant in the high prevalence of infertility in women with endometriosis, and high levels of purines may be considered in connection with this.

In addition, a significant decrease in the level of carnitine in the peritoneal fluid was found in women with endometriosis. It is believed that L-carnitine may be useful in the treatment of infertility due to its antioxidant effect [28,34].

In ectopic cells, the high energy requirement leads to altered biochemistry, including dysfunction of the citric acid cycle. As a result, alternative ways of delivering the carbon component are needed. The elevated levels of L-arginine, L-tyrosine, leucine, lysine, and asparagine observed in the ectopic endometrium are most likely caused by altered energy metabolism and a high level of structural protein catabolism. Such changes can also be reflected in blood plasma [28,34].

Endometriosis, being a polygenic and multifactorial disease, has increased angiogenesis and proteolysis, contributing to its development and progression. Studies demonstrate the prominent involvement of several factors associated with angiogenesis, such as delta-like 4 (Dll4)-Notch signaling pathways, angiopoietin, vascular endothelial growth factor, and vascular endothelial growth factor receptor [8].

Vascular endothelial growth factor and vascular endothelial growth factor receptor are the best-known molecules involved in the process of angiogenesis. They are able to regulate cell proliferation, migration, and permeability. They promote intraperitoneal angiogenesis, supporting existing ectopic lesions and the development of new ones. This has been reflected in studies in the form of changes in plasma concentrations of IL-17A, which promotes increased expression of various angiogenic factors such as VEGF, IL-8 and bFGF, according to published results. In addition, their significant decrease was noted after surgical removal of ectopic endometrial tissue [8,15,33].

Discussion.

Summing up, it should be noted that metabolomic screening for endometriosis in general and endometrioid cystadenomas in particular is characterized by a number of changes. The described disorders reflect the processes of oxidative stress, mitochondrial dysfunction, endothelial dysfunction, metabolic disorders of amino acids, organic acids, purines, lipid metabolism, and active angiogenesis.

The highlighted metabolomic changes can improve and speed up the process of diagnosing endometriosis in general and endometrioid cystadenomas in particular in a non-invasive way. Through the study of large samples, the stereotyped metabolic profile of patients with endometrioid cystadenomas can be distinguished. Certain detailed metabolic disorders may be a promising point of application for the correction of symptoms and the treatment of endometriosis and endometrioid cystadenomas.

Our research team plans to review the detailed metabolomic profile of patients and identify metabolomic markers characteristic of this pathology. The exact timing of application is being discussed. In the future, metabolomic analysis can be used to assess the dynamics of therapy for patients who do not require surgical treatment according to standards, and they can also be considered in the future for the differential diagnosis of the disease in the early stages. The markers that we plan to consider reflect changes in the metabolism of pathological tissue, thanks to which we will be able to influence pathological processes. In addition, markers discovered in the future may be a useful point for applying new therapy or additional correction of the condition.

Conclusion.

Metabolomics undoubtedly deserves attention for understanding the pathophysiology of diseases at a more detailed level. It can act as a new tool in the search for diagnostic markers of gynecological diseases and application points for therapeutic approaches in disturbed metabolic processes. However, the number of large studies is small, and the existing work has limitations. It is necessary to expand research in this direction with a more thorough consideration of controversial issues and the use of a deeper analysis.

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მეტაბოლური მარკერები ენდომეტრიოზში: ხედვა

რეზიუმე

აქტუალობა: ენდომეტრიოზი ფართოდ გავრცელებული პათოლოგიაა რეპროდუქციული ასაკის ქალებში. დაავადების პათოფიზიოლოგიური მექანიზმები ჯერ კიდევ კარგად არ არის გასაგები. გარდა ამისა, დიაგნოსტიკის „ოქროს“ სტანდარტი კვლავ ლაპაროსკოპიაა. მთელ მსოფლიოში, პაციენტებს შეიძლება განიცადონ ენდომეტრიოზის დიაგნოზის დაგვიანება დაახლოებით 6-დან 12 წლამდე. კვლევის მიზანი: ზოგადად ენდომეტრიოზის და კერძოდ ენდომეტრიოიდული ცისტადენომის მეტაბოლური დიაგნოსტიკის თანამედროვე ლიტერატურაში წარმოდგენილი მონაცემების სისტემატური ანალიზი. მასალები და მეთოდები: მიმოხილვა მოიცავს მონაცემებს მსოფლიო კვლევებიდან ბოლო 7 წლის მანძილზე ენდომეტრიოზის მეტაბოლურ სკრინინგთან დაკავშირებით. შედეგები: წარმოდგენილია ენდომეტრიოზისთვის დამახასიათებელი მეტაბოლური ცვლილებები, რომლებიც აღინიშნება ამინომჟავების, ორგანული მჟავების, ლიპიდების, პურინების ცვლაში. აღწერილი დარღვევები ასახავს ოქსიდაციური სტრესის, მიტოქონდრიული დისფუნქციის, ენდოთელიუმის დისფუნქციის და აქტიური ანგიოგენეზის პროცესებს. დასკვნა: გამოვლენილმა მეტაბოლურმა ცვლილებებმა შეიძლება გააუმჯობესოს და დააჩქაროს ზოგადად ენდომეტრიოზის და, კერძოდ, ენდომეტრიოიდული ცისტადენომის დიაგნოსტიკის პროცესი არაინვაზიური გზით. მეტაბოლური პროცესების გარკვეული დეტალური დარღვევა შეიძლება გახდეს პერსპექტიული პუნქტი სიმპტომების გამოსწორებისა და ამ პათოლოგიის მკურნალობისთვის.

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